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Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

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Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

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Executive Summary

Humans have harnessed the power of genetics throughout history, beginning with selectively breeding agricultural crops and livestock to increase the prevalence of beneficial traits, such as enhanced growth rate and disease resistance. With advances in science and technology, the field of genetics expanded from agricultural fields and livestock barns into research laboratories and medical institutions. As knowledge of genetics increased, medical professionals and society at large looked for the potential benefits for health and the prevention of human suffering this knowledge could bring.

In more recent history, by tracking the prevalence of diseases in families, medical researchers were able to identify the genetic underpinnings of certain human diseases, such as Huntington's disease and sickle cell anemia. In some instances, if scientists discovered that a genetic mutation associated with a disease prevented the body from producing an essential gene product, they were able to develop treatments that delivered the missing essential gene product to the patient, thereby alleviating the disease symptoms. Unfortunately, until more recent advances in the field of genetics, few genetic diseases were amendable to such treatments.

The 1980s brought developments in genetic engineering techniques. These advances allowed scientists to develop crops and livestock with desired traits far more quickly than conventional breeding techniques, but the process was still labor-intensive, time consuming and imprecise. Scientists could not target where the new genetic material would be inserted into the recipient organism's genome. As a result, genetic engineering (also known as gene therapy) carried too high a risk for human patients: the new genetic material, while potentially beneficial as a treatment for the patient's current disease, might be inserted into the middle of, and therefore disrupt the functioning of, an essential gene, causing potentially harmful or even fatal side effects.

Recent advances in genome-editing technologies, such as CRISPR-Cas9 (the acronym for clustered regularly interspaced short palindromic repeats (CRISPR) and CRISPR-associated protein 9), have revolutionized the field of genetics and renewed hope that gene-editing technologies will be able to bring about the eradication of many deadly human diseases and save countless lives, immeasurable heartache and large health care expenditures in perpetuity. These technologies allow scientists to make more precise alterations to the genetic makeup of an organism in an extraordinarily short period of time. Although first discovered only a decade ago, CRISPR-Cas9 and related genome-editing technologies are already leading to the development of potentially lifesaving medical treatments, such as for sickle cell anemia and spinal muscular atrophy. CRISPR-Cas9 has also been successfully used to genetically alter crops, animals, insects and microorganisms.

Recent advances in genome-editing technologies, such as CRISPR-Cas9, have revolutionized the field of genetics and renewed hope that gene-editing technologies will bring about the eradication of many deadly human diseases and save countless lives, immeasurable heartache and large health care expenditures in perpetuity.

Nevertheless, as history has shown, society must examine not only the enormous potential benefits, but also the potential risks, ethical issues and societal implications of these technologies. Policymakers must ask, for example: Should gene editing only be permitted as a method to treat patients with a genetic disease, or should it also be used to alter the genetic makeup of those patients in a way that allows them to pass the altered genes on to their children? How will agricultural uses of genome-editing technology affect biodiversity and can these technologies be used in a way that will not impact organic farming? How

As history has shown, society must examine not only the enormous potential benefits but also the potential risks, ethical issues and societal implications of these technologies.

can we ensure that access to these new, often expensive treatments is equitable and that these technologies are not developed or used in a way that will intentionally or unintentionally harm historically disadvantaged members of society? The impact of these technologies and their applications is increasingly evident in medicine, agriculture and the economy – and the pace of innovation is accelerating.

Genome-editing technologies have the potential to fundamentally improve the human experience and life for Mainers. Without the proper safeguards, however, they also could fundamentally harm our health, our natural environment, our social fabric and our economy. While federal funding restrictions and international professional society agreements and conventions provide current safeguards, until now, no state has examined how genome-editing technology broadly affects their state and its people. Thus, the 130th Maine Legislature established the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State. In Resolve 2021, chapter 177, the Legislature tasked the panel with studying the implications of genome-editing technology and with making recommendations to the joint standing committee of the 131st Legislature having jurisdiction over health and human services matters on the legislative, administrative or other steps the State should take to both capitalize on the potential benefits, and avoid the hazards, of genome-editing technology. The resolve identified the following areas of expertise and background knowledge that could inform a legislative and regulatory framework for genome-editing technologies: ethics; clinical medicine for children and adults; public health; bioscience research; environmental protection; forestry; agriculture or aquaculture; fishing; state economics; tourism, business or commerce; military or security affairs; experience with the University of Maine System or Maine Community College System; hospice or hospital chaplaincy; the history of race, ethnicity or eugenics; and persons living with or who are the parents of persons living with a single-gene disorder, such as sickle cell anemia, cystic fibrosis or Duchenne muscular dystrophy. (A copy of Resolve 2021, chapter 177 is included as Appendix A.)

Pursuant to the resolve, the panel was comprised of 14 residents of the State as follows:

- Six legislators, with preference given to Legislators having expertise or backgrounds in one of the areas described above;
- One bioethicist;
- One person under 30 years of age at the time of appointment;
- One member of a federally recognized Indian nation, tribe or band in the State;
- One fiction author or poet whose published works have explored the humanity of all people;
- One person living with a single-gene disorder; and
- Three persons having expertise or background in one of the areas described above.

Additionally, the resolve directed the Presiding Officers to invite the participation of the Chief Justice of the Supreme Judicial Court or the chief justice's designee and the Governor or the Governor's designee. (A list of panel members is included as Appendix B.)

Over the course of its four meetings, the panel sought input from numerous experts, including panel members, and received presentations focused on four areas of inquiry:

- ***Gene Editing in Health and Bioscience***, including the medical, public health and bioscience research opportunities and implications of this technology;

- ***Gene Editing in the Natural World***, including the environmental, agricultural, forestry, fisheries and aquaculture opportunities and implications of this technology;
- ***Gene Editing and the Humanities***, including the historical context of the eugenics movement and the ethical, legal and religious considerations attendant to this technology; and
- ***Gene Editing in Systems and Institutions***, including the state economy, business and industry and education system opportunities and implications of this technology.

After carefully considering these presentations and follow-up information gathered in response to panel member questions, the panel developed the following set of consensus recommendations regarding the appropriate path for Maine in this new era of genome-editing technology.

	Recommendations
Genetic literacy and workforce development	A. To affirm the importance of genetics, genomics and related technologies, including data science, the Maine Department of Education should: i. Gather, assemble and aggregate more educational resources for educators teaching in these content areas. ii. Explore ways to enhance professional development opportunities for pre-Kindergarten through grade 12 educators in the State. B. The University of Maine System, the Maine Community College System and the Maine Department of Education should jointly participate in a genetics education summit in order to: i. Enhance the connections between the State's higher education institutions and the pre-Kindergarten through grade 12 system, including the State's career and technical education system, regarding the teaching of genetics, genomics and related technologies. ii. Consider how to develop and promote community-based education regarding genetics, genomics and related technologies outside of the formal education setting.
Economic opportunities and workforce development	C. The Department of Economic and Community Development should convene a statewide conference on genomic and gene-editing research. D. The Legislature should enact legislation directing the Maine Department of Agriculture, Conservation and Forestry to study both: i. The current uses and applications of gene-edited organisms and gene-editing technologies in the State's agriculture and forestry industries, including the potential this technology may provide to enhance those industries in the future; and ii. The impact that gene-editing technologies and gene-edited organisms may have on the State's organic farming industry – specifically, whether current state and federal legal and regulatory safeguards maintain the appropriate balance between the potential benefits of gene-editing technologies to non-organic farmers and the importance of preserving the integrity of organic farming methods and products. The legislation should direct the department to submit a combined report or separate reports on these issues, including its findings and recommendations, to the joint standing committee of the 131st Legislature having jurisdiction

	over agriculture and forestry issues, which should be authorized to report out legislation related to the report.
Cost of and access to genomic medicine	E. The Legislature should amend the statute establishing the Rare Disease Advisory Council to require that the Commissioner of Health and Human Services: i. Appoint at least one person whose rare disease is the result of a single-gene disorder, with preference given to a person who is eligible to participate in a clinical trial involving genomic medicine for that rare disease, when appointing the two members of the council who are over 18 years of age and who have had or who currently have a rare disease under 22 M.R.S. §1700-B(2)(L); ii. Appoint at least one parent or guardian of a child whose rare disease is caused by a single-gene disorder, with preference given to the parent or guardian of a child who is eligible to participate in a clinical trial involving genomic medicine for that rare disease, when appointing the two members of the council who are parents or guardians of a child with a rare disease under 22 M.R.S. §1700-B(2)(M). F. The Rare Disease Advisory Council should specifically address the financial burdens and potential benefits of genomic medicine as it completes its statutory duties, set forth in 22 M.R.S. §1700-B(5)(D) & (E), to distribute educational resources to providers and patients regarding treatment for rare diseases and to develop recommendations to improve patient quality of life and to provide services and reimbursement for such services. G. In conducting its statutory duties, the Office of Affordable Health Care, established by 5 M.R.S. §3122, should examine not only historic drivers of health care costs but also future cost-drivers, such as genomic medicine, which may have large up-front treatment costs but might also dramatically improve the lives of patients with rare diseases and yield long-term cost savings for both patients and insurance carriers.
Access to high-quality genetic counseling services	H. The Legislature should enact legislation directing the Department of Professional and Financial Regulation to conduct a sunrise review and report back to the Legislature on the benefits and drawbacks of establishing a professional licensing program for genetic counselors in the State. In conducting this evaluation, the department should examine not only the statutory sunrise review criteria set forth in 32 M.R.S. §60-J but also the impact licensure may have on insurance coverage, the availability of genetic counseling services to Maine patients across the State and the quality of genetic counseling services in the State.
Genetic privacy and discrimination	I. The State should make every effort possible to avoid engaging in activities similar to the historical wrongs that the State perpetrated on Malaga Island as well as the historical wrongs committed during the eugenics movement. J. The Legislature should reconsider whether to adopt a state law prohibiting discrimination based on genetic information in coverage and premium-setting decisions by insurers that issue life, disability, long-term care and related types of insurance.

I. Introduction

The 130th Maine Legislature established the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State through the passage of Resolve 2021, chapter 177. (A copy of Resolve 2021, chapter 177 is included as Appendix A.) The Legislature tasked the panel with studying the implications of genome-editing technology and with making recommendations to the joint standing committee of the 131st Legislature having jurisdiction over health and human services matters on the legislative, administrative or other steps the State should take to capitalize on the potential benefits, and avoid the hazards of, genome-editing technology. The resolve directed the panel to solicit testimony, advice or participation of persons having the following backgrounds or areas of expertise: ethics; clinical medicine caring for children; clinical medicine caring for adults; public health; bioscience research; environmental protection; forestry; agriculture or aquaculture; fishing; state economics; tourism, business or commerce; military or security affairs; University of Maine System or Maine Community College System; living with a single-gene disorder, such as cystic fibrosis, Duchenne muscular dystrophy or sickle cell anemia, or a parent or guardian of a person living with such a single-gene disorder; hospital or hospice chaplaincy; and history of race, ethnicity or eugenics.

The Legislature tasked the panel with studying the implications of genome-editing technology and with making recommendations on the legislative, administrative or other steps the State should take to both capitalize on the potential benefits of and avoid the hazards of genome-editing technology.

Pursuant to the resolve, the panel was comprised of 14 residents of the State appointed as follows:

- Six legislators, including three members of the Senate appointed by the President of the Senate and three members of the House of Representatives appointed by the Speaker of the House, who were encouraged to appoint legislators having expertise or backgrounds in one of the areas described above;
- One member who is a bioethicist, appointed by the President of the Senate;
- One member who was a person under 30 years of age at the time of appointment, appointed by the Speaker of the House;
- One member from a federally recognized Indian nation, tribe or band in the State, appointed by the President of the Senate;
- One member who is a fiction author or poet whose published works have explored the humanity of all people, appointed by the Speaker of the House;
- One member who is a person living with a single-gene disorder, appointed by the President of the Senate; and
- Three members, two appointed by the President of the Senate and one appointed by the Speaker of the House, having expertise or background in one of the areas described above.

Additionally, the resolve directed the Presiding Officers to invite the participation of the Chief Justice of the Supreme Judicial Court or the chief justice's designee and the Governor or the Governor's designee. (A list of panel members is included as Appendix B.)[1]

[1] The resolve further directed the panel to seek funding contributions to fully fund the costs of the study; sufficient contributions were received and accepted by the Legislative Council.

II. Brief Glossary of Helpful Genetic Terms[2]

Chromosome: A threadlike structure made of protein and a single, long molecule of DNA that contains the genes that determine an organism's genetic traits. Different types of organisms have different numbers of chromosomes.

Deoxyribonucleic acid (DNA): The molecule that carries genetic information for an organism's genetic traits. DNA is a long molecule made up of nucleotides composed of sugars, phosphates, and derivatives of four bases: adenine (A), guanine (G), cytosine (C), and thymine (T). The sequence of the bases along the DNA strand encodes biological information for different developmental and functional traits of an organism.

Gene: The basic unit of inheritance. Genes contain the information needed to specify different physical and biological traits of an organism. Genes are typically specific segments of a chromosome and encode specific functional products (such as proteins), which have differing functions within the body.

Genome: The entire set of DNA instructions found in the chromosomes of a particular organism. A genome contains all of the genetic information needed for an organism to develop and function.

Genome editing (also known as "gene editing"): Specific changes to the DNA of an organism made by scientists using a variety of technologies that add, remove or alter DNA within some or all of the organism's cells, leading to changes in a specific trait.

Germ cells (also called "germ line cells"): Germ cells are the sex cells (eggs and sperm) that sexually reproducing organisms use to pass on their genomes from one generation to the next (parents to offspring). Mutations in germ cells can be passed on to the organism's offspring.

Mutation: A change in the DNA sequence of an organism. Naturally occurring mutations can result from errors in DNA replication during cell division, exposure to mutagens or a viral infection. Mutations in germ cells can be passed on to an organism's offspring, while mutations in somatic cells are not passed on to an organism's offspring.

Somatic cells: Somatic cells are the cells of an organism other than germ cells. Mutations in somatic cells can affect the individual organism, but these mutations cannot be passed on to the organism's offspring.

III. Panel Process

The panel held four meetings on August 17, September 7, September 21 and October 19, 2022, using a hybrid format in which panel members were either present in person or attended remotely using the Zoom platform. All meetings were open to the public and were livestreamed with closed captioning on the Legislature's publicly accessible website. Meeting materials and background materials were posted online and remain archived on the following website: https://legislature.maine.gov/genome-editing-technology-advisory-panel.

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[2] These definitions primarily derive from the National Human Genome Research Institute's *Talking Glossary of Genomic and Genetic Terms*, https://www.genome.gov/genetics-glossary, the U.S. Department of Agriculture's *Agricultural Biotechnology Glossary*, https://www.usda.gov/topics/biotechnology/biotechnology-glossary, and the introductory presentations from Dana Waring Bateman, panel member and genetics educator, which are included in Appendix D.

At the outset of the first meeting, co-chairs Senator Claxton and Representative Zager explained the panel's work would begin with an introduction to genetics, genomics and recent advances in gene-editing technology. The chairs then organized the panel's examination of the opportunities and emerging issues surrounding genomics and gene-editing technology by focusing, over the course of the panel's four meetings, on the following areas:

- ***Gene Editing in Health and Bioscience***, including the medical, public health and bioscience research opportunities and implications of this technology;
- ***Gene Editing in the Natural World***, including the environmental, agricultural, forestry, fisheries and aquaculture opportunities and implications of this technology;
- ***Gene Editing and the Humanities***, including the historical context of the eugenics movement and the ethical, legal and religious considerations attendant to this technology; and
- ***Gene Editing in Systems and Institutions***, including the state economy, business and industry and education system opportunities and implications of this technology.

Each presenter invited to speak on one of these topics was asked to provide background information regarding the presenter's expertise or specific interest in gene-editing technology and then answer the questions: "What should the State of Maine do regarding gene editing within your field in order to best benefit Mainers in the next five years and, subsequently, over the next generation?"

Throughout the panel's four meetings, members engaged in preliminary discussions during which they proposed and debated a wide variety of recommendations the panel could consider making to the Legislature and other state actors regarding genome-editing technology. Ultimately, the panel chose to adopt only recommendations supported by a consensus of all members. Accordingly, this report does not summarize each of the preliminary discussions and instead focuses on panel members' rationale for adopting each consensus recommendation in Part IV of this report.

A. First Meeting - August 17, 2022[3]

The panel held its first meeting on August 17, 2022. The meeting began with panel member introductions, opening remarks by co-chairs Senator Ned Claxton and Representative Samuel Zager, and an overview by legislative staff of the panel's authorizing legislation (Resolve 2021, chapter 177 in Appendix A) and duties. Legislative staff also oriented members to the panel's website, including by reviewing the list of selected background materials gathered by legislative staff and curated by co-chairs Representative Zager and Senator Claxton, which include summaries of recent advances in gene-editing technology; examples of medical, agricultural and environmental applications of this emerging technology; and proposed regulations and reports prepared by national and international governmental and scientific organizations regarding the bioethical implications of human genome editing. (A copy of the final list of background materials, which was periodically updated during the course of the panel's work, is included as Appendix C.) Legislative staff then reviewed the agenda for the day, which included an introduction to gene-editing technology followed by presentations focused on the topic of gene editing in health and bioscience.

1. Introduction to Gene-Editing Technology

Dana Waring Bateman, co-founder of the Genetics Education Project at Harvard Medical School and panel member, next provided context for the panel's work by presenting an overview of the new frontiers

[3] A recording of the August 17th meeting is available at the following link: https://legislature.maine.gov/Audio/#209?event=86313&startDate=2022-08-17T09:00:00-04:00.

of genetic technology entitled "Genome Editing and CRISPR." Ms. Bateman began by explaining that the advent of genetic testing over the past two decades has allowed humans to unlock a wealth of information about their family history, inherited traits and predisposition to certain diseases and conditions. Genetic testing technology and the information it provides raises complicated questions regarding, for example, whether individuals choose to obtain their own genetic information about their predisposition to disease, whether parents choose to pursue non-invasive prenatal testing to predict the traits of a fetus or pre-implantation genetic diagnosis to predict the traits of an embryo produced through in vitro fertilization, and what use individuals, entities—including, for example, law enforcement and insurance companies—and society can and should be allowed to make of genetic testing information. Challenges also arise in ensuring fairness and equity in access to genetic testing, especially in light of the existing disparities in access to health care by different socioeconomic, racial and ethnic groups.

More recently, Ms. Bateman observed, researchers have developed several new genome-editing tools including CRISPR (the acronym for Clustered Regularly Interspaced Short Palindromic Repeats), which allow scientists to make specific, targeted changes to an organism's DNA. CRISPR technology has been successfully employed to make precise genome edits in a variety of organisms—including plants, animals and bacteria. This tool holds great potential to cure or to develop treatments for many human diseases, especially rare diseases that arise from single-gene mutations.

As with genetic testing, genome-editing technology raises complicated questions, including whether genome editing should be limited to somatic cells – for example, to edit the hemoglobin gene in a sickle cell patient's blood cells to alleviate the symptoms and complications of the disease – or also permitted in germline cells – for example, to edit the hemoglobin gene in the sperm or egg of an individual with sickle cell disease, allowing the individual to pass on the edited gene to a new generation. Ms. Bateman noted that more of a consensus exists among doctors, scientists and bioethicists for allowing somatic as opposed to germline editing. Yet, because the costs and impact of different diseases vary greatly, panel members observed that each patient and family, if given a choice, may reach a different decision regarding whether they might opt to pursue somatic or germline gene-editing treatments.

Difficult questions have arisen regarding whether parents should have access to genome-editing technology to make non-therapeutic changes for their children and, if not, where to draw the line between therapies to treat diseases and disabilities and enhancements. The answer to these questions remains clouded by the country's troubled history of eugenics.

Ms. Bateman noted that difficult questions have also arisen regarding whether parents should have access to genome-editing technology to make non-therapeutic changes for their children and, if not, where to draw the line between therapies to treat diseases and disabilities and enhancements utilizing genome-editing technology. The answer to these questions remains clouded by the country's troubled history of eugenics, through which the emerging science of genetics was used to justify discriminatory actions, including forced sterilization of individuals deemed to be different or inferior to others. In addition, Ms. Bateman cautioned that it may be necessary to reassess the manner in which society currently characterizes certain differences, for example deafness or certain forms of autism, as disabilities. Individuals who possess these traits do not always agree that their differences constitute disabilities or disorders that necessitate treatments or cures.

Research is also underway on a wide variety of other methods for employing CRISPR and other genome-editing technologies to enhance human health, including, for example: to genetically alter pigs so that their organs might be transplanted into humans without triggering the immune response that traditionally causes such organs to be rejected; to alter the genes of insects that spread devastating human diseases, including malaria; and to prevent the spread of tickborne

diseases by altering the germline cells of white-footed mice, which are currently responsible for infecting many ticks in North America. (A copy of Ms. Bateman's presentation is included in Appendix D.[4])

2. Gene Editing in Health and Bioscience

After a lunch break, the panel heard from the following slate of presenters, who possess a variety of perspectives and expertise regarding gene editing in the fields of health and bioscience:[5]

- Nirav Shah, M.D., J.D., Director, Maine Center for Disease Control & Prevention
- Jennifer A. Jewell, M.D., pediatric hospitalist, Barbara Bush Children's Hospital and representative of the Maine Chapter of the American Academy of Pediatrics
- Abbie Hunnewell, panel member and person living with a single-gene disorder (cystic fibrosis)
- Christina Riley, panel member and parent of a child with a single-gene disorder (Duchenne muscular dystrophy)
- Benjamin King, Ph.D., Assistant Professor of Bioinformatics, the University of Maine
- Laura Reinholdt, Ph.D., Associate Professor and co-Director, Genetic Resource Sciences, The Jackson Laboratory

Dr. Nirav Shah opened the panel by explaining that new genome-editing technologies allow scientists to change an organism's genetic information by adding, removing or editing DNA at a particular location. While CRISPR (also known as CRISPR/Cas9) is currently the fastest, cheapest and most effective genome-editing technology tool, undoubtedly newer genome-editing technologies will be developed in the future. The emergence of these technologies generates opportunities for Maine's cutting-edge institutions and universities to position themselves as leaders in this field; opportunities to improve the public health of Mainers as this technology is used to generate faster and more accurate diagnoses, targeted and precise treatments and the potential to cure certain genetic disorders; and the potential to foster an even more vibrant biotechnology sector in Maine, which could serve as a location to develop and test new potential treatments and therapies. For example, Maine could position itself to become the hub of research into reversing the course of neurodegenerative diseases using CRISPR technology. Dr. Shah cautioned the panel to consider the ethical challenges and safety concerns that might arise, however, if genome-editing technologies were used to alter germline cells in a manner that could enable altered genes to be passed on to new generations. He also noted that these technologies raise important questions of equity—who can and should benefit from these technologies?

The emergence of genome-editing technologies generates opportunities for Maine's cutting-edge institutions and universities to position themselves as leaders in this field; opportunities improve the public health of Mainers; and the potential to foster an even more vibrant biotechnology sector in Maine.

[4] Ms. Bateman did not have time during the first meeting to review in detail the portions of her presentation discussing potential non-human-health environmental and agricultural applications of CRISPR and other genome-editing technologies.

[5] Dr. Jonathan Zuckerman, Director of the Adult Cystic Fibrosis Program at Maine Medical Center, had been invited to join the presenters discussing Gene Editing in Health and Bioscience, but was unable to attend. He submitted written remarks that were distributed to panel members during the September 7, 2022 meeting. (A copy of Dr. Zuckerman's remarks is included in Appendix E.)

Many of the diseases that are amenable to gene editing, including sickle cell disease and spinal muscular atrophy, are the cruelest.

Dr. Jennifer Jewell focused her remarks regarding genome-editing technology and pediatric patients on three topics. First, she noted the potential value of this technology to her patients. Many of the diseases that are amenable to gene editing, including sickle cell disease and spinal muscular atrophy, are the cruelest. Treatments developed from genome-editing technology can save patients and families from both the pain of these diseases and from the financial and emotional strain of repeated hospitalizations. Second, she observed that, as with every medical treatment, we must recognize that there are safety concerns and potentially unknown long-term side effects from these new treatments. Third, she cautioned that these emerging technologies raise several ethical conundrums, not only regarding the potential for parents to pursue genetic enhancements and not just treatments for their children (and the difficulty of distinguishing between the two) but also the social justice implications for families who cannot access these new treatments based on financial or educational barriers to understanding the new technology. In addition, Dr. Jewell expressed her concern that industry will either neglect diseases that primarily affect minority populations or will test new treatments on minority patients without fully disclosing the new treatments' potential risks. For these reasons, she urged panel members to ask the difficult questions necessary to ensure that gene editing is accomplished safely, ethically and in a manner that protects the best interests of individual Maine patients and of Mainers as a population.

Abbie Hunnewell described her life with cystic fibrosis, a single-gene disorder. Cystic fibrosis causes thick and sticky mucus to build up in her lungs, which clogs her airways, enhances the growth of bacteria and leads to frequent respiratory illness. The build-up of mucus in her other organs prevents her body from absorbing nutrients, resulting in the need to surgically insert a gastronomy tube and causing her to develop cystic fibrosis-related diabetes. She has been hospitalized approximately 2-4 times per year for several weeks at a time. Even when she is not in the hospital, she must maintain a demanding health regimen of up to 20 pills per day and many hours of airway clearance therapies and nebulizing treatments. Genome-editing technology, which has already been used to correct the genetic cause of cystic fibrosis in cultured cells, has the exciting potential to revolutionize the treatment and management of cystic fibrosis. As this technology develops, Ms. Hunnewell recommended that the State take steps to ensure that research into potential treatments is performed in an ethical and responsible way and that treatments are provided to patients in a fair and equitable manner.

Research into potential gene-editing treatments should be performed in an ethical and responsible way and treatments should be provided to patients in a fair and equitable manner.

Christina Riley, former state representative and parent of an adult son with Duchenne muscular dystrophy (DMD), next described the enormous toll this single-gene disorder has taken on both her son and her family. DMD patients have a variety of mutations in the dystrophin gene on the X chromosome, and the disease is more common in boys than in girls. DMD causes progressive muscle weakening, and many, but not all, patients also experience cognitive difficulties and impairments. Without intervention, patients often die in their late teens and early twenties. Ms. Riley's son, a bright young man who graduated from high school with honors, was diagnosed shortly before he was two years old, developed his first bout with pneumonia in third grade, lost the ability to walk at age 12, and has undergone multiple surgeries to address the complications of DMD. Ms. Riley eventually left her career to provide full-time care for her son, who requires constant assistance navigating daily life. The loss of her career negatively impacted her family's financial resources, which were already strained by medical expenses as well as the cost of accessible vehicles and adaptive equipment. While government assistance programs provide a vital lifeline, the processes to qualify for such programs are lengthy and intrusive. Parents of DMD patients often cannot accept the reality of this progressive and ultimately fatal disease, causing them, out of desperation, to spend thousands of dollars pursuing harmful "therapies" that ultimately do not work. While the first genetic therapies are being developed for different forms of DMD,

these therapies remain out-of-reach financially for many patients. She urged the panel to explore methods of increasing equitable access to these types of treatments.

> Investments in public pre-Kindergarten through post-graduate science education and biotechnology research will not only increase the public's awareness of these emerging technologies but will also expand the number of citizens who can contribute to important ethical conversations regarding these technologies.

Dr. Benjamin King highlighted the revolution in genomics and bioinformatics that has allowed companies to offer full sequencing of an individual's genome for less than $150.[6] With this new technology, genomic science will impact all of our lives, not only as a genealogical tool but also to help doctors decide which drugs to prescribe based on genetic variations potentially impacting various drugs' effectiveness in individual patients. He further observed that scientists' new ability to make precision edits to various organisms' genomes is an incredible tool, which has allowed the students in his laboratory to edit the genes of zebrafish to study the ways in which different types of immune cells respond to infections from different viruses. In the face of these emerging technologies and research, Dr. King suggested that the panel ensure that citizens in the State engage in a productive dialogue on the ethical issues surrounding human genome editing. Increased investments in public pre-Kindergarten through post-graduate science education and biotechnology research will not only increase the public's awareness of these emerging technologies but will also expand the number of citizens who can contribute to these important ethical conversations. In addition, he suggested that Maine should support communities of patients and families who experience a broad spectrum of diseases. Maine should, for example, expand its investment in clinical research to expand the number of clinical trials that take place in Maine, increasing access for patients who cannot regularly travel out of state to receive cutting-edge treatments.

Dr. Laura Reinholdt focused on the positive, transformational impact that gene-editing technology has had on biomedical and clinical research both broadly and locally at The Jackson Laboratory in Maine. In response to the specific questions posed of all presenters, Dr. Reinholdt recommended that over the next five years, Maine promote life sciences awareness and education both in K-12 schools and in community organizations. Building sufficient knowledge regarding biomedical technology among Maine citizens will help them engage in meaningful policy conversations about the uses and regulation of gene editing and other biomedical technologies. In the longer term, Dr. Reinholdt encouraged Maine to invest in medical research talent and infrastructure, so that Maine patients are not prevented from accessing future genomic treatments due to lack of proximity to a major research hub. (A copy of Dr. Reinholdt's remarks is included in Appendix E.)

3. *Public Comment*

Following the Gene Editing in Health and Bioscience presentations, the panel co-chairs granted a request by Michael McKernan, Director of Government and Community Relations at The Jackson Laboratory, to comment on the panel's discussion of the importance of attracting college graduates with degrees in biosciences and related fields to live and work in Maine. He informed the panel that The Jackson Laboratory employs approximately 1,800 people in the State and, as of August 17, 2022, has 108 open positions. Over the 2021 calendar year, the average age of new hires at The Jackson Laboratory was 31 years. In addition, out of 233 employees hired during the 2021 calendar year, just 31 were hired from outside the State of Maine.

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[6] By contrast, it is estimated to have cost approximately $300 million to sequence the first human genome as part of the Human Genome Project. "The Cost of Sequencing a Human Genome," Genome.gov (National Human Genome Research Institute, November 1, 2021), https://www.genome.gov/about-genomics/fact-sheets/Sequencing-Human-Genome-cost.

B. Second Meeting – September 7, 2022[7]

The panel held its second meeting on September 7, 2022. The meeting began with panel member introductions and remarks by co-chair Senator Claxton on the value of the diversity of panel member backgrounds outside of the scientific and medical fields. Legislative staff then reviewed the agenda for the day, which included a review of core concepts related to gene-editing technology and follow-up information related to the topic of gene editing in health and bioscience that had been explored during the first meeting, followed by presentations focused on the topic of gene editing in the natural world.

1. Review of Core Concepts Related to Gene-Editing Technology

The co-chairs next invited panel member and genetics educator Dana Waring Bateman to clarify several core concepts related to gene-editing technology. Ms. Bateman began by observing that, as a genetics educator, she approaches this topic from a humanities perspective, similar to how other panel members without formal training as a scientist or doctor are approaching this work.

Ms. Bateman explained that deoxyribose nucleic acid, or DNA, can be found in virtually every cell of the body. DNA is a unique code, which contains the instructions for all of our traits. The code is determined by the arrangement of four nucleotide bases along each strand of DNA: Adenine (A), Cytosine (C), Guanine (G), and Thymine (T). A gene is a unit of DNA that provides the instructions for a specific purpose and a chromosome is a packaged bundle of genes. Changes in the DNA code at any level can create variations in our traits, some of which can be detrimental to human health. For example, sickle cell anemia results from a change in one nucleotide base within a single gene, Cystic Fibrosis results from the deletion of three nucleotide bases within a single gene, and Down syndrome results from the presence of an entire additional chromosome.

CRISPR is a gene-editing tool derived from a bacterial immune system that recognizes specific DNA sequences and can alter them by removing, replacing, or adding specific base pairs or even entire genes to an organism's chromosomes. CRISPR was first used in human cell culture in 2013 and has been successfully used in every type of species in which it has been attempted, and is just one of an array of gene-editing tools that can be used to change our DNA code. Gene therapies, including those developed using CRISPR, can be delivered to our bodies in a variety of ways. For example, to treat sickle cell anemia, blood cells can be removed from the body, treated with the gene therapy tool outside of the body and then reinjected back into our bloodstream. With other gene therapies, it is necessary to target a specific organ system. This can be done either by injecting the gene therapy system directly into the target organ or by using genetically-altered viruses (called "viral vectors") that are designed to deliver specific genetic changes to specific cells within a patient's body.

Ms. Bateman also highlighted the critical difference between gene therapies targeted to somatic cells and gene therapies targeted to germline cells. Somatic cells are the "body cells" – essentially all of the cells in the body other than sperm and eggs. Germline cells are reproductive cells, sperm and eggs, which contain genetic information that can be passed on to future generations. Gene therapies that affect somatic cells, such as blood cells or eye cells, will only affect the individual receiving the treatment and will not be passed on to their offspring. Gene therapies that target germline cells, sperm or eggs, can be passed on to future generations, however. The ability to alter germline cells raises questions around possible unintended consequences and the lack of individual autonomy and consent of the child who is born

[7] A recording of the September 7th meeting is available at the following link: https://legislature.maine.gov/Audio/#209?event=86381&startDate=2022-09-07T09:00:00-04:00.

from those altered germline cells. Ms. Bateman shared that currently there is a worldwide consensus that making permanent genetic changes, or changes to the germline, should not be performed at this stage in our understanding of gene-editing technology and its potential consequences.[8] (A copy of Ms. Bateman's presentation is included in Appendix D.)

2. Additional Information Related to Gene Editing in Health and Bioscience

Panel co-chair Senator Claxton next directed panel members' attention to information received by the panel related to the first meeting's slate of presentations on Gene Editing in Health and Bioscience:

- Written testimony from Jonathan Zuckerman, M.D., Director of the Adult Cystic Fibrosis Program at Maine Medical Center, who had been invited to present but was unable to attend. (A copy of Dr. Zuckerman's testimony is included in Appendix E.)
- A public comment from Kent Redford, Ph.D., in response to the first meeting's presentations. (A copy of Dr. Redford's public comment is included in Appendix F.)

Legislative staff next provided panel members with copies of the following items, which had been requested by panel members during the first meeting:

- Public Law 2021, chapter 740, *An Act To Establish the Rare Disease Advisory Council*, which was enacted during the Second Regular Session of the 130th Legislature;[9]
- LD 1085, *An Act Relating to the Use of Genetic Information for Insurance Purposes*, which had been considered, but ultimately not enacted, by the 130th Legislature;[10] and
- Information regarding the federal Genetic Information Nondiscrimination Act of 2008, which prohibits most health insurers and employers from engaging in certain discriminatory practices on the basis of a (potential) customers' or employees' genetic information.[11]

3. Gene Editing in the Natural World

During the balance of the meeting, the panel heard from the following slate of presenters, who possess a variety of perspectives and expertise regarding gene editing in the natural world:[12]

- Dana Waring Bateman, panel member and genetics educator
- Chris Okonkwo, Ph.D., Assistant Professor of Biotechnology, the Roux Institute at Northeastern University

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[8] The background materials list, included as Appendix C, includes several of these policy statements.

[9] *See* http://www mainelegislature.org/legis/bills/display_ps.asp?ld=972&PID=1456&snum=130.

[10] *See* http://www mainelegislature.org/legis/bills/display_ps.asp?ld=1085&PID=1456&snum=130.

[11] "Genetic Discrimination," Genome.gov (National Human Genome Research Institute, January 6, 2022), https://www.genome.gov/about-genomics/policy-issues/Genetic-Discrimination.

[12] Kent Redford, Ph.D., an expert in conservation and synthetic biology and the Maine Aquaculture Innovation Center were invited to join the presenters discussing Gene Editing in the Natural World, but were unable to attend. They each submitted written remarks, which were distributed to panel members during the September 7, 2022 and September 21, 2022 meetings. (Copies of these materials are included in Appendix G.) At the request of the panel's co-chairs, legislative staff also sent inquires to Gulf of Maine Research Institute, Natural Resources Council of Maine, Maine Forest Products Council, Maine Lobstermen's Association, and Syngenta on this topic. For various reasons, these organizations declined to participate.

- Diane Rowland, Ph.D., Dean of the College of Natural Sciences, Forestry and Agriculture and Director of the Maine Agricultural and Forest Experiment Station, the University of Maine
- Melody N. Neely, Ph.D., Associate Professor of Molecular and Biomedical Sciences, the University of Maine
- Hillary Peterson, Ph.D., Integrated Pest Management Specialist, Maine Department of Agriculture, Conservation and Forestry
- Heather Spaulding, Deputy Director and Senior Policy Director of the Maine Organic Farmers and Gardeners Association

Ms. Bateman began by sharing the portions of the presentation she had prepared for the first panel meeting that illustrate how CRISPR and other genome-editing technologies are being used outside of the medical field. For example, researchers have altered the genome of the cassava plant to reduce the toxicity of this globally important food crop and, in an effort to prevent the extinction of Hawaiian honeycreepers, mosquitos that have the potential to spread avian malaria have been genetically altered to prevent them from carrying this disease. Researchers have even discussed the "Hail Mary" idea of using genome editing to bring back the woolly mammoth, a currently extinct animal whose size and habits might help prevent the thawing of permafrost by compressing it. While each use of genome-editing technology was designed to achieve a worthy goal, each also raises many questions. In case of cassava, for example, do the genetic changes that reduce this crop's toxicity also negatively affect the plant's drought tolerance or insect resistance? Will someone own the edited plants or seeds, hindering their use in less affluent countries? Is gene editing the most appropriate approach to a problem (hunger) that is a result of many factors, including poverty and changing climate conditions? (A copy of Ms. Bateman's presentation is included in Appendix D.)

Dr. Chris Okonkwo's presentation focused on the impact that gene editing could have on three of Maine's heritage industries: forestry, marine fisheries, and agriculture. He reiterated that CRISPR revolutionized science by providing a simple, fast, relatively inexpensive and accurate method of gene editing. Dr. Okonkwo explained that CRIPSR can be used to genetically alter microorganisms in a way that will allow them to transform agricultural and forest waste into, for example, efficient biofuels and biochemicals, synthetic rubber or bioplastics and resins, all of which will add value to the forestry sector in Maine. Similarly, biotechnology researchers have used genome-editing technology to enhance the efficiency of microorganisms that degrade bioplastics. In the future, these genetically altered microorganisms could be used to clean up the marine environment and improve the health of marine fisheries. Genome editing can also be used enhance the efficiency and efficacy of microorganisms that remove pollutants, such as ammonia, phosphorous, and heavy metals, from wastewater. Dr. Okonkwo noted that gene editing might be used to increase agricultural crops' resistance to drought, disease, and pests. These alterations would not only increase crop yields but also might make crops more resilient in the face of climate change and potentially increase food security globally. He advised the panel and the State to invest more resources in genome-editing technologies and educational opportunities, which will help attract biotechnology companies to the State and make Maine a biotechnology hub. (A copy of Dr. Okonkwo's presentation is included in Appendix G.)

> Gene-editing technology has the potential to add value to the forestry sector in Maine; to clean up the marine environment and improve the health of Maine fisheries; to remove pollutants from wastewater; and potentially to enhance food security globally by increasing crop yields and making crops more resilient in the face of climate change.

Dr. Diane Rowland explained that, although she is not a geneticist, she has 20 years of experience in crop research as a whole plant physiologist. Whole plant physiologists work in the field to examine traits at the whole plant level and to assist breeders in targeting traits of interest. Many of these traits, such as drought

Maine should explore ways to enhance partnerships between post-secondary institutions and private industry.

resistance, are very complex. It can take long periods of time to develop crops with these traits using conventional breeding techniques. Gene-editing technologies accelerate this process, especially given the tremendous advances that have been made in genome sequencing that have identified genetic sequences of importance in various agricultural crops. Dr. Rowland highlighted the importance of Maine taking part in conversations about the agricultural uses of gene-editing technology, particularly with respect to Maine's signature crops, including potatoes and blueberries, both of which are the focus of current and proposed future research. She also urged the panel to explore ways to enhance partnerships between post-secondary institutions and private industry, especially by increasing student internship opportunities. Finally, Dr. Rowland recommended that the State take steps to increase both the general population's understanding of basic genetic technology and terminology and the preparation of university graduates to ensure that they have the expertise necessary to enter this field.

Dr. Melody Neely next shared that, around the world, research using gene-editing technologies on potatoes, blueberries and salmon could have beneficial impacts on Maine's agriculture and fisheries industries. In addition, at the University of Maine, research is currently being conducting using the CRISPR gene-editing tool in zebrafish to examine how its immune system functions and how to make the genetic underpinnings of its immune system more robust. The results of this research may in the future be used to develop treatments for human diseases or to enhance aquaculture by making other fish species more resistant to disease. Dr. Neely emphasized the importance of ensuring that these technologies are used safely, however. As genome-editing technologies are developed—for example, to increase the resistance of blueberries to disease—the university believes it is critical to consult experts from many disciplines, including geneticists; bioinformatics and large data analysis; proteomics, transcriptomics and metabolomics; agricultural testing; food and nutrition analysis; and bioethicists. In this way, the university can ensure that the products it creates are not only safe but also a great benefit to Maine and the industry. Dr. Neely further cautioned that, while the U.S. Department of Agriculture (USDA) provides regulatory oversight for genetically modified organisms (GMOs) that cannot be created through conventional breeding or found in nature – *i.e.,* if a gene from one organism is introduced into a new organism – the USDA does not regulate GMOs that are generated through genome-editing technologies including CRISPR that merely make targeted changes to the organism's own genes. (A copy of Dr. Neely's presentation is included in Appendix G.)

By consulting with a consortium of experts across multiple disciplines as it develops new genome-editing technologies, the University of Maine can ensure that the products it creates are not only safe but also a great benefit to Maine and the industry.

Following a lunch break, Dr. Hillary Peterson described the role that gene editing could play in an integrated pest management system and in reducing pesticide use.[13] Integrated pest management (IPM) combines several methods to prevent and mitigate pest related problems in a biologically based manner: (1) setting plants up for success with ideal growth conditions; (2) monitoring plants for pests and disease and keeping detailed records; (3) properly identifying pests and disease before treating the plants; and (4) mitigating pesticide use though other means, including, traditionally, biological controls, natural pest enemies, mass trapping, repelling and physical barriers. Gene editing can fit into steps (1) and (4) of the IPM toolbox by helping scientists engineer more resistant plants and by mitigating the use of pesticides. Dr. Peterson cautioned that the development and application of gene-editing technologies in agriculture, while certainly beneficial, requires a significant amount of research, grant dollars, time and personnel.

[13] Dr. Peterson also informed the panel that the Maine Department of Agriculture, Conservation and Forestry does not currently have a set policy or position regarding the use of gene-editing technology.

Therefore, Dr. Peterson recommended that Maine provide financial support for this research and for growers who are willing to implement these new technologies. Additionally, she advised the State to increase public awareness and understanding regarding these technologies while respecting the many perspectives that exist. (A copy of Dr. Peterson's presentation is included in Appendix G.)

Organic farmers are concerned that genetically altered plant varieties will mix with, and potentially alter, natural or heirloom plant varieties.

Heather Spalding, speaking on behalf of the Maine Organic Farmers and Growers Association, or MOFGA, the oldest and largest organic food association in the country, expressed concerns about the use of gene-editing technology in agriculture. MOFGA opposes genetic engineering and advocates for significant changes in regulatory framework governing the technology at local, state and national levels. Ms. Spaulding explained that the National Organic Standards Board (NOSB) has recommended that the U.S. Department of Agriculture's National Organic Program prohibit the use of all genetically modified organisms, including all products of gene-editing technology, by organic farmers. MOFGA believes the health and safety of this technology has not been adequately assessed. Organic farmers are also concerned that genetically altered plant varieties will mix with, and potentially alter, natural or heirloom plant varieties. In addition, MOFGA has significant concerns about the impact that genetically altered plants will have on the health of the environment. For example, crops that have been genetically altered to withstand the increased use of herbicides, while beneficial in reducing pesticide use, have led to the destruction of milkweed, endangering the survival of the monarch butterfly. Ms. Spalding recommended that the State provide more funding towards methods that advance organic agriculture and that Maine take a precautionary approach to novel technologies, especially before products engineered using these techniques are released in the environment. She also stressed that the State already has at its fingertips the necessary knowledge and resources to rebuild the health and diversity of the environment in Maine, without these novel technologies.

C. Third Meeting – September 21, 2022[14]

The panel's third meeting on September 21, 2022 began with panel member introductions and an overview of the agenda for the day, which included a review of additional information related to gene editing in health and bioscience and gene editing in the natural world, the topics that had been the focus of the first two panel meetings, as well as overviews of the applicable regulatory structures for genome-editing research, followed by presentations focused on the topic of gene editing and the humanities.

1. Additional Information Related to Gene Editing in Health and Bioscience and Gene Editing in the Natural World

At the outset of the third meeting, panel members received the following items of information related to the topics of Gene Editing in Health and Bioscience and Gene Editing in the Natural World:

- Public Law 2021, chapter 459, *An Act To Lower Health Care Costs through the Establishment of the Office of Affordable Health Care*, which was enacted during the First Special Session of the 130th Legislature;[15]
- A memorandum prepared by legislative staff in response to questions posed by panel members regarding whether a recommended number of genetic counselors has been established for a given

[14] A recording of the September 21st meeting is available at the following link: https://legislature.maine.gov/Audio/#209?event=86393&startDate=2022-09-21T09:00:00-04:00.

[15] *See* http://www.mainelegislature.org/legis/bills/display_ps.asp?ld=120&PID=1456&snum=130.

population and, if so, whether this standard has been met in the State of Maine (A copy of this memorandum is included in Appendix F);

- A public comment from Lisa Harvey-McPherson of Northern Light Health advocating that the State establish a professional licensing program for genetic counselors (A copy of this comment is included in Appendix F);
- Written testimony from Kent Redford, Ph.D., an expert in conservation and synthetic biology, who had been invited but was unable to present during the second meeting on Gene Editing in the Natural World (A copy of this testimony is included in Appendix G);
- Written testimony from Anne Langston Noll, Ph.D., Project Director from the Maine Aquaculture Innovation Center, who had been invited but was unable to present during the second meeting on Gene Editing in the Natural World (A copy of this testimony is included in Appendix G);
- Copies of several publicly available documents summarizing the federal government's regulatory oversight of non-medical uses of genome-editing technology;[16]
- A memorandum prepared by legislative staff at the direction of the panel co-chairs regarding the types of gene-editing technologies prohibited in organic farming under applicable federal regulations (A copy of this memorandum is included in Appendix H);
- Information from the Maine Department of Education in response to questions about Science, Technology, Engineering and Math (STEM) education programs in Maine's public high schools and career and technical education centers (Copies of the original email containing this information, as well as a later clarifying email, are included in Appendix L); and
- Information from the websites of the Maine Technology Institute, describing its targeted technology sectors, and the Finance Authority of Maine, describing the Maine Seed Capital Tax Credit Program.[17]

2. *Overview of the Current Regulatory Structure for Research Involving Genome-editing Technologies*

In response to questions posed during the first two panel meetings, the panel co-chairs invited the following individuals to present overviews of the applicable regulatory structure for the conduct of genome-editing research in medical and non-medical fields:

- Andrew P. Holmes, Ph.D., Institutional Biosafety Officer at the University of Maine
- Frank Chessa, Ph.D., panel member and Director of Clinical Ethics at Maine Medical Center

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[16] U.S. Library of Congress, Congressional Research Service, *Agricultural Biotechnology: Overview, Regulation, and Selected Policy Issues*, by Genevieve K. Croft, R46737 (March 29, 2021), https://crsreports.congress.gov/product/pdf/R/R46737; U.S. Department of Agriculture, U.S. Department of Health and Human Services' Food and Drug Administration, and U.S. Environmental Protection Agency, *Modernizing the Regulatory System for Biotechnology Products: Final Version of the 2017 Update to the Coordinated Framework for the Regulation of Biotechnology* (January 4, 2017), https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/2017_coordinated_framework_update.pdf; "Unified Website for Biotechnology Regulation," U.S. Department of Agriculture, https://usbiotechnologyregulation.mrp.usda.gov/biotechnologygov/home (accessed September 21, 2022).

[17] "Technology Sectors," The Maine Technology Institute, https://www.mainetechnology.org/who-is-mti/technology-sectors/ (accessed September 21, 2022); "Maine Seed Capital Tax Credit Program," Finance Authority of Maine, https://www.famemaine.com/business-financing/for-business-owners/fame-financing-programs/equity-capital-tax-credits/maine-seed-capital-tax-credit/ (accessed September 21, 2022).

Dr. Andrew P. Holmes first discussed the federal government's *Coordinated Framework for the Regulation of Biotechnology (2017)*, which applies to gene-editing research conducted outside of the medical context. He explained that he would only provide a brief overview of the framework and urged panel members to review the materials distributed by staff for further information. The coordinated framework, originally created in 1986, was most recently updated in 2017 in response to the development of the CRISPR/Cas9 system and related genome-editing technologies. Under the coordinated framework, three separate agencies, the U.S. Department of Agriculture (USDA), the U.S. Food & Drug Administration (FDA) and the U.S. Environmental Protection Agency (EPA), play distinct roles in regulating products and organisms that appear on the market. The USDA evaluates plants and other organisms, as well as animals and veterinary biologics. The FDA regulates a variety of products, including food, animal feed and drugs for humans and animals. The EPA regulates pesticides, including by regulating the amount of pesticides that may be present in food. Products falling within more than one category are subject to regulatory overlap. Unlike the approach taken by some other countries, these federal agencies employ a risk-based assessment process that focuses on the characteristics of the product, as opposed to the type of process (like gene-editing technology) used to create the product. Under this system, products that have proven to be safe in the past receive more expedited reviews—for example, the USDA exempts plants that have been modified by genetic engineering from regulation if the modification could otherwise be accomplished through conventional breeding. In Dr. Holmes' opinion, this approach properly balances the need to ensure product safety and the importance of promoting product innovation. Applying an alternative process-based approach to regulation would, in Dr. Holmes' view, impede the economic development of small businesses by imposing costs that could only be absorbed by large, multinational corporations.

The federal government's *Coordinated Framework for the Regulation of Biotechnology (2017)* applies to gene-editing research conducted outside of the medical context.

Beyond the coordinated framework, research institutions impose additional checks and balances on gene-editing research. Dr. Holmes explained that the University of Maine employs a multi-layered approach to safety. The university established an institutional biosafety committee comprised of experts and community members to ensure that all research is performed safely and ethically. In addition, all university research projects involving genome-editing technologies are conducted either on campus or within other controlled environments that prevent the release of genetically altered organisms into the environment. As a recipient of federal funding, the university also adheres to National Institutes of Health (NIH) guidelines. Dr. Holmes urged the panel to ensure members of the public receive sufficient education in the basics of molecular biology, which will help alleviate the public's uncertainties regarding these technologies and allow them to better assess the various applications of these technologies.

Dr. Frank Chessa next provided an overview of the regulatory guardrails applicable to gene-editing technology in a medical research context. He began by explaining the history underlying the development of institutional review boards (IRBs). After World War II, German scientists who were tried for the atrocities they committed while experimenting on human subjects in concentration camps, claimed that their research practices were no different than practices in other countries, including the United States. These scientists also pointed out that, at the time, there were no published standards for medical experimentation on human beings. The Nuremberg Code was developed to provide standard protections for human subjects and survives today as an important document stating the ethical principles underlying the protection of human subjects: (1) human subjects must voluntarily consent to the experiment; (2) the experiment should be designed to yield fruitful results for the good of society; (3) the experiment must be conducted so as to avoid all unnecessary physical and mental suffering; (4) the experiment should not be conducted if it is likely that

The Nuremberg Code was developed after World War II to provide standard protections for human subjects and survives today as an important document stating the ethical principles underlying the protection of human research subjects.

death or disabling injury will occur; and (5) at all times, human subjects should be at liberty to bring the experiment to an end. Unfortunately, research continued to violate these principles in the decades following development of the Nuremberg. The progress towards the standards and regulations in place today continued to develop over time. The National Research Act of 1974 established Institutional Review Boards, or IRBs, which were further regulated by the promulgation in 1991 of a set of federal regulations protecting human subjects in research known as the Common Rule.[18] IRBs are charged with the ethical review of research involving human subjects. IRBs must be diverse and community specific and must include at least a scientist, a nonscientist and a member of the community. IRBs examine five elements of proposed research involving human subjects: informed consent; study design; subject selection; safety monitoring; and confidentiality. While IRBs were designed to allow local norms to guide the research process, Dr. Chessa noted that recent shifts in clinical research practices – including a decrease in the number of trials conducted by academic medical centers and increase in trials conducted by for-profit companies – have resulted in a shift away from local university IRBs toward the use of a few for-profit IRBs.

Dr. Chessa concluded his presentation by providing an overview of federal laws and international agreements and conferences addressing the use of gene-editing technologies. Although no federal law expressly prohibits the use of gene editing in germ line cells, federal funding restrictions effectively prevent such research in the United States. He also shared information related to the number and location of countries with policies regulating human germ line genome editing and highlighted a series of reports issued by international organizations that make specific recommendations regarding whether and how researchers should approach human genome editing. (A copy of Dr. Chessa's presentation is included in Appendix F.[19])

Although no federal law expressly prohibits the use of gene editing in germ line cells, federal funding restrictions effectively prevent such research in the United States.

3. Gene Editing and the Humanities

After a short break, the panel heard from the following slate of presenters, who possess a variety of perspectives and expertise regarding gene editing in the humanities:[20]

- Dimitry Bam, Esq., Vice Dean of the University of Maine School of Law
- Kate McBrien, Maine State Archivist
- Frank Chessa, Ph.D., panel member and Director of Clinical Ethics at Maine Medical Center
- John Hennessy, co-chair of the Maine Council of Churches' Public Policy Committee
- Lois Lowry, panel member and author whose published works have explored the humanity of all people
- Marcques Houston, panel member representing persons under 30 years of age

[18] Protection of Human Subjects, 45 C.F.R. pt. 46 (2018), https://www.ecfr.gov/on/2018-07-19/title-45/subtitle-A/subchapter-A/part-46.

[19] Links to many of the federal and international materials referenced in the latter half of Dr. Chessa's presentation are included in the list of background materials included as Appendix C.

[20] Mr. Dwayne Tomah was invited to speak during the September 21st meeting, but due to a scheduling conflict he provided his remarks during the October 19th meeting. At the request of the panel's co-chairs, legislative staff also sent inquires to the Maine Association for the Deaf, Inc., The Maine Education Center for the Deaf and Hard of Hearing/Governor Baxter School for the Deaf, Disability Rights Maine, Temple Beth El in Portland, the Center for Small Town Jewish Life at Colby College and the Islamic Center of Maine. For various reasons these organizations declined to participate.

Dimitry Bam opened his remarks by explaining that he was not an expert in the laws governing genome editing but would share his thoughts regarding the types of legislation governments should consider and the human rights implications of genome-editing technology. He cautioned that, as with any novel technology, lawmakers must clearly define the term "genetic engineering" in any legislation designed to regulate this technology. He suggested that lawmakers consider creating a tiered approach for research involving gene-editing technology, with decreased oversight of routine applications of this technology and different types of regulatory structures applicable to research leading to the development of medical therapies as opposed to cosmetic enhancements. State lawmakers should also carefully consider whether federal regulations sufficiently regulate the products of gene-editing research. Topics to consider include whether consumers are adequately informed about the potential risks of these products; whether civil fines or criminal penalties should be designed to address situations when these products produce negative environmental or social consequences or whether the value these products provide to society justifies the creation of tort liability protections to spur innovation; and whether there should be mandatory insurance coverage for medical applications of this technology. Vice Dean Bam further cautioned lawmakers that human genome-editing research and applications implicate several fundamental individual rights, including the right to privacy, substantive due process and equal protection and parental rights.

In the early 1900s, the State evicted all of the residents of Malaga Island, some of whom were institutionalized in Maine School for the Feeble Minded. During this same time period, the State performed eugenically based sterilizations under both compulsory and voluntary laws, including on residents of the Maine School for the Feeble Minded.

Maine State Archivist Kate McBrien next shared the history of Malaga Island, a small island off the coast of Maine that was home to a multi-race community from about 1863 until 1912, and the impact that the eugenics movement had on that community. The eugenics movement aimed to increase the incidence within the community of what the movement's scientific and political leaders regarded as desirable characteristics and to decrease the incidence of characteristics viewed as less desirable. Influenced by eugenic theories, a report submitted to the Governor of Maine and the State's Executive Council in 1911 described, using racist terminology, the people of Malaga Island – a poor, multi-race community whose lives had become the subject of popularly disseminated myths including stories of theft, inbreeding and illiteracy. In 1911, the State of Maine decided to break up the community, evicting them from the island in an attempt to prevent further procreating and possible community growth. The State also took title to the island to prevent individuals from attempting to resettle there. Some Malaga Island residents were institutionalized at the newly opened Maine School for the Feeble Minded, including one entire family. By 1912, the community on Malaga Island was gone. During this same time period, the State performed eugenically based sterilizations under both compulsory and voluntary laws, including on residents of the Maine School for the Feeble Minded. The popularity of eugenics theories continued to grow in Maine and, in 1917, a report commissioned by the Governor concluded that the "intellectual and moral standards of the State's inhabitants as a whole may be advanced faster and their efficiency be increased by seeking to humanely diminish the burden of feeblemindedness."[21] While it is easy for modern society to dismiss the movement as misguided, Ms. McBrien observed that throughout the turn of the century and up through the 1940s, eugenics-based theories were the leading scientific theories championed by doctors, educators and politicians. Governor John Baldacci, Governor Paul LePage and the Maine Legislature eventually apologized on behalf of the State and established the Malaga 1912 Scholarship Fund for

Governor John Baldacci, Governor Paul LePage and the Maine Legislature eventually apologized on behalf of the State and established the Malaga 1912 Scholarship Fund.

[21] State of Maine. *The Report of The Maine Commission for The Feebleminded and of the Survey by The National Committee for Mental Hygiene*, 1918, https://archive.org/details/reportofmainecom00nati/page/n7/mode/2up.

descendants of former residents of Malaga Island. [22] Nevertheless, the lingering effects of the eugenics movement remain today. Following Ms. McBrien's presentation, the panel paused to take a moment of silence to reflect upon the harm the State inflicted on the people of Malaga Island and other disadvantaged populations during the eugenics movement. (A copy of Ms. McBrien's presentation is included in Appendix I.)

After a lunch break, Dr. Frank Chessa again addressed the panel, this time from his perspective as a bioethicist. He explained his excitement about the potential for somatic-cell gene-editing therapies to treat human diseases and urged the State to do everything it can to increase access to established therapies as well as clinical trials involving new therapies within the State. He also stressed the importance of creating robust protections for research subjects, especially given the potential for the development of unsafe therapies caused by a dangerous mix of patient therapeutic misconceptions[23] and researcher profit motives. Dr. Chessa cautioned, however, that the State should consider adopting the recommendations made by the National Academies in their Human Genome Editing Report that would limit research and therapies involving human germ-cell gene-editing to single-gene heritable diseases.[24] He also cautioned the State to learn from its history of eugenics and guard against using science and pseudoscience to advance political rather than therapeutic agendas. The State should restrict the use of gene-editing technologies to the prevention of diseases that have definite negative effects on patients, rather than allowing these technologies to be harnessed to promote broader social movement aimed at creating "better" people. Dr. Chessa also noted the difference between "negative eugenics" – preventing the birth of people whom society deems undesirable – and "positive eugenics" – taking steps to enhance the traits of people who are born. Each poses danger requiring society to guard against the use of these technologies to pursue concepts of racial superiority and genocide. Finally, Dr. Chessa asked the panel to consider the value that society places on "wild nature." Environmental ethicists have noted that there is probably no segment of nature completely untouched by human technology. Nevertheless, it may make sense, especially given how quickly changes in a population can spread through the use of new genome-editing technologies, to contemplate preserving and protecting some segments of nature from these technologies.

[22] Governor LePage originally proposed a one-time appropriation of $500,000 for the scholarship fund, but this figure was reduced to $300,000 by the Legislature as part of the biennial budget process. For more information on the gubernatorial and legislative apologies as well as the scholarship fund, see the staff memorandum in Appendix J.

[23] Dr. Chessa had described the therapeutic misconceptions held by patients during his presentation earlier in the day. *See* Appendix F.

[24] Dr. Chessa described the National Academies' recommendations during his presentation earlier in the day. *See* Appendix F.

In 1985, the Episcopal Church cautioned that gene therapies should be available equally, regardless of financial status, and that genetic information should not be used to discriminate against individuals in employment, insurance or other contexts. It also warned against potential misuses of this technology, especially for personal glory, power or wealth.

John Hennessey began his presentation by informing panel members that he testified on behalf of the Maine Council of Churches and the Episcopal Diocese in support of LD 1771, the legislation establishing this panel, to encourage Maine's citizens to engage in the important conversations the panel has undertaken regarding genome-editing technology.[25] In 1985, the Episcopal Church voted to encourage genetic engineering research to increase human understanding of vital processes. The Church concluded that it held no theological or ethical objections to the use of gene therapies for diagnostic or therapeutic purposes aimed at the prevention or alleviation of human suffering. Yet, the Church cautioned that these treatments should be available equally, regardless of financial status, and genetic information should not be used to discriminate against individuals in employment, insurance or other contexts. Mr. Hennessy also noted that the Church has warned against potential misuses of this technology, especially for personal glory, power, or wealth.

The State should to invest in in its young people and their education as we approach the time when gene editing will be a part of their existence. We should teach young people not only about bioscience, but also about the art or science of making choices.

Lois Lowry, panel member and author of award-winning books on the Holocaust, dystopian futures and poetry, began her presentation by explaining that as a fiction writer, she lives in a world of nuance and metaphor. A world quite different from scientists. Ms. Lowry next spoke about her book, *The Giver*, which is set in an undated future time and in a place that is seemingly utopian – there is no war, no poverty, no discrimination, no illness, no conflict, no politics. The protagonist is a young boy living in a safe and well managed community, who eventually realizes that things are ominously missing from his world – there is no literature, no music, no art. The central question raised by this novel is central to the work of this panel: What sacrifices or trade-offs are required to develop a society free of problems? Ms. Lowry asked the panel to consider Giuseppe Verdi's *Requiem*. He could not have written the work if he had never experienced grief. The musicians and performers could not perform the music if they did not know grief. The audience, if they had never mourned, might be able to listen to *Requiem*, but would not really hear it. Is the loss of music too high a trade-off for freedom from grief? The same is true of gene editing. It is an amazing technology that can enhance our lives, health and future. But what losses, dangers and tradeoffs lurk within the use of this technology? Ms. Lowry noted that the speakers who preceded her had reminded the panel of some of the dangers that might be involved. She admitted that she cannot pretend to answer the question posed of all presenters: "What should the State of Maine do or consider with regard to gene-editing technology over the next five years or over the next generation?" Instead, she advised the State to invest in its young people and their education as we approach the time when gene editing will be a part of their existence. We should teach them not only about bioscience, but also about the art or science of making choices. There will always be blurred, murky areas with no right or wrong answers. The type of world we live in will depend on the seriousness with which they, and we, answer those questions.

[25] A copy of Mr. Hennessey's testimony in support of LD 1771 may be accessed from the Legislature's website through the following link: http://www.mainelegislature.org/legis/bills/getTestimonyDoc.asp?id=10001129.

The State should invest in education and the growth of the biotechnology sector, which will encourage young people both to move to the State and to remain here.

Marcques Houston, the panel member representing persons under 30 years of age, also began by sharing that he lacks experience or training in genetics. He attended Colby College, majoring in English and American Studies. As a result, he approaches the issues raised by genome-editing technologies through the lens of books and creative fiction pieces. Mr. Houston explained that his studies focused on science fiction, which often includes themes involving eugenics and the creation of an ideal human. He noted though, that the "what if?" of science fiction has now become the "what now?" as a result of CRISPR and similar technologies. Mr. Houston gave an example of a recent work of fiction, *Upgrade* by Blake Crouch, that grapples with many of the questions raised by advances in gene editing. One powerful theme from the book is that one can't sacrifice humanity to save humanity. The book also emphasizes that greed can lead one in the wrong direction, a sentiment he noted that Dr. Doudna, one of the scientists awarded the Nobel Prize in Chemistry for developing the CRISPR/Cas9 system, has also expressed. Mr. Houston advised the panel that regulation of gene-editing technology is necessary to prevent these technologies from causing harm to people, the climate and the world we live in. He believes researchers should focus on how this technology can be used positively, such as to cure diseases and to reduce climate change. Society must ensure that marginalized people and people of color have access to these technologies. Finally, Mr. Houston encouraged the State to invest in education and to promote the growth of the biotechnology sector here in Maine, which will help encourage young people both to move to the State and to remain here.

D. Fourth Meeting – October 19, 2022[26]

The panel's fourth meeting on October 19, 2022 began with panel member introductions and an overview of the agenda for the day, which included a review of information provided by Legislative staff in response to questions raised by panel members at the third meeting as well as a presentation related to the topic of gene editing and the humanities, which the speaker had been unable to present during the third meeting, followed by presentations focused on the topic of gene editing in systems and institutions and an opportunity for panel members to discuss and adopt recommendations to the Legislature.

1. Information Gathered in Response to Information Requests

After panel member introductions, Legislative staff-oriented panel members to the following information, which had been gathered at the direction of the panel co-chairs in response to questions raised by panel members at the third meeting:

- Information submitted via email by Katherine Lafferty of the Broad Institute regarding Maine's existing genetic counselor workforce and the current challenges to insurance coverage for genetic counseling services in the State. (A copy of Ms. Lafferty's email is included in Appendix F.);
- Information submitted via email by Molly Bogart, Director of Government Relations for the Maine Department of Health and Human Services, regarding MaineCare coverage for the cost of clinical trials, genetic testing and genetic counselor services. (A copy of Ms. Bogart's email is included in Appendix F.);

[26] A recording of the October 19th meeting is available at the following link: https://legislature.maine.gov/Audio/#209?event=86412&startDate=2022-10-19T09:00:00-04:00.

- Excerpts from the *Maine Learning Results: Parameters for Essential Instruction*, the State's parameters for essential teaching and learning for public school students in pre-Kindergarten through grade 12, focusing on the State's Life Sciences strand within the Science, Technology, and Engineering standards;[27]
- A chart from the National Institutes of Health's National Human Genome Research Institute of state laws that expand upon the protections provided by the federal Genetic Information Nondiscrimination Act of 2008[28] and the full text of Florida Statute §627.4301 (2022),[29] which prohibits life, long-term care and disability insurers from engaging in specific forms of genetic discrimination; and
- A memorandum prepared by legislative staff providing further information on the Legislative apology to and creation of a scholarship fund for the descendants of former residents of Malaga Island. (A copy of this memorandum is included in Appendix J.)

1. Additional Presentation related to Gene Editing and the Humanities

The panel next heard from Dwayne Tomah, panel member and member of the Passamaquoddy Tribe at Sipiyak, who had been invited but was unable to present during the portion of the third panel meeting focused on Gene Editing and the Humanities. Mr. Tomah began by explaining that he and other members of the Indian tribes within the State want to learn more about the potential uses of emerging genome-editing technologies that enable scientists to make specific changes to the DNA of human cells and other organisms. Mr. Tomah emphasized the crucial importance of making decisions regarding genome-editing technology that are moral, ethical and honest. While indigenous populations want to embrace this new technology and are honored to have their voices included in the panel's discussions, they have concerns grounded in the deplorable manner in which they have historically been treated by the State. To illustrate his point, Mr. Tomah shared a video recording of Dennis Saddleman reading his poem "Monster," which describes the trauma he experienced when he was sent to a residential school designed to eradicate his connection to his tribal culture at a young age.[30] The discussion between Mr. Tomah and other panel members that followed the video centered on how to build trust and relationships as science and society embarks on this new technological path. The discussion touched upon the importance of ensuring equitable access to this powerful new medical tool, providing outreach and education of tribal members, the benefits of collaboration between the State and tribal members to share historical, societal and scientific expertise, and the importance of autonomy over genetic data. All panel members expressed their joint desire to build better relationships, increase collaboration, and learn from the lessons of history in order to avoid repeating the atrocities of the past.

While indigenous populations want to embrace this new technology and are honored to have their voices included in these conversations, they have concerns grounded in the deplorable manner in which they have historically been treated by the State.

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[27] The Maine Learning Results: Parameters for Essential Instruction are codified in Chapter 132 of the rules adopted by the Maine Department of Education and can be accessed through the following link: https://www.maine.gov/sos/cec/rules/05/chaps05.htm. The excerpt focusing on the life sciences strand that was distributed to panel members is posted on the panel's website at the following link: https://legislature.maine.gov/doc/9126.

[28] "Genome Statute and Legislation Database," Genome.gov (National Human Genome Research Institute, August 3, 2020), https://www.genome.gov/about-genomics/policy-issues/Genome-Statute-Legislation-Database. (Search for "other lines of insurance nondiscrimination" under "Topic" and "enacted" under "Bill Status".)

[29] *See* Fla. Stat. §627.4301 (2022), https://www flsenate.gov/Laws/Statutes/2022/627.4301 (accessed Sept. 7, 2022).

[30] Dennis Saddleman, "Powerful Poem Captures Residential School Survivor's Experience," CBCnews, October 1, 2022, https://www.cbc.ca/player/play/2079043651723.

2. Gene Editing in Systems and Institutions

After Mr. Tomah's presentation, the panel heard from the following slate of presenters, who possess a variety of perspectives and expertise regarding gene editing in systems and institutions:

- Brian Whitney, President of the Maine Technology Institute
- Dana O'Brien, President of FocusMaine
- Joan Ferrini-Mundy, Ph.D., University of Maine System Vice Chancellor for Research & Innovation and President of the University of Maine and the University of Maine at Machias
- Lon Cardon, Ph.D., President and CEO of The Jackson Laboratory

A focus on the biotechnology sector is both warranted and strategic: The number of jobs within Maine in the biotechnology sector has increased dramatically by 42% over the last five years, and the average annual wage for Maine jobs in this sector was just under $109,000.

Brian Whitney began his presentation by explaining that the Maine Technology Institute is a unique public-private partnership designed to help catalyze innovation in Maine. MTI focuses on diversifying and growing Maine's technology within seven technology sectors, including biotechnology. Mr. Whitney noted that a recent report issued by the Bioscience Association of Maine illustrates why the State's focus on this sector is both warranted and strategic. There are approximately 500 establishments engaged in the life sciences sector in Maine and those entities employ nearly 10,000 people. The number of jobs within Maine in this sector increased dramatically by 42% over the last five years, and the average annual wage for Maine jobs in this sector was just under $109,000. Federal research granting institutions and private equity investors have also significantly increased their investments within the Maine biotechnology sector over the past few years. Despite these advances, there are still areas for improvement, specifically in the number of patents developed in Maine and the State's level of spending on higher education research and development. Maine's ten-year economic development strategy, developed in 2019, recommends that Maine continue to invest in research and development to support innovation in the private and nonprofit sectors and that the State should utilize its strengths and abundant natural resources to grow and diversify its economy by developing new and innovative ways to leverage those resources. Mr. Whitney believes that Maine's life science sector can, and will, help Maine achieve these attainable goals through continued innovation and sustained growth. He shared an example of a recent conditional funding award granted by MTI to a Cambridge-based life sciences firm specializing in genetics and genomics, which will offer emerging companies a turnkey lab space and office space as well as a very impressive list of laboratory equipment to be shared among the tenants. (A copy of Mr. Whitney's remarks is included in Appendix K.)

Dr. Joan Ferrini-Mundy next provided the panel with an education and research perspective on fostering a vibrant biotechnology sector in the state. She identified three important factors that will assist Maine in achieving this goal: strong curricular preparation of pre-Kindergarten through grade 12 students in all STEM areas; enhanced awareness of and exposure to STEM career choices for pre-Kindergarten through grade 12 students; and expanded options and student retention in STEM career pathways and postsecondary programs. While progress has been made, students within the University of Maine System face ongoing challenges, including a need for instruction in developmental mathematics and time management and study skills. Dr. Ferrini-Mundy described the wide variety of programs that the system has created to cultivate primary and secondary students' interest in STEM college and careers as well as several innovative and exciting new programs that the system has implemented that have enhanced undergraduate students' exposure to, and thus their interest in, bioscience research and data analytics. She also explained that the university's Maine Center for Research in STEM Education conducts research, leads graduate education and professional development, and builds community partnerships to improve evidence-based STEM education for pre-Kindergarten through grade 12 educators both in Maine and beyond. Dr. Ferrini-Mundy concluded her remarks by recommending that the State continue to foster a vibrant biotechnology sector by: supporting investments in the University of Maine System; maintaining rigorous standards for pre-Kindergarten through grade 12 Maine students and educators; and investing in hands-on pre-Kindergarten through grade 12 student and educator learning opportunities within the biosciences. (A copy of Dr. Ferrini-Mundy's presentation is included in Appendix K.)

The State should continue to foster a vibrant biotechnology sector by supporting investments in the University of Maine System; maintaining rigorous standards for elementary and secondary science education; and investing in hands-on student and educator learning opportunities within the biosciences.

The State should not only educate the public about science, but also enhance workforce and business opportunities centered on science to help society meet the pressing challenges currently facing our planet, our health and well-being and our food system.

Dana O'Brien opened his presentation by explaining that FocusMaine is a private-sector led economic development organization that seeks both to accelerate the growth of Maine's highest potential industries, including biotechnology, and to promote workforce opportunities across all industries. He then urged the State to embrace science as society confronts pressing monumental challenges to our planet, our health and well-being, and our food systems. The State must not only educate the public about science, but also enhance workforce and business opportunities centered on science to meet these urgent societal needs. Mr. O'Brien reminded the panel that genome editing is just one of many biotechnologies in use today and suggested that the State should invest in biotechnologies and data analytics more broadly. He also recommended that Maine capitalize on the opportunity presented by recent reports that demonstrate that the demands for new research facilities and enterprises placed on other geographic areas typically known as centers for biotechnology, such as Boston-Cambridge, have outpaced those areas' existing biomanufacturing infrastructure and workforce capacities. He noted that the State has quality existing life science infrastructure that we can build upon, including the State's universities, community colleges and private industry scientific institutions. He advised the State to invest in education, workforce and business development as it focuses on growing the State's biotechnology sector. (A copy of Mr. O'Brien's remarks is included in Appendix K.)

Dr. Lon Cardon reminded the panel that gene editing has transformed basic research. Before the development of this technology, the field of medical genetics was passive: scientists waited until they observed a disease or cluster of symptoms and then began the lengthy process of uncovering its potential genetic underpinnings in an effort to develop treatments. Gene-editing technologies have dramatically changed that process, allowing scientists to create thousands of genetic variants and examine their effects. In addition, when scientists in the past discovered that a rare genetic disease was caused by the inability of the patient's "broken" gene to produce an essential gene product, perhaps an enzyme, they developed processes to manufacture that gene product in a laboratory and inject it into the patient. The next generation of therapies, known as gene therapies, were designed to deliver a therapeutic copy of the affected gene to operate alongside the patient's own broken gene. New therapeutic gene editing, by contrast, will allow scientists to precisely and directly repair the patient's own defective gene. In the future, this technology may also enable scientists to render a permanent change to the patient's broken gene that can be passed on to new generations, which, if safe and effective, is about as good as it can get. Dr. Cardon also highlighted The Jackson Laboratory's Rare Disease Translational Center, which has worked with dozens of rare disease foundations and their associated research teams to generate custom mouse models of rare conditions using CRISPR/Cas9 and other new gene-editing methods in order to lay the groundwork for new therapeutic interventions. It is now expanding its focus to include working with pharmaceutical companies to conduct pre-clinical test of new therapeutics. Accordingly, Dr. Cardon suggested that the panel recommend the appointment of a scientist like Dr. Cat Lutz, vice president of the Center, to the State's soon-to-be-created Rare Disease Advisory Council. He also recommended that the State increase its investments in genetics education and teacher professional development to prepare students both to pursue careers in this field and to be the consumers of precision therapeutics and other products developed and implemented using gene-editing technology. Relatedly, he asked the panel to support recommendations that increase access to teacher professional development in genomics, which combines genetics and computer sciences to enable data-intensive research in one or many genomes. Increasingly, genetics research is performed using only computational methods, demonstrating the need to grow the State's digitally capable workforce. Finally, he reminded the panel that investments in education and teacher professional development must be accompanied by parallel investments in the State biosciences economy; otherwise, Maine's support of STEM education will increasingly benefit other states. (A copy of Dr. Cardon's remarks is included in Appendix K.)

The State should increase access to teacher professional development in genomics, which combines genetics and computer sciences to enable data-intensive research in one or many genomes.

IV. Recommendations

At co-chair Senator Claxton's suggestion, the panel agreed that it would not include any recommendation in the report unless it garnered the support of all panel members present at the time[31] when it was finally considered.[32] Accordingly, each of the following recommendations represents the panel's consensus about the appropriate path for Maine in this new era of genome-editing technology.

Genetic Literacy and Workforce Development

Recommendation A. To affirm the importance of genetics, genomics and related technologies, including data science, the Maine Department of Education should:

[31] Dr. Amy Belisle explained that, in her role as a member of the Executive Branch, she would abstain from weighing in on whether the recommendations should be adopted.

[32] When a draft of the report was circulated to all panel members, no panel member objected to any of the consensus recommendations that had been adopted in that panel member's absence.

i. **Gather, assemble and aggregate more educational resources for educators teaching in these content areas.**

ii. **Explore ways to enhance professional development opportunities for pre-Kindergarten through grade 12 educators in the State.**[33]

Recommendation B. The University of Maine System, the Maine Community College System and the Maine Department of Education should jointly participate in a genetics education summit in order to:

i. **Enhance the connections between the State's higher education institutions and the pre-Kindergarten through grade 12 system, including the state's career and technical education system, regarding the teaching of genetics, genomics and related technologies.**

ii. **Consider how to develop and promote community-based education regarding genetics, genomics and related technologies outside of the formal education setting.**[34]

The panel's work demonstrates the myriad ways in which the recent evolution in genomics and gene-editing technologies has reshaped and will continue to shape bioscience research and medicine, natural resources industries, the environment and the State's economy. It also demonstrates the critical need for the Maine populace as a whole and the State's government and institutions to critically explore the ethical, legal, and social implications of this technology. Throughout the course of the panel's meetings, the medical professionals, academic researchers, industry leaders, ethicists, and other experts who appeared before the panel emphasized the importance or promoting awareness of and education regarding gene-editing technologies. Maine citizens faced with personal or public health crises cannot properly evaluate potential genomic medicine and related treatment options or decide whether to avail themselves of preventative health measures developed with novel genetic technologies unless they have a strong foundational understanding of genetics, genomics and related technologies. Similarly, the State's populace cannot engage in important conversations regarding whether and how society should proceed with gene-editing and related technologies and grapple with complicated bioethical and environmental issues related to these technologies without a firm foundation of scientific knowledge. Representatives from Maine's existing life sciences industries report that their growth depends on a highly educated and skilled workforce, with expertise not only in genetics but also in data science and analytics. The State will not be able to grow its life sciences economy and position itself as a future hub of genomic and gene-editing research, unless it invests additional resources in promoting genetics, genomics and data science education at all levels, from primary school through post-secondary and graduate school programs.

Given the importance of this topic, the panel developed a multi-pronged approach to enhancing education in gene-editing and related technologies. First, the panel has sent a letter to Commissioner of Education A. Pender Makin, encouraging the Department of Education to affirm the importance of primary and secondary education in genetics, genomics and related technologies by gathering educational resources to assist teachers as they teach these concepts to their students and enhancing professional opportunities for teachers on these topics. These technologies lie on the cutting edge of science, and many teachers may not have an up-to-date understanding of how these technologies work or the potential benefits and detriments of these technologies. Programs like The Jackson Laboratory's Teaching the Genome Generation have helped bridge that gap in educator knowledge and more teachers should be made aware of this and related programs. The panel has also sent a letter urging Maine's congressional delegation to advocate for

[33] Recommendation I was developed by consensus of panel members Claxton, Zager, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

[34] Recommendation J was developed by a consensus of panel members Claxton, Zager, Hymanson, Arata, Chessa, Hunnewell and Wray.

increased federal funding and grant opportunities to enhance professional development in genetics, genomics, data science and related technologies. This funding will help the State not only expand existing, successful teacher professional development programs to reach educators across the State but also develop new and innovative programs to augment the options currently available within the State.

Second, as part of its correspondence with Commissioner Makin, the panel recommended that she, Chancellor Dannel P. Malloy of the University of Maine System and President Dave Daigler of the Maine Community College System jointly convene and participate in a genetics education summit that will allow primary and secondary educators to tap into the expertise of Maine's post-secondary education system regarding genetics, genomics and related technologies. Educators at all levels have developed innovative programs designed both to spark students' interest in bioscience related fields and to prepare them to enter the competitive bioscience workforce, including the many programs described by University of Maine President Dr. Ferrini-Mundy during the fourth panel meeting and the biomedical research support program offered to high school students by the Hancock County Technical Center in part through a partnership with The Jackson Laboratory. The panel suggests that summit participants also consider whether to create new scholarship opportunities within genetics and related fields for indigenous and other populations that were disadvantaged and mistreated by unethical genetic research and eugenics policies in the past.

The genetics education summit should not focus solely on formal education settings, however. The panel urges summit participants to consider how to develop community-based education programs and resources in genetics, genomics and related technologies. As an initial step, summit participants should consider whether to conduct a baseline survey to assess public knowledge of and attitudes toward genetics, genomics and gene-editing technologies, including the public's view of the potential benefits of and its concerns about these emerging technologies. (Copies of these letters are included in Appendix M.)

Economic opportunities and workforce development

Recommendation C. The Department of Economic and Community Development should convene a statewide conference on genomic and gene-editing research.[35]

The panel was excited to learn about the cutting-edge genomic and gene-editing research being performed at the University of Maine, the Roux Institute, The Jackson Laboratory and other public and private institutions across the State. Existing and potential areas of future research that might be harnessed to benefit Maine span a broad spectrum, from the development of genomic medicines to treat patients with rare diseases; to the creation of sterile strains of gene-edited salmon to be grown by aquaculture facilities without risking the integrity of wild salmon; to the engineering of microorganisms that decrease the presence of phosphorous, heavy metals and other environmental pollutants in municipal and industrial wastewater. Maine's institutions of higher education and private industry have drawn hundreds of millions of grant dollars for bioscience research from the National Science Foundation, National Institutes of Health, Small Business Innovation Research and Small Business Technology Transfer Research programs and the State has invested millions of dollars in the biotechnology sector through the Maine Technology Institute and other innovative programs. Research conducted by the Bioscience Association of Maine (BioME)[36] reveals that these investments in the biotechnology sector were demonstrably

[35] Recommendation G was developed by consensus of panel members Claxton, Zager, Moore, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

[36] Bioscience Association of Maine, *Life Sciences in Maine: State of the Industry 2022*, https://biomaine.org/industry-impact/.

successful in catalyzing growth in this industry. Life science jobs grew by 42% in Maine over the past five years, far outpacing the State's 1% overall job growth and the growth in life sciences jobs across New England over the same time period. These occupations provide workers with significantly higher median hourly earnings than average workers in the State.

The panel has therefore written a letter to Commissioner Heather Johnson encouraging the Department of Economic and Community Development to harness the potential of existing and future research in genomic and gene-editing technologies and the benefits these technologies can bring to Mainers' health, Maine's agricultural and fishery industries and the Maine economy by convening a statewide conference on genomic and gene-editing research. (A copy of the letter is included in Appendix M.) Suggested topics for exploration by conference attendees include:

- Surveying the genomic and gene-editing research currently being performed in public and private institutions of higher education and in the private sector in the State;
- Developing methods to enhance research collaborations between the State's institutions of higher education and the private sector; and
- Grappling with and making recommendations regarding the ethical, legal, and social implications of genomic and gene-editing research, including data privacy issues.

Recommendation D. The Legislature should enact legislation directing the Maine Department of Agriculture, Conservation and Forestry to study both:

i. The current uses and applications of gene-edited organisms and gene-editing technologies in the State's agriculture and forestry industries, including the potential this technology may provide to enhance those industries in the future; and

ii. The impact that gene-editing technologies and gene-edited organisms may have on the State's organic farming industry – specifically, whether current state and federal legal and regulatory safeguards maintain the appropriate balance between the potential benefits of gene-editing technologies to non-organic farmers and the importance of preserving the integrity of organic farming methods and products.

The legislation should direct the department to submit a combined report or separate reports on these issues, including its findings and recommendations, to the joint standing committee of the 131st Legislature having jurisdiction over agriculture and forestry issues, which should be authorized to report out legislation related to the report.[37]

As previously described in Part III of this report, the panel learned a great deal about the potential applications of gene-editing technologies in Maine's agricultural and forestry industries. To mention just a few examples, published and emerging areas of research include:

- Engineering new strains of blueberries and other crops designed to resist drought and other potential effects of climate change;
- Engineering potatoes and other agricultural crops to increase crop yields and to enhance nutrient density, disease resistance and pest resistance without increased use of pesticides; and
- Engineering microorganisms that increase the efficiency of converting agricultural and forestry waste products into bioenergy.

[37] Recommendation H was developed by consensus of panel members Claxton, Zager, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

Experts also advised the panel on the potential benefits that gene-editing and related technologies provide in the field of conservation and biodiversity preservation, including by increasing the genetic diversity of threatened species, remediating degraded ecosystems and product replacement.

While the applications of gene-editing technology hold great promise for many of Maine's natural resource industries, concerns have arisen within Maine's important organic agriculture sector. The current federal regulatory framework for non-medical applications of technology relies on a complex network of oversight by the United States Department of Agriculture (which has regulatory oversight over new plants and organisms based on their plant-pest and noxious weeds risks; new products that are animal pests or that have the potential to cause disease in livestock; and new veterinary biologics), Federal Drug Administration (which regulates food, animal feed additives and human and animal drugs), and the Environmental Protection Agency (which regulates the use of all pant pesticides, including pesticides incorporated in plant genomes through genetic engineering).[38] While these regulations govern many aspects of the intrinsic safety of the products of biotechnology, the United States Department of Agriculture's Natural Organic Program places the impetus on organic farmers and food producers to take steps to ensure that the products they produce and sell under an "organic" label have not been produced or handled using certain genetic engineering technologies that "would not be possible under natural conditions." (See Staff memorandum on the types of genetic engineering prohibited in organic farming and processing in Appendix H.) Although applicable regulations do not penalize organic farmers and processers for the inadvertent cross-contamination of their products by genetically modified organisms, organic farmers remain concerned that the health and safety risks to humans and the environment of emerging genetic technologies has not be fully assessed and that potential cross-contamination may lead to the eradication of natural or heirloom varieties of agricultural products. The organic industry thus generally urges that the government take a more precautionary approach toward novel technologies, especially before these products are released into the environment.

For the foregoing reasons, the panel recommends that the Legislature direct the Department of Agriculture, Conservation and Forestry to closely examine both the potential benefits and the potential detriments of gene-editing technologies and gene-edited organisms to Maine's agriculture and forestry industries, including the organic farming industry. After studying these issues in depth, the Department should be directed to report its findings and recommendations to the Legislature, which may then enact legislation that will allow Maine to harness the potential of these new technologies in a safe and responsible way.

Cost of and Access to Genomic Medicine

The high costs and potential benefits of genomic medicine emerged as one of the primary themes during the first meeting's presentations on the topic of Gene Editing in Health and Bioscience. The phrase "genomic medicine" refers to a panoply of therapies and medical treatments that includes, but is not limited to, both gene therapy and gene editing. Gene-editing technology stands as a powerful tool through which physicians and research geneticists have begun developing therapies that provide targeted corrections to genetic mutations carried by patients who suffer from single-gene disorders. Yet, because this is an emerging field of medicine and many of these diseases are rare, there are only small patient populations available to share the cost of developing such treatments. For example, the panel learned that a new and exciting genomic medicine treatment for Spinal Muscular Atrophy (SMA), a rare but devastating progressive genetic motor neuron disease, costs approximately $2 million. It is crucial that policymakers establishing policies affecting patients' access to this treatment and other types of genomic

[38] U.S. Library of Congress, Congressional Research Service, *Agricultural Biotechnology: Overview, Regulation, and Selected Policy Issues*, by Genevieve K. Croft, R46737 (March 29, 2021), https://crsreports.congress.gov/product/pdf/R/R46737.

medicine weigh not only the exceedingly high cost of these treatments but also the toll that untreated disease can take on patients and their families.

Recommendation E. The Legislature should amend the statute establishing the Rare Disease Advisory Council to require that the Commissioner of Health and Human Services:

i. **Appoint at least one person whose rare disease is the result of a single-gene disorder, with preference given to a person who is eligible to participate in a clinical trial involving genomic medicine for that rare disease, when appointing the two members of the council who are over 18 years of age and who have had or who currently have a rare disease as described by 22 M.R.S. §1700-B(2)(L);**

ii. **Appoint at least one parent or guardian of a child whose rare disease is caused by a single-gene disorder, with preference given to the parent or guardian of a child who is eligible to participate in a clinical trial involving genomic medicine for that rare disease, when appointing the two members of the council who are parents or guardians of a child with a rare disease as described by 22 M.R.S. §1700-B(2)(M).**

Recommendation F. The Rare Disease Advisory Council should specifically address the financial burdens and potential benefits of genomic medicine as it completes its statutory duties, set forth in 22 M.R.S. §1700-B(5)(D) & (E), to distribute educational resources to providers and patients regarding treatment for rare diseases and to develop recommendations to improve patient quality of life and to provide services and reimbursement for such services.[39]

The Rare Disease Advisory Council, recently established by legislation enacted during the Second Regular Session of the 130th Legislature, provides an important forum for engaging in policy discussions regarding access to and the cost of genomic medicine. Although the council has not yet been formed, it is charged by law with advising the State's Commissioner of Health and Human Services and disseminating information to the public on issues related to rare diseases, which are defined to include any condition or illness affecting fewer than 200,000 persons in the United States.

Pursuant to 22 M.R.S. §1700-B(2), the Rare Disease Advisory Council will be comprised of 20 members appointed by the Commissioner of Health and Human Services, including medical professionals, insurance industry representatives, academic and biopharmaceutical company representatives, as well as:

> L. Two persons over 18 years of age who have had or currently have a rare disease; [and]
>
> M. Two parents or guardians who each have a child with a rare disease[.]

To achieve its statutory purposes, §1700-B(5) directs the council to perform a series of statutorily defined activities, including:

> D. Identify[ing] and distribut[ing] publicly available educational resources to providers of health care in order to foster recognition of symptoms of and treatment for rare diseases among patients of those providers; [and]
>
> E. Evaluat[ing] the systems for delivery of treatment for rare diseases in place in the State and develop[ing] recommendations to improve quality of life and to provide services and reimbursement for those services for persons with rare diseases;

[39] Recommendations C & D were developed by consensus of panel members Claxton, Zager, Moore, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

As it performs these duties, the panel recommends that the council specifically address the financial burdens and potential benefits of genomic medicine for Maine patients with rare diseases, their families and the State as a whole. To ensure that issues surrounding access to genomic medicine for rare diseases are given priority in council discussions, the panel further recommends that, when the Commissioner of Health and Human Services appoints two adults with a rare disease and two parents or guardians of a child with a rare disease to the panel, at least one adult and one parent or guardian be affected by a rare disease that is the result of a single-gene disorder, with preference given to an adult with a rare disease who is eligible to participate in a clinical trial involving genomic medicine and to the parent or guardian of a child who is similarly eligible for clinical trial participation.

The panel therefore sent a letter to Commissioner of Health and Human Services, Jeanne Lambrew, urging her to take these recommendations into consideration as she begins making appointments to the council and as the council commences its duties. (A copy of this letter is included in Appendix M.) The panel also suggests that the Legislature amend 22 M.R.S. §1700-B(2)(L) and (2)(M) to require continued appointments to the council of at least one adult patient with a rare disease that is the result of a single-gene disorder and at least one parent or guardian of a child whose rare disease is caused by a single-gene disorder, to ensure that the voices of patients with single-gene disorders and their families continue to be heard.

> **Recommendation G. In conducting its statutory duties, the Office of Affordable Health Care, established by 5 M.R.S. §3122, should examine not only historic drivers of health care costs but also future cost-drivers, such as genomic medicine, which may have large up-front treatment costs but might also dramatically improve the lives of patients with rare diseases and yield long-term cost savings for both patients and insurance carriers.[40]**

The panel similarly believes that the Office of Affordable Health Care, which was also established by the 130th Legislature but is not yet operational, provides a helpful forum for ensuring that State policies governing access to medicine, including health insurance policy, are not created without a careful consideration of the costs and benefits of genomic medicine. The office will be staffed by an executive director appointed by the Governor who operates independently under the general policy direction of both the joint standing committee of the legislature with jurisdiction over health coverage matters and a newly appointed Advisory Council on Affordable Health Care. Pursuant to 5 M.R.S. §1322(3), the office shall report at least annually to the Governor and to the Legislature "on matters affecting the cost of health care in the State" after engaging in specific statutorily prescribed duties, including:

> A. Analyz[ing] health care cost growth trends and correlation to the quality of health care;
>
> B. Analyz[ing] health care spending trends by consumer categories, payer type, provider categories or any other measurement that presents available data in a manner that may assist the legislative oversight committee in understanding health care cost drivers, health care quality and utilization trends, consumer experience with the health care system or any other aspect of the health care system;
>
> C. Monitor[ing] the adoption of alternative payment methods in this State and other states that foster innovative health care delivery and payment models to reduce health care cost growth and improve the quality of health care;
>
> D. Based upon the data obtained and the analysis pursuant to paragraphs A to C, develop[ing] proposals for consideration by the legislative oversight committee on potential methods to improve the cost-efficient provision of high-quality health care to the residents of this State; [and]

[40] Recommendation E was developed by consensus of panel members Claxton, Zager, Moore, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

> E. Based upon the data obtained and the analysis pursuant to paragraphs A to C, conduct[ing] a systemic review of the health care system and develop proposals to improve coordination, efficiency and quality of the health care system[.]

As it carries out these duties, the panel recommends that the office examine not only traditional drivers of health care costs but also newly emerging cost drivers including genomic medicine, which may involve large up-front treatment costs but might also dramatically improve the lives of patients with rare diseases and generate long-term costs savings for both patients and insurance carriers. Because the Governor has not yet selected an executive director for the Office of Affordable Health Care, the panel has sent a letter to the Governor's Senior Policy Advisor on health matters, copying members of the advisory council, urging the office to implement this recommendation. (A copy of this letter is included in Appendix M.)

Access to high-quality genetic counseling services

> **Recommendation H. The Legislature should enact legislation directing the Department of Professional and Financial Regulation to conduct a sunrise review and report back to the Legislature on the benefits and drawbacks of establishing a professional licensing program for genetic counselors in the State. In conducting this evaluation, the department should examine not only the statutory sunrise review criteria set forth in 32 M.R.S. §60-J but also the impact licensure may have on insurance coverage, the availability of genetic counseling services to Maine patients across the State and the quality of genetic counseling services in the State.[41]**

The services provided by genetic counselors have assumed increasing importance in recent years as the availability and scope of genetic testing and gene-editing technologies has increased dramatically and the role of genetics in health care continues to grow. According to the National Society of Genetic Counselors, genetic counselors possess specialized graduate-level degrees and experience in both medical genetics and counseling and serve an important role in the health care system by "empower[ing] patients and their families with information, guidance and emotional support to help them understand their family history, evaluate genetic testing options," including by explaining the benefits and limitations of specific genetic tests, "and make informed choices based on test results."[42] According to Katherine Lafferty, a clinical genetic counselor from the Broad Institute, Maine has approximately 15 clinical genetic counselors, the majority of whom serve patients in the greater Portland area. Rural Mainers are vastly underserved, requiring them to wait up to a year to obtain genetic counseling appointments. (See the information provided by Ms. Lafferty in Appendix F.)

Because genetic counseling services are not directly covered by most health insurance providers in the State, including MaineCare, it is difficult for medical practices, clinics and hospitals to invest in genetic counseling services and attract providers to the State. Ms. Lafferty and Lisa Harvey-McPherson, Vice President of Government Relations at Northern Light Health, urged the panel to recommend that the State adopt a professional licensure program for genetic counselors. (See the email correspondence from Ms. Lafferty and Ms. Harvey-McPherson in Appendix F.) While licensure is not a guarantee for insurance payment, licensing programs increase the likelihood that private and public insurance will cover these services. A professional licensing program may also increase patient outcomes and satisfaction by ensuring that genetic counselors practicing in the State possess the required education and expertise to provide high-quality services to patients. For these reasons, the panel recommends that the Legislature

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[41] Recommendation F was developed by consensus of panel members Claxton, Zager, Moore, Hymanson, Arata, Chessa, Lowry, Hunnewell, Wray, Bateman and Mulhern.

[42] "Genetic Counseling Key Messages and Interview Tips," National Society of Genetic Counselors, November 10, 2022, https://www.nsgc.org/Portals/0/x221014%20Genetic%20Counseling%20Key%20Messages%20and%20Interview%20Tips.docx.

direct the Department of Professional and Financial Regulation to conduct a sunrise review and report back to the legislature regarding the benefits and drawbacks of implementing a genetic counseling licensing program. In conducting this evaluation, the department should examine not only the statutory sunrise criteria for sunrise reviews set forth in 32 M.R.S. §60-J, but also should specifically examine the impact licensure may have on insurance coverage, the availability of genetic counseling services to Maine patients across the State and the quality of genetic counseling services in the State.

Genetic Privacy and Discrimination

Recommendation I. The State should make every effort possible to avoid engaging in activities similar to the historical wrongs that the State perpetrated on Malaga Island as well as the historical wrongs committed during the eugenics movement. [43]

Panel members are deeply troubled by the manner in which science, specifically the emerging field of genetics, was used to justify discrimination, forced sterilization and genocide in the United States and in other countries (most notably Nazi Germany) during the end of the nineteenth century and first half of the twentieth century. Respected academics and intellectuals cited the heritability of traits as they encouraged people or groups who they viewed as possessing positive traits to have more children while also arguing that people or groups who they viewed as having negative traits should be discouraged or prevented from reproducing. Eugenicists succeeded in co-opting the power of the government to implement their discriminatory policies, including through the establishment of state institutions for individuals considered to be intellectually or morally inferior and the enactment and use of forced sterilization laws. Related philosophies were also used to justify conducting sometimes horrific medical experiments on minority and disadvantaged populations and efforts to eradicate indigenous cultures through, for example, the residential school movement.

As Kate McBrien, the Maine State Archivist, explained to the panel, the State's forced eviction of the entire multi-race and economically poor community living on Malaga Island in 1912 serves as an alarming illustration of the power that eugenics, discrimination and racism held in the State at that time. After forcibly removing residents, the State took title to the island to prevent residents from returning. The State also institutionalized several island residents, including all of the members of a single family, in the then newly established Maine School for the Feeble Minded, where some of them were sterilized. (See Ms. McBrien's presentation in Appendix I.)

Panel members strongly recommend that the State make every effort possible to learn from its past mistakes and to avoid repeating the atrocities perpetrated by society and the government, partly in the name of science, on Malaga Island and through the eugenics movement more broadly.

Recommendation J. The Legislature should reconsider whether to adopt a state law prohibiting discrimination based on genetic information in coverage and premium-setting decisions by insurers that issue life, disability, long-term care and related types of insurance.[44]

Recent advances in genetics and genomics have led to dramatic increases in the scope of potentially helpful medical information available through genetic testing. Genetic testing can reveal the existence of multiple mutations throughout a person's genome, some of which may have been characterized by scientists as associated with an increased risk of developing certain types of diseases. Patients whose

[43] Recommendation A was developed by consensus of panel members Claxton, Zager, Hymanson, Arata, Chessa, Hunnewell and Wray.

[44] Recommendation B was developed by consensus of panel members Claxton, Zager, Hymanson, Arata, Chessa, Hunnewell and Wray.

close relatives have a history of certain types of cancer, for example, may wish to obtain genetic testing to determine whether they carry the relevant cancer-associated genetic mutations. Patients who carry such mutations may choose to engage in more frequent cancer screenings or may choose to change aspects of their lifestyle (diet, exercise, etc.) that will reduce their risk for developing that type of cancer.

During the course of its meetings, the panel learned that patients are sometimes wary of pursuing genetic testing because they worry that insurance companies may learn about their genetic test results and either deny coverage or impose higher premiums based on a suspected predisposition to disease revealed by those results. Although the Genetic Information Nondiscrimination Act of 2008 protects individuals from discrimination on the basis of genetic information by health insurers in making coverage, underwriting or premium-setting decisions, this federal law does not apply to life insurers, disability insurers or long-term care insurers. Several states have taken steps to fill this void by enacting laws prohibiting genetic discrimination within these additional categories of insurance. When similar legislation was introduced in the 130th Legislature by panel member Representative Patty Hymanson, however, the insurance industry expressed its strong concern that the legislation could lead to adverse selection. Adverse selection occurs when an individual has access to information that increases the individuals' risk of mortality or morbidity, causing the individual to be more likely to seek insurance coverage, but does not share that information with the insurance company. Because the insurance company does not know about the test results, it assigns a lower risk of disease to and sets lower premiums for the individual than it might if it had access to the genetic testing information. As a result, individuals who do not have a known heightened risk of disease may end up subsidizing the costs of insuring individuals with an elevated genetically-linked susceptibility to disease.

While many panel members felt strongly that the State should prohibit genetic discrimination by life insurance, disability insurance and long-term care insurance, panel members also understood the potential concerns raised by insurers. The panel ultimately agreed to recommend that the 131st Legislature carefully reconsider whether the adoption of legislation extending the federal law's protections against genetic discrimination to life, disability and long-term care insurance will protect Mainers from genetic discrimination without unduly burdening Maine's overall pool of insurance customers. The panel believes that a bill identical to the majority committee amendment to Representative Hymanson's bill from the 130th Legislature, LD 1085, *An Act Relating to the Use of Genetic Information for Insurance Purposes*, would provide a useful vehicle for collecting public hearing testimony and for engaging in these deliberations.

APPENDIX A

Authorizing Legislation: Resolve 2021, c. 177

APPROVED
MAY 3, 2022
BY GOVERNOR

CHAPTER
177
RESOLVES

STATE OF MAINE

IN THE YEAR OF OUR LORD

TWO THOUSAND TWENTY-TWO

H.P. 1322 - L.D. 1771

Resolve, To Establish the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Preamble. Whereas, genome-editing technologies, such as clustered regularly interspaced short palindromic repeats, also known as CRISPR, CRISPR-associated protein 9, also known as Cas9, and gene drive, have been discovered and dramatically refined in recent years, enabling innumerable opportunities around the world to inexpensively edit the genetic code of any living thing; and

Whereas, many deadly human diseases could be eradicated with genome-editing technology, thereby saving countless lives, immeasurable heartache and large health care expenditures in perpetuity; and

Whereas, a genetic alteration in a species of marine, terrestrial or airborne animal, plant, fungus, protozoan, bacteria or virus could rapidly alter the natural beauty, ecology, security and economy of Maine; and

Whereas, Maine's higher education system and technology sector can further position themselves as leaders in innovation and ethical implementation, reaping enduring benefits for Maine citizens, through the use of these technologies; and

Whereas, there are significant ethical, social and legal considerations for genome editing in humans and other species; and

Whereas, in the past, scientific ideas have been used in the implementation of and to promote eugenics programs and other forms of oppression; and

Whereas, throughout history living organisms have been used as weapons, and genome-editing technologies create new security needs in the endless effort to protect the people of Maine and the United States; and

Whereas, genome editing has the potential to fundamentally improve or diminish our health, our natural environment, our social fabric and our economy; and

Whereas, the pace of innovation is accelerating and over the next several years Maine can capitalize on the changes in our world that genome editing can bring about or risk being left behind; now, therefore, be it

Sec. 1. Panel established. Resolved: That the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, referred to in this resolve as "the panel," is established.

Sec. 2. Panel membership. Resolved: That, notwithstanding Joint Rule 353, the panel consists of 14 members who are residents of this State and appointed as follows:

1. Two members of the Senate appointed by the President of the Senate from the party holding the largest number of seats in the Senate. In making the appointments pursuant to this subsection, the President of the Senate shall endeavor to appoint members having expertise in areas or backgrounds listed in section 6;

2. One member of the Senate appointed by the President of the Senate from the party holding the 2nd largest number of seats in the Senate. In making the appointment pursuant to this subsection, the President of the Senate shall endeavor to appoint a member having expertise in areas or backgrounds listed in section 6;

3. Two members of the House of Representatives appointed by the Speaker of the House from the party holding the largest number of seats in the House. In making the appointments pursuant to this subsection, the Speaker of the House shall endeavor to appoint members having expertise in areas or backgrounds listed in section 6;

4. One member of the House of Representatives appointed by the Speaker of the House from the party holding the 2nd largest number of seats in the House. In making the appointment pursuant to this subsection, the Speaker of the House shall endeavor to appoint a member having expertise in an area or background listed in section 6;

5. One member who is a bioethicist, appointed by the President of the Senate;

6. One member who is a person under 30 years of age at the time of the appointment, appointed by the Speaker of the House;

7. One member who is from a federally recognized Indian nation, tribe or band in the State, appointed by the President of the Senate;

8. One member who is a fiction author or poet whose published works have explored the humanity of all people, appointed by the Speaker of the House;

9. One member who is a person living with a single-gene disorder, such as cystic fibrosis, Duchenne muscular dystrophy or sickle cell anemia, appointed by the President of the Senate;

10. One member having expertise in an area or a background listed in section 6, appointed by the President of the Senate; and

11. Two members having expertise in areas or backgrounds listed in section 6, appointed by the Speaker of the House.

The Presiding Officers shall invite the participation on the panel of the Chief Justice of the Supreme Judicial Court or the chief justice's designee and the Governor or the Governor's designee.

Sec. 3. Chairs. Resolved: That the first-named Senate member is the Senate chair and the first-named House of Representatives member is the House chair of the panel.

Sec. 4. Vacancies. Resolved: That Legislators may serve as members on the panel only while they are members of the Legislature. The Presiding Officers shall fill any vacancy according to the requirements of section 2, subsections 1, 2, 3 and 4.

Sec. 5. Appointments; convening of panel. Resolved: That all appointments must be made no later than 30 days following the effective date of this resolve. The appointing authorities shall notify the Executive Director of the Legislative Council once all appointments have been completed. After appointment of all members, the chairs shall call and convene the first meeting of the panel. If 30 days or more after the effective date of this resolve a majority of but not all appointments have been made, the chairs may request authority and the Legislative Council may grant authority for the panel to meet and conduct its business.

Sec. 6. Duties. Resolved: That the panel shall study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology. In performing its duties under this section, the panel shall solicit the testimony, advice or participation of persons having the following backgrounds or areas of expertise:

1. Ethics;
2. Clinical medicine caring for children;
3. Clinical medicine caring for adults;
4. Public health;
5. Bioscience research;
6. Environmental protection;
7. Forestry;
8. Agriculture or aquaculture;
9. Fishing;
10. State economics;
11. Tourism, business or commerce;
12. Military or security affairs;
13. University of Maine System or Maine Community College System;
14. Living with a single-gene disorder, such as cystic fibrosis, Duchenne muscular dystrophy or sickle cell anemia, or a parent or guardian of a person living with such a single-gene disorder;
15. Hospital or hospice chaplaincy; and
16. History of race, ethnicity or eugenics.

Sec. 7. Staff assistance. Resolved: That the Legislative Council shall provide necessary staffing services to the panel, except that the Legislative Council staff support is not authorized when the Legislature is in regular or special session.

Sec. 8. Report. Resolved: That, no later than November 2, 2022, the panel shall submit a report that includes its findings and recommendations, including suggested legislation, to the joint standing committee of the Legislature having jurisdiction over health and human services matters. The joint standing committee of the Legislature having jurisdiction over health and human services matters is authorized to report out legislation to the First Regular Session of the 131st Legislature.

Sec. 9. Outside funding. Resolved: That the panel shall seek funding contributions to fully fund the costs of the study. All funding is subject to approval by the Legislative Council in accordance with its policies. If sufficient contributions to fund the study have not been received within 30 days after the effective date of this resolve, no meetings are authorized and no expenses of any kind may be incurred or reimbursed.

Sec. 10. Appropriations and allocations. Resolved: That the following appropriations and allocations are made.

LEGISLATURE

Study Commissions - Funding 0444

Initiative: Allocates funds for the costs to the Legislature of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State.

OTHER SPECIAL REVENUE FUNDS	**2021-22**	**2022-23**
Personal Services	$0	$1,320
All Other	$0	$1,930
OTHER SPECIAL REVENUE FUNDS TOTAL	$0	$3,250

APPENDIX B

Membership List: Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Resolve 2021, ch. 177

Membership List

Name	Representation
Senator Ned Claxton – Chair	Member of the Senate
Representative Samuel Zager – Chair	Member of the House
Senator Joe Baldacci	Member of the Senate
Senator Marianne Moore	Member of the Senate
Representative Patricia Hymanson	Member of the House
Representative Amy Arata	Member of the House
Frank Chessa	Bioethicist
Marcques Houston	Person under 30 years of age
Dwayne Tomah	Member of a federally recognized Indian nation, tribe or band in the State
Lois Lowry	Fiction author or poet whose published words have explored the humanity of all people
Abbie Hunnewell	Person living with a single-gene disorder
Charles Wray	Member having expertise or a background in bioscience research
Hon. Christina Riley	Parent of a person living with a single-gene disorder
Dana Waring Bateman	Member having expertise or a background in bioscience research
Hon. Richard Mulhern	Chief Justice or Chief Justice's designee
Amy Belisle	Governor or Governor's designee

APPENDIX C

List of Background Materials

Genome-editing Technology Advisory Panel Background Materials

Legislative History of Advisory Panel Legislation:

LD 1771, Resolve, To Establish the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

- Bill tracking and testimony: available here
- Finally passed as: Resolve 2021, Ch. 177

Similar legislation proposed in the prior session:

LD 1601, Resolve, To Establish an Advisory Panel To Study the Implications of Genome-editing Technology for the Citizens of the State

- Bill tracking and testimony: available here

Selected Background Materials:

Date	Item (or author, title, publication info., date)	Notes
2000	Mark S. Frankel & Audrey R. Chapman, Human Inheritable Genetic Modifications: Assessing Scientific, Ethical, Religious and Policy Issues (2000)	Report prepared for the American Association for the Advancement of Science (AAAS) and made available online by AAAS.
February 2017	National Academies of Sciences, Engineering & Medicine, Human Genome Editing: Science, Ethics and Governance, The National Academies Press (2017).	Consensus study report of the: *Committee on Human Gene Editing: Scientific, Medical, and Ethical Considerations*
February 2017	WNYC Studios, Radiolab Podcast: Update: CRISPR (2019)	A closed-captioned version of the podcast is available here.
2018	Nuffield Council on Bioethics, Genome editing and human reproduction: social and ethical issues (2018)	Also available on the website are: • a shorter guide to the report; and • a separate document listing the key report recommendations
2019	Joanna Buchthal, et al., Mice Against Ticks: an experimental community-guided effort to prevent tick-borne disease by altering the shared environment, Phil. Trans. R. Soc. B, **374**: 20180105 (2019)	
January 2019	George Q. Daley, et al., After the Storm – A Responsible Path for Genome Editing, NEJM.org (2019)	Full-text access requires either registration or a subscription.

March 2019	Wonder Collaborative, Human Nature (2019)	The trailer for this documentary is available here.
March 2019	Eric Lander, et al., Comment: Adopt a moratorium on heritable genome editing, 567 Nature 165 (2019)	
December 2019	Further Consolidated Appropriations Act, 2020, Pub. L. No. 116-94	*See* Division B, Title VII, Section 745, which appears on page 120 of the PDF file.
September 2020	National Academy of Medicine, National Academy of Sciences & The Royal Society, Heritable Human Genome Editing, The National Academies Press (2020)	Consensus study report of the: *International Commission on the Clinical Use of Human Germline Genome Editing*
October 2020	The Royal Swedish Academy of Sciences, Press Release: The Nobel Prize in Chemistry 2020	Also available on this website are: • Genetic scissors: a tool for rewriting the code of life (popular science background) • A Tool for Genome .333Editing (scientific background)
October 2020	Francois Baylis, et al., Human Germline and Heritable Genome Editing: The Global Policy Landscape, 3 CRISPR J. 365 (2020)	A Supplementary Appendix listing policies in countries around the world, with links to original policy documents, is posted online and frequently updated.
December 2020	John M. Conley, et al., A New Governance Approach to Regulating Human Genome Editing, 22 N.C. J.L. & Tech. 107 (2020)	
2021	Masafumi Omori, et al., Targeted mutagenesis of ***CENTRORADIALIS*** using CRISPR/Cas9 system through the improvement of genetic transformation efficiency of tetraploid highbush blueberry, 96 J. of Horticultural Science & Biotech., 153 (2021)	Article abstract (full text access requires a subscription).
March 2021	Walter Isaacson, The Code Breaker: Jennifer Doudna, Gene Editing, and the Future of the Human Race, Simon & Schuster (2021)	Nonfiction book available for purchase and at several public libraries in the State.

May 2021	International Society for Stem Cell Research, ISSCR Guidelines for Stem Cell Research and Clinical Translation: Version 1.0, (2021)	*See* Section 1: Fundamental Ethical Principles.
July 2021	World Health Organization Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing, Human Genome Editing: A Framework for Governance (2021)	Also available on the website are: • A separate document outlining the Committee's recommendations; and • A shorter position paper summarizing the framework for governance and recommendations
March 2022	U.S. Food & Drug Administration, Human Gene Therapy Products Incorporation Human Genome Editing: Draft Guidance for Industry (2022)	*See* Introduction and Background on pp. 3-4.
June 2022	Casey Crownhart, This CRISPR pioneer wants to capture more carbon with crops, MIT Technology Review (2022)	
Ongoing	U.S. Food & Drug Administration, Feed Your Mind: Agricultural Biotechnology *See also* How GMOs Are Regulated in the United States	Originally created in March 2020, this website is an FDA education initiative "to help consumers better understand genetically engineered foods, commonly called GMOs or genetically modified organisms."

Background Materials Proposed After First Meeting of Advisory Panel:

- **Article:** *Her Discovery Changed the World. How Does She Think We Should Use It?*, The New York Times (Aug. 15, 2022), available at: https://www.nytimes.com/interactive/2022/08/15/magazine/jennifer-doudna-crispr-interview.html. (A subscription is required to access this article, which profiles Dr. Jennifer Doudna, who won the Nobel Prize in Chemistry for helping develop CRISPR gene-editing technology.)

- **Documentary:** New Zealand Geographic documentary about Duchenne Muscular Dystrophy entitled ***The Death Gene***: https://www.nzgeo.com/video/the-death-gene/

- **Documentary**: Directed by Renee Tajima-Peña about the sterilization of Mexican immigrant mothers in Los Angeles in the 1960s and 1970s entitled ***No Más Bebés***: a preview of the

documentary is available at https://www.pbs.org/independentlens/documentaries/no-mas-bebes/ and the film's website is available at: http://www.nomasbebesmovie.com/film.

- **Book:** Siddhartha Mukherjee, *The Song of the Cell: An Exploration of Medicine and the New Human* (Simon & Schuster 2002) – this book will be published on October 25, 2022 and is described by the publisher as "an exploration of medicine and our radical new ability to manipulate cells." Information about the book is available here, on the publisher's website: https://www.simonandschuster.com/books/The-Song-of-the-Cell/Siddhartha-Mukherjee/9781982117351.

Background Materials Proposed During or After Second Meeting of Advisory Panel:

- **Article:** Zhang, Y., Pribil, M., Palmgren, M. *et al.*, *A CRISPR way for accelerating improvement of food crops*, 1 Nature Food 200–05 (March 3, 2020), available at https://doi.org/10.1038/s43016-020-0051-8 (A subscription or institutional access is required to access this article, which provides an overview of CRISPR technology, its application to food crops, and implications of regulatory policy for deploying the technology in the developing world.)

- **Book**: Kent H. Redford & William M. Adams, *Strange Natures: Conservation in the Era of Synthetic Biology* (Yale University Press 2021). The publisher's website is available here: https://books.google.com/books?id=rnkwEAAAQBAJ&printsec=frontcover&source=gbs_ViewAPI&hl=en#v=onepage&q&f=false.

- **Article:** Kent H. Redford & William M. Adams, *COP26: Synthetic Biology and Nature-Based Solutions* (Yale University Press; Nov. 4, 2021), available at: https://yalebooks.yale.edu/2021/11/04/cop26-synthetic-biology-and-nature-based-solutions/.
    - Note: this article was published before May 28, 2020, when the USDA's Animal and Plant Health Inspection Service published its final rule revising the Sustainable, Ecological, Consistent, Uniform, Responsible, and Efficient (SECURE) rule. The SECURE rule regulates the movement (including environmental release) of genetically engineered organisms that are likely to pose plant pest risks.

- **Opinion / Insight Piece:** Matthew J. Kan & Jennifer A. Doudna, *Treatment of Genetic Diseases With CRISPR Genome Editing*, 328 JAMA 980 (Sept. 13, 2022), available at: https://jamanetwork.com/journals/jama/fullarticle/2796264.

- **Advertisement:** Representative Hymanson has asked us to share the following advertisement from Boston Children's Hospital about novel new genetics-based diagnostic and treatment tools: https://www.nytimes.com/paidpost/boston-childrens/flipping-the-diagnostic-playbook.html.

Background Materials Proposed During or After Third Meeting of Advisory Panel:

- **Articles on Florida laws:**
    - Jeff Schmerker, *New Florida Law Protects Genetic Testing Info. from Life, Disability, and Long-Term Care Insurance Policy Decisions*, Integrated DNA Technologies' Community Blog Post (Oct. 26, 2020), available at:

https://www.idtdna.com/pages/community/blog/post/new-florida-law-protects-genetic-testing-info-from-life-disability-and-long-term-care-insurance-policy-decisions

- Aldo M. Leiva, Baker Donelson, *New Florida Genetic Privacy Law Imposes Criminal Penalties* (Oct. 14, 2021), available at https://www.bakerdonelson.com/new-florida-genetic-privacy-law-imposes-criminal-penalties.

- Mark Rothsetin and Kyle Brothers, *Banning Genetic Discrimination in Life Insurance – Time to Follow Florida's Lead*, 383 N. England J. Med. 2099 (Nov. 26, 2020), available at https://www.nejm.org/doi/pdf/10.1056/NEJMp2024123 (Full-text access to this article requires either registration or a subscription.)

- **Community Engagement Research Model**: Organizing Committee for Assessing Meaningful Community Engagement in Health & Health Care Programs & Policies, *Assessing Meaningful Community Engagement: A Conceptual Model to Advance Health Equity through Transformed Systems for Healthi,* NAM Perspectives, Commentary, National Academy of Medicine (Feb. 14, 2022), available at https://doi.org/10.31478/202202c.

- **Maine Bioscience Day** information: https://biomaine.org/event/me-bioscience-day-2022/

- **Bioscience Association of Maine (BioME)'s Industry Report.** The report, entitled *Life Sciences in Maine: State of the Industry 2022* is available as a free download on the following webpage: https://biomaine.org/industry-impact/.
  - The following article also describes the results of this report: Vivien Leigh, *Life Sciences are Maine's Fastest-Growing Industry*, News Center Maine (Oct. 14, 2022), available at https://www.newscentermaine.com/article/money/business/life-sciences-are-maines-fastest-growing-industry-business-money-maine-health-technology-local/97-745728a5-2f32-44fc-bce6-531d588f840d.)

- **Article:** Jennifer Couzin-Frankel, *As gene testing surges, lawsuits aren't far behind*, Science (May 7, 2019), available at: https://www.science.org/content/article/gene-testing-surges-lawsuits-arent-far-behind#:~:text=doi%3A%2010.1126/science.aax9577

- **Article:** Scott P. McGrath, *et al.*, *Legal Challenges in Precision Medicine: What Duties Arising From Genetic and Genomic Testing Does a Physician Owe to Patients?*, Frontiers in Medicine, Vol. 8, Article 663014 (July 26, 2021), available at: https://www.frontiersin.org/articles/10.3389/fmed.2021.663014/full.

- **Legal research resource**: University of Minnesota & Vanderbilt University Medical Center, LawSeq: Mapping & Shaping the Law of Genomics (website with searchable databases of federal laws, state laws and secondary legal materials relevant to genomics), available at https://lawseq.umn.edu/ (last visited Oct. 18, 2022).

APPENDIX D

Introductory Presentations by Dana Waring Bateman, genetics educator

- *Genome Editing and CRISPR* (Aug. 17, 2022)
- *What is a gene? What are germ cells, somatic cells, and stem cells? How are CRISPR therapies delivered?* (Sept. 7, 2022)

Genome Editing and CRISPR

August 17th, 2022
Maine State House

Dana Waring Bateman – danabateman@gmail.com

Adapted for PBS LearningMedia in partnership with WETA for use with:

KEN BURNS PRESENTS
THE GENE
AN INTIMATE HISTORY

2022

WETA

New advances in genetics are becoming personal

Learning about our DNA can offer:

- Insights about our health, behavior, family history and other traits.
- Information with personal, social and familial impact.
- Improved health care.
- Complicated questions about how to use genetics personally and as a society.
- Challenges about how to ensure fairness and equity in genetic advances.

Technology out of the lab and into the world: Rapid, portable DNA analysis is on the horizon

2002

Applied Biosystems 3730 DNA Analyzers

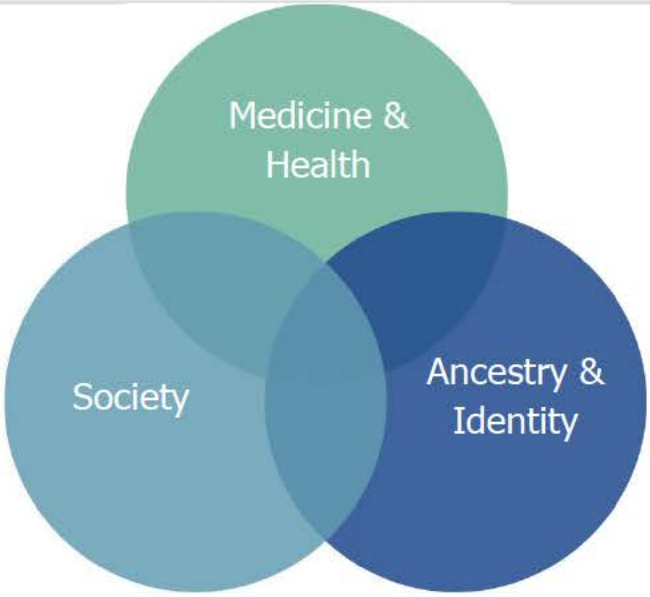
Jurvetson, CC BY 2.0

2019

MinION DNA Sequencer

NASA

How is personal genetics affecting real people?



Genetic testing:

Solving medical mysteries
& connecting families

2022 Update: there are now over 130 patients and the condition has a name – Hao-Fountain Syndrome.

Personal choices based on genetic information

Actor Angelina Jolie reveals she chose to undergo a double mastectomy.

Jolie had a genetic test and found she carried a mutation in the BRCA1 gene. Doctors estimated there was a very high chance she would get breast cancer.

Image: Gage Skidmore, CC BY 2.0

Genetics can determine safety and effectiveness of certain medications

CYP2D6 gene, involved in converting codeine to morphine - 100 known variants and counting!

- **Typical metabolizer** - medication works as expected
- **Slow metabolizer** - gets very little effect from the medicine
- **Rapid metabolizer** - standard dose of medication can be lethal

Adapted from http://www.ensrmedical.com/pharmacogenetics/

Genetic testing during pregnancy: More information and at an earlier date

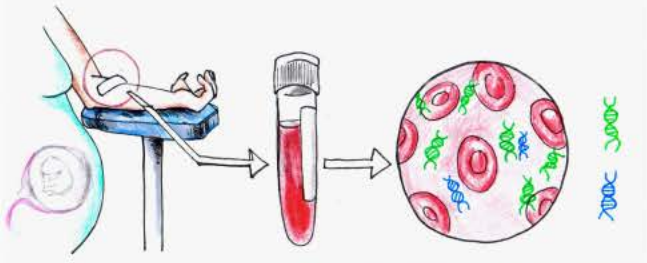
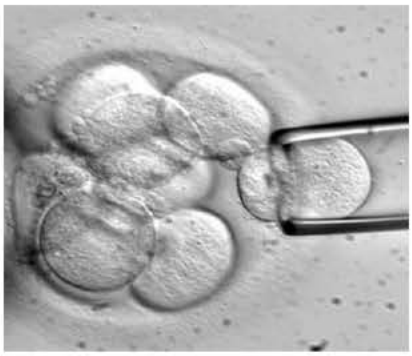


Image: Personal Genetics Education Project (Patricia Hautea)

- **Non-invasive prenatal testing (NIPT)** involves analyzing a blood sample taken from a pregnant person to learn about traits of the fetus.
- This test looks at small pieces of DNA that circulate in the pregnant person's bloodstream.
- Some of these pieces of DNA come from cells of the placenta that broke open and can reveal information about the developing fetus.

Reproductive technology opens the door to analyze embryos for certain genetic traits

- Eggs, harvested from ovaries, can be combined with sperm in a petri dish in a process called in-vitro fertilization (IVF).
- After 3-5 days of development, one or more cells can be removed from the embryo and assessed for certain traits in a process called pre-implantation genetic diagnosis (PGD).



Biazotti et al. (2015), CC BY 4.0

"Golden State Killer" suspect arrested in April 2018

The search was aided by a DNA match from a database created to find relatives for family history/genealogy hobbyists.

[GED match] **Tools for DNA and Genealogy Research**

Photo via Sacramento county policy department

Forensic genetic genealogy in use in Maine

Maine man to stand trial for 1993 Alaska murder after genetic genealogy tied him to crime scene DNA

Share

Updated: 6:48 PM EDT Apr 29, 2021

Infinite Scroll Enabled

Phil Hirschkorn
Political Reporter

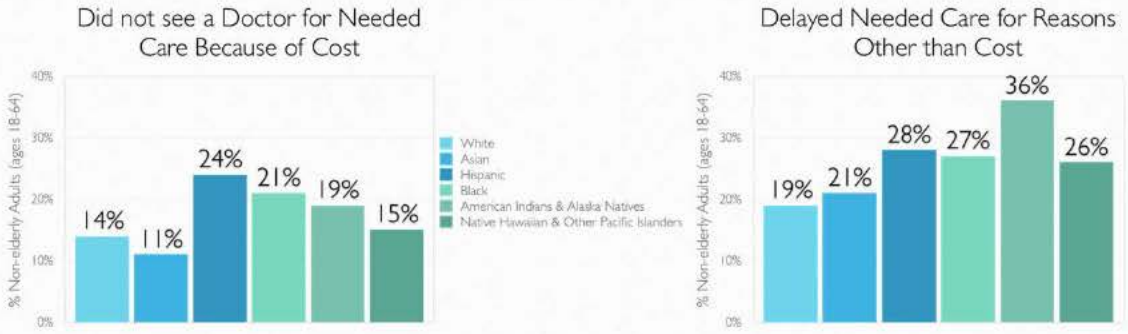
A key step is comparing crime scene DNA with DNA profiles accessible from two popular consumer DNA testing sites, GEDmatch and FamilyTreeDNA, which currently store a combined 1.6 million profiles.

"We reverse engineering people's family tree," Moore said. "But we're not actually accessing anyone's DNA file or DNA code. All we're getting is a list of matches, which is generated through comparing the unknown crime-scene DNA to all those DNA files of the people that are participating in those two databases."

https://www.wmtw.com/article/maine-man-to-stand-trial-for-1993-alaska-murder-after-genetic-genealogy-tied-him-to-crime-scene-dna/36292803

Healthcare access is key to personal genetics being shared fairly

Percent of Non-elderly Adults in US who did not Receive or Delayed Care in past 12 months by Race/Ethnicity (2014)



Data from Kaiser Family Foundation analysis of CDC Behavior Risk Factor Surveillance System (2014)

Diné (Navajo Nation) setting their own terms: Making decisions regarding their participation in genetic research

dbking, CC-BY 2.0

"To us, any part of ourselves is sacred. Scientists say it's just DNA. For an Indian, it is not just DNA, it's a part of a person, with a deep religious significance. It is part of the essence of a person."
– Frank Dukepoo, Hopi geneticist

Erin Blakemore, *History* (Nov 3, 2017)

Navajo Nation reconsiders ban on genetic research

Tribal leaders are developing a policy for genetic research and data sharing, potentially ending a 15-year moratorium

Sara Reardon, *Nature* (Oct 6th, 2017)

Proposed policy included power for Nation to:

- Approve or reject research proposals
- Maintain control over the samples

Where does CRISPR fit in to this conversation?

What is **CRISPR**?

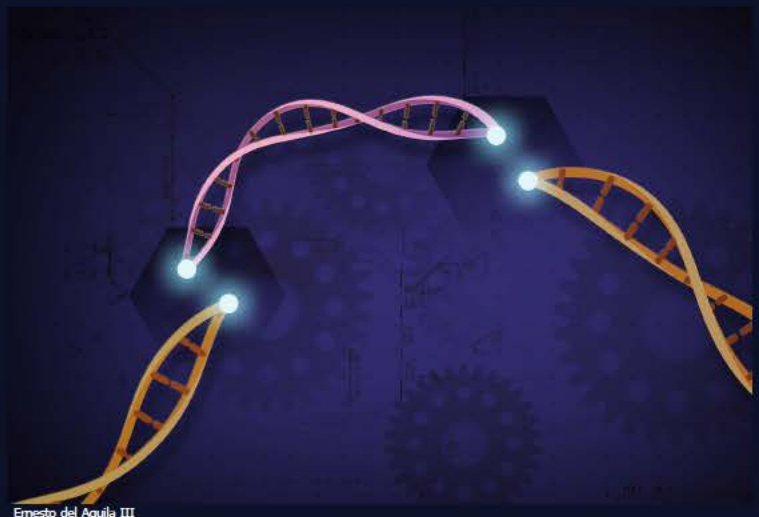
(Clustered regularly interspaced short palindromic repeats)

A genome editing technique that:

- Targets a specific section of DNA
- Makes a precision cut/break at the target site
- Can do one of two things:
  - Makes a gene non-functional
  - Replace one version of a gene with another

What are the potential applications of CRISPR to human health?

What is genome editing?



Ernesto del Aguila III

Genome editing is making a change to an organism's DNA at a specific site.

CRISPR is a genome editing tool that can be used to make these specific DNA changes.

Genetic testing during pregnancy: More information and at an earlier date

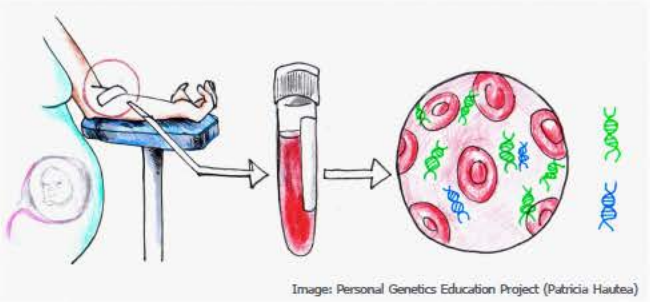


Image: Personal Genetics Education Project (Patricia Hautea)

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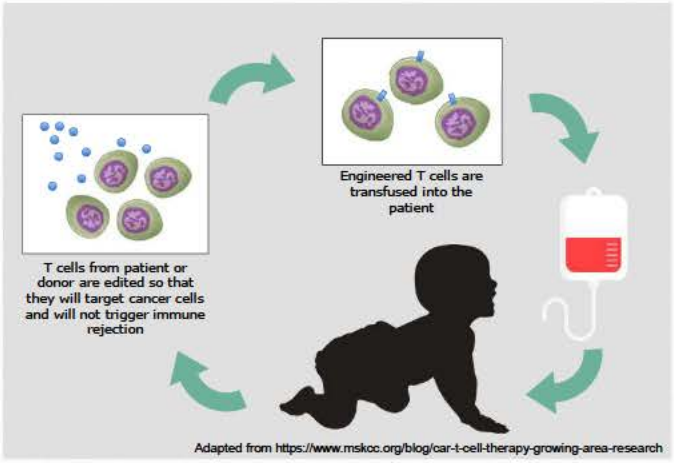


The possibility of changing your DNA

Layla Richards: the first success of genome editing-based gene therapy

Do Now: Discuss the following with the person (or people) next to you:

Imagine you've been offered a deal from a genomics company. You can get a free genome sequence – an analysis of all your DNA that includes a report of your ancestry, traits and a medical profile. The medical profile tells you about diseases for which you have a low risk of getting, and also those you have a high risk of getting.

Are you interested? Why or why not?

Do Now: Discuss the following with the person (or people) next to you:

For the first 100 volunteers, the company is offering to "correct" several of the disease-related genes found by the analysis. Imagine this were a very new procedure approved by the government for safety, but without a great deal of long-term study.

Would you volunteer for this added service?

(This service is not currently available and will not be in the near future, so use your imagination.)

Watch this clip from *The Gene: An Intimate History*

https://ny.pbslearningmedia.org/resource/9795d5d3-2b03-4d50-b193-ae6eb918392f/genome-editing-and-crispr/

What is Gene Therapy?

Research is on-going to develop gene therapies for conditions such as cystic fibrosis and sickle cell disease

Image: Blausen.com staff, CC BY 3.0

Image: Wellcome Images, CC BY-NC-ND 2.0

Researchers have used genome editing to cure a type of liver disease in adult mice

Image: Lex McKee, CC BY-NC 2.0

This type of research is an important step towards developing new gene therapies in humans

Image: Maidiel1, CC BY-SA 4.0

Might genome editing one day lead to a solution to the global shortage of organs?

Should genome editing be used in the hopes of reducing malaria?

Image: YoHandy, CC BY-NC-ND 2.0

> Philos Trans R Soc Lond B Biol Sci. 2019 May 13;374(1772):20180105.
doi: 10.1098/rstb.2018.0105.

Mice Against Ticks: an experimental community-guided effort to prevent tick-borne disease by altering the shared environment

Joanna Buchthal [1], Sam Weiss Evans [2 3 4], Jeantine Lunshof [1 5 6], Sam R Telford 3rd [7], Kevin M Esvelt [1]

Affiliations + expand

PMID: 30905296 PMCID: PMC6452264 DOI: 10.1098/rstb.2018.0105

Free PMC article

Abstract

Mice Against Ticks is a community-guided ecological engineering project that aims to prevent tick-borne disease by using CRISPR-based genome editing to heritably immunize the white-footed mice (Peromyscus leucopus) responsible for infecting many ticks in eastern North America. Introducing

https://pubmed.ncbi.nlm.nih.gov/30905296/#:~:text=Mice%20Against%20Ticks%20is%20a,ticks%20in%20eastern%20North%20America.

Image: The National Academies, CC BY-NC-SA 2.0

2018: Claims of CRISPR being used to edit genomes of twin girls

"New eugenics" and "designer babies": What are the underlying concerns?

Eugenics lurk in the shadow of CRISPR

Robert Pollack, *Science* (May 22, 2015)

What's the difference between genetic engineering and eugenics?

Robert Gebelhoff, *Washington Post* (February 22, 2016)

Designer babies aren't futuristic. They're already here.

Are we designing inequity into our genes?

Laura Hercher, *MIT Technology Review* (October 22, 2018)

Scientists confront the ghost of eugenics

Amy Marcus, *Wall Street Journal* (August 17, 2018)

American eugenics movement

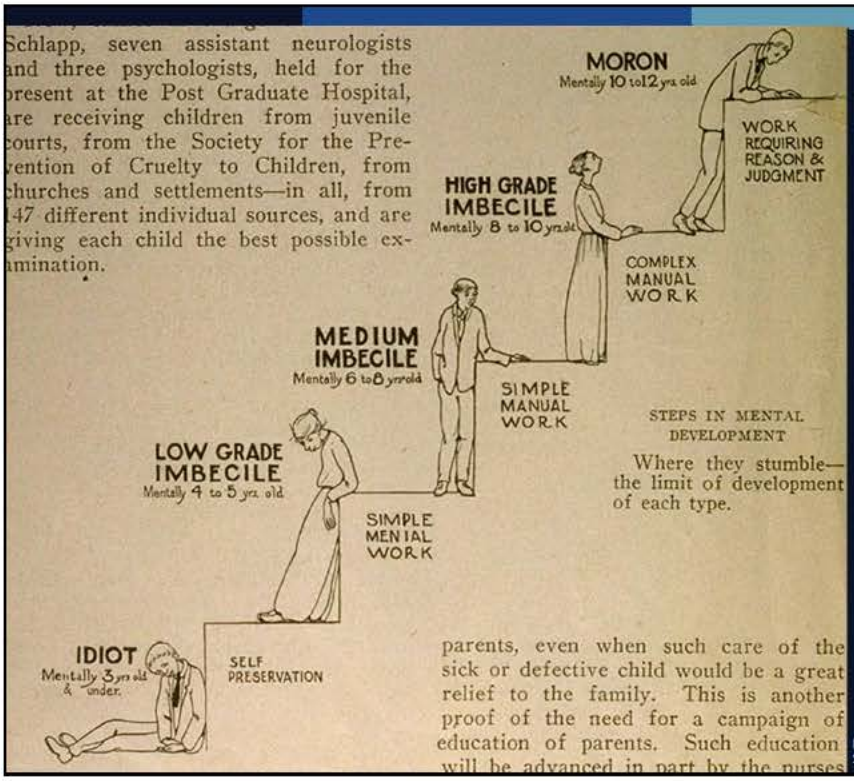
- Began in US in early 1900s
- Social movement that worked to "improve" society by encouraging or discouraging people to have babies
- Promoted reproduction by people or groups with "positive" qualities
- Discouraged or sometimes stopped reproduction by groups with "negative" qualities
- State and Federal laws addressing issues ranging from immigration to mandatory sterilization

OCTOBER 29, 1926.

HEREDITY IS BIG PROBLEM

Home for Feeble-Minded Is Filled With Those Whose Parents Were Not as Carefully Selected as Dairymen Breed Cattle

The Women's Auxiliary to the dairymen, who met in the roof garden of the Hotel Vermont yesterday afternoon, listened to talks by Miss Sara M. Holbrook, department of education, U. V. M., and Prof. H. F. Perkins of the University, head of the zoology department.



Schlapp, seven assistant neurologists and three psychologists, held for the present at the Post Graduate Hospital, are receiving children from juvenile courts, from the Society for the Prevention of Cruelty to Children, from churches and settlements—in all, from 147 different individual sources, and are giving each child the best possible examination.

MORON
Mentally 10 to 12 yrs. old
WORK REQUIRING REASON & JUDGMENT

HIGH GRADE IMBECILE
Mentally 8 to 10 yrs. old
COMPLEX MANUAL WORK

MEDIUM IMBECILE
Mentally 6 to 8 yrs old
SIMPLE MANUAL WORK

LOW GRADE IMBECILE
Mentally 4 to 5 yrs. old
SIMPLE MENTAL WORK

IDIOT
Mentally 3 yrs. old & under.
SELF PRESERVATION

STEPS IN MENTAL DEVELOPMENT

Where they stumble—the limit of development of each type.

parents, even when such care of the sick or defective child would be a great relief to the family. This is another proof of the need for a campaign of education of parents. Such education will be advanced in part by the nurses

Making the case for eugenics:

Arguing certain people are destined to become a "burden"

Photo: 1906. Source: American Philosophical Society, ERO, MSC77,Ser1,Box35: Trait Files

US Library of Congress

Supreme Court ruling: Buck v. Bell allows forced sterilization

"...society can prevent those who are manifestly unfit from continuing their kind... Three generations of imbeciles are enough."
-Justice Oliver Wendell Holmes, Jr.

Quote source: Buck v. Bell, 274 US 200 – Supreme Court 1927

Pedigrees used to justify sterilization

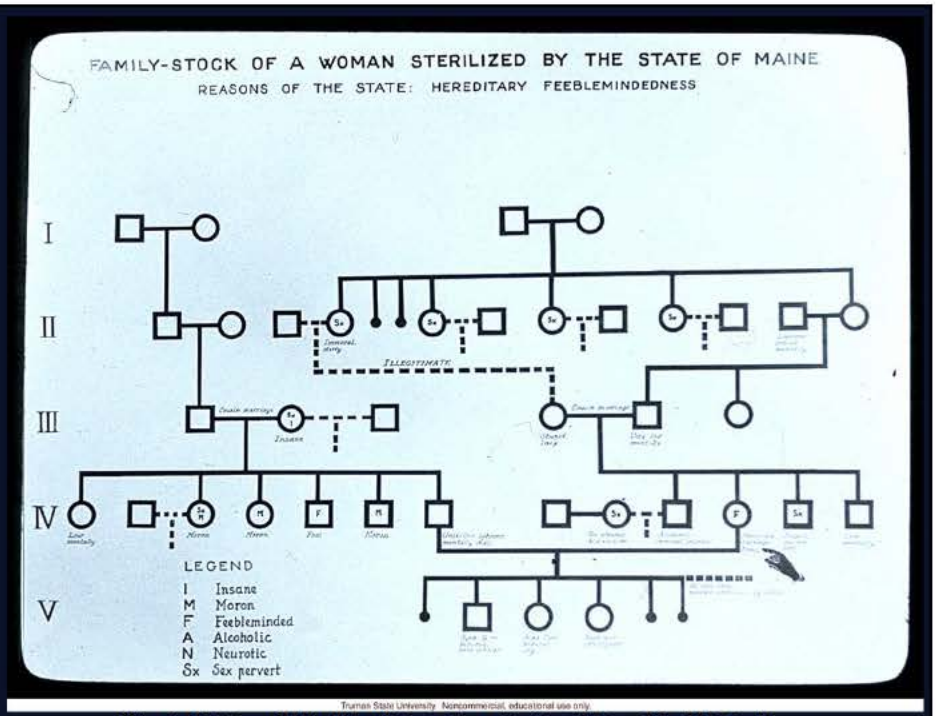


Photo: circa 1935. Source: The Harry H. Laughlin Papers, Truman State University, Lantern Slides, IBM Box,Box 10

Echoes of the past: Sterilization in the 2000s

Judge to inmates: Get sterilized and I'll shave off jail time

Derek Hawkins, *Washington Post* (July 21, 2017)

Following reports of forced sterilization of female prison inmates, California passes ban

Hunter Schwarz, *Washington Post* (September 26, 2014)

Many perspectives are needed to forge a path forward

Upcoming webinars in this series

Difference, not deficit: Reframing the conversation around genetics, deafness, and disability

CRIPSR has extensive medical and health implications – but what about other sectors of society?

How could genome editing impact our environment?

Cassava

Neil Palmer, CC BY-SA 2.0

Agriculture case study: Using genome editing to lower the toxicity of an important food crop – cassava.

Honeycreeper

USFWS – Pacific Region, CC BY-NC 2.0

Insect-borne disease case study: Using genome editing to engineer mosquitoes to prevent them from infecting Hawaiian honeycreepers with avian malaria.

Mammoth

Mammut, CC BY-SA 2.0

De-extinction and permafrost preservation case study: Using genome editing to bring back the woolly mammoth to help prevent thawing of permafrost.

Cassava

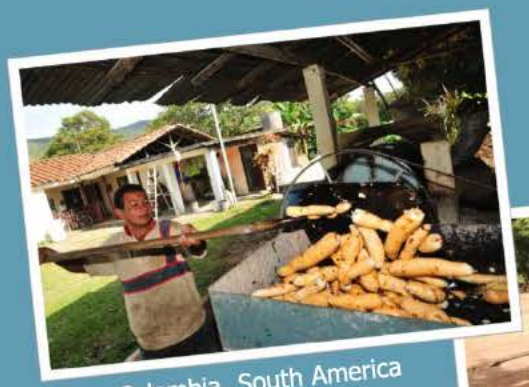
Do Now: Discuss the following with the person (or people) next to you:

You live in a rural village and your relatives are suffering from Konzo, a disease that causes paralysis. You rely on a plant called cassava as your main source of food. Cassava naturally produces a toxin. At high concentration, this toxin can make people sick with Konzo. However, soaking the cassava in water for a couple of days before eating it prevents this problem.

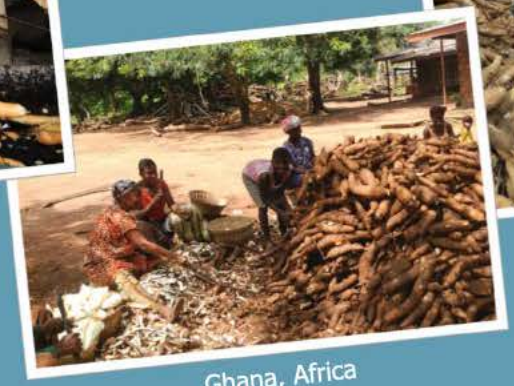
Scientists have proposed to genetically alter the cassava plant to make it less dangerous. You wonder whether providing a clean source of water, such as a well, to your village could be a better solution. What are the questions you have for the scientists about their plan?

Cassava

Cassava is an important food crop for over 800 million people worldwide



Colombia, South America



Ghana, Africa

Vietnam, Asia

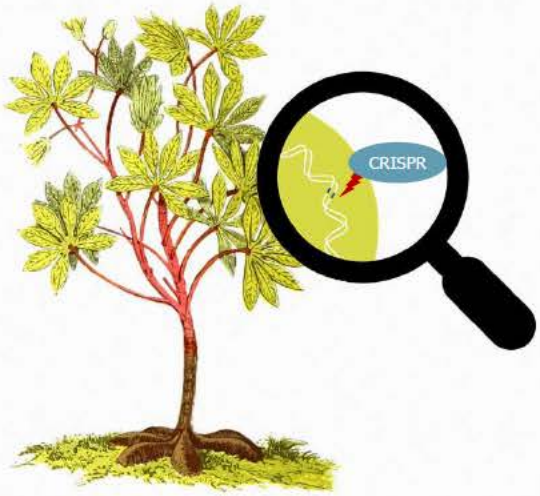
Cassava

Cassava can cause a disease called Konzo

- Cassava naturally produces a toxin, which is present at higher levels when the plant is grown in drought conditions.
- At high levels, this toxin can cause Konzo, a disease that leads to paralysis and can potentially be deadly.
- Soaking the cassava in water and eating a protein-rich diet can prevent Konzo and make cassava a safe source of food.
- Konzo is a disease of poverty, because poverty often limits access to water and a protein-rich diet.

Cassava

Genome editing of the cassava's DNA could be used to lower the plant's toxicity.



- Cassava has 2 genes that are responsible for the plant's toxic effects.
- CRISPR could be used to edit these genes to reduce the toxicity of cassava.

Schematic created by pgEd (Nadine Vincenten)

Cassava

Major questions and considerations

- Could genome editing negatively affect the plant's drought-tolerance, a very beneficial trait for many regions across the globe?
- Could genome editing of cassava make the plant more vulnerable to insects? If so, would farmers need to use pesticides to grow their crop?
- Will someone own the edited plants? What about the seeds?
- Should efforts in preventing Konzo lie with this genome editing approach? Or should the focus be on breaking the cycle of poverty? Might a combination of approaches be the best way forward?

Neil Palmer, CC BY-SA 2.0

This CRISPR pioneer wants to capture more carbon with crops

New research at Jennifer Doudna's institute aims to create faster-growing, carbon-hungry plants using the gene-editing tool.

By Casey Crownhart June 14, 2022

INNOVATIVE GENOMICS INSTITUTE

https://www.technologyreview.com/2022/06/14/1053843/carbon-capture-crispr-crop

Agricultural issues closer to home?

nature › horticulture research › review articles › article

Review Article | Open Access | Published: 01 January 2021

Can gene editing reduce postharvest waste and loss of fruit, vegetables, and ornamentals?

Emma N. Shipman, Jingwei Yu, Jiaqi Zhou, Karin Albornoz & Diane M. Beckles

Horticulture Research **8**, Article number: 1 (2021) | Cite this article

11k Accesses | **22** Citations | **54** Altmetric | Metrics

Abstract

https //www.nature com/articles/s41438-020-00428-4

Approximately 33% of the produce that is harvested is never consumed since these products naturally have a short shelf-life…This loss, however, could be reduced by breeding new crops that retain desirable traits and accrue less damage over the course of long supply chains.

New gene-editing tools promise the rapid and inexpensive production of new varieties of crops with enhanced traits more easily than was previously possible.

Agricultural issues closer to home?

AP U.S. News World News Politics Sports Entertainment Business Technology Health Science Oddities Lifestyle

Maine's blueberry crop faces climate change peril

By PATRICK WHITTLE June 5, 2021

SYSTEMATIC REVIEW article

Front. Sustain. Food Syst., 07 September 2021

Sec. Crop Biology and Sustainability

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Application of Gene Editing for Climate Change in Agriculture

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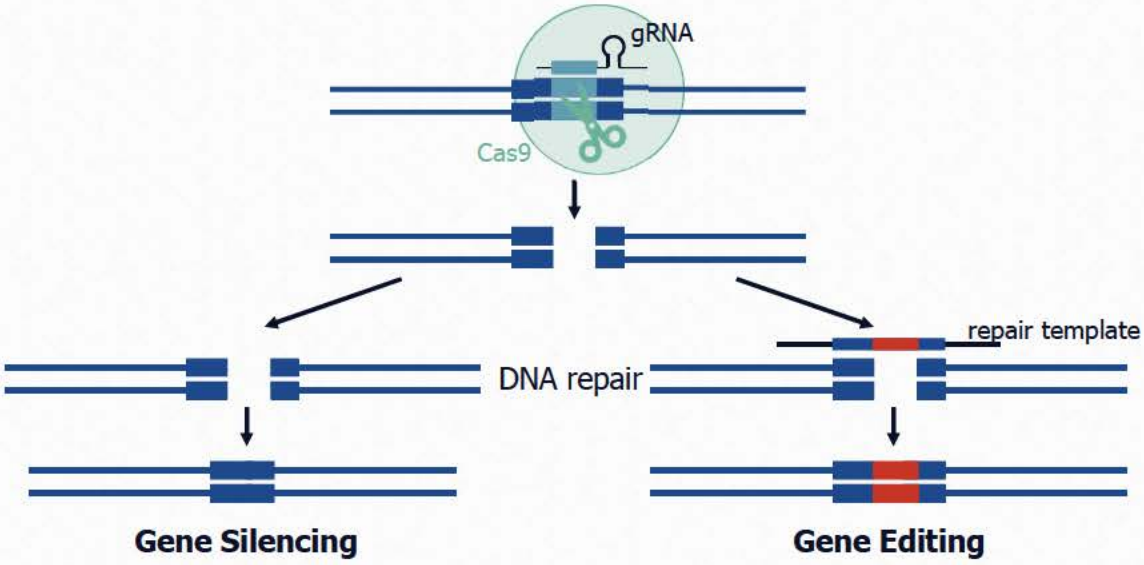
Mechanism of CRISPR gene editing system



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Slide 3: (left) "Riding Shotgun" by Steve Jurvetson (http://www.flickr.com/photos/jurvetson/57080968/, accessed Jan 25, 2016). Available under a Creative Commons Attribution 2.0 Generic license (https://creativecommons.org/licenses/by/2.0/).

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Slide 4: Personal Genetics Education Project (Patricia Hautea).

Slide 5: "Wanted" poster courtesy of Bo Bigelow, founder USP7 foundation (https://www.usp7.org/, accessed Oct 4, 2018).

Slide 6: "Angelina Jolie" by Gage Skidmore (https://www.flickr.com/photos/gageskidmore/4860509634/, accessed Jan 25, 2016). Available under a Creative Commons Attribution-ShareAlike 2.0 Generic license (https://creativecommons.org/licenses/by-sa/2.0/).

Slide 7: Adapted from http://www.ensrmedical.com/pharmacogenetics/

Slide 8: Personal Genetics Education Project (Patricia Hautea).

Slide 9: "8-cell human embryo, day 3" by ekem, Courtesy: RWJMS IVF Program (https://commons.wikimedia.org/wiki/File:Embryo,_8_cells.jpg, accessed Jan 13, 2017). Public domain.

Slide 10: Photo via Sacramento county police department

Slide 11 Educational purposes only, https://www.wmtw.com/article/maine-man-to-stand-trial-for-1993-alaska-murder-after-genetic-genealogy-tied-him-to-crime-scene-dna/36292803

Slide 12: Data from: Data from Kaiser Family Foundation analysis of CDC Behavior Risk Factor Surveillance System (2014): https://www.kff.org/report-section/key-facts-on-health-and-health-care-by-race-and-ethnicity-section-2-health-access-and-utilization/

Slide 13: "Navajo Nation flag" by dbking (https://flic.kr/p/8tW3e9, accessed Oct 4, 2018). Available under a Creative Commons Attribution 2.0 Generic license (https://creativecommons.org/licenses/by/2.0/).

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Slide 17: Personal Genetics Education Project (Patricia Hautea).

Slide 18: Adapted from https://www.mskcc.org/blog/car-t-cell-therapy-growing-area-research

T cell image from "The Hematopoietic System of the Bone Marrow" by OpenStax College (https://commons.wikimedia.org/wiki/File:2204_The_Hematopoietic_System_of_the_Bone_Marrow_new.jpg, accessed Oct 16, 2018). Available under a Creative Commons Attribution 3.0 Unported license (https://creativecommons.org/licenses/by/3.0/deed.en). Image cropped.

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Slide 21: Ken Burns Presents The Gene: An Intimate History (https://ny.pbslearningmedia.org/resource/9795d5d3-2b03-4d50-b193-ae6eb918392f/genome-editing-and-crispr/, accessed May 11, 2020)

Slide 22: (right) "B0000521 SEM sickled and other red blood cells" by Wellcome Images, Credit: EM Unit, UCL Medical School, Royal Free Campus (https://www.flickr.com/photos/wellcomeimages/7112270353/, accessed Jan 12, 2017). Available under a Creative Commons Attribution-NonCommercial-NoDerivs 2.0 Generic License (https://creativecommons.org/licenses/by-nc-nd/2.0/). No changes made.

(left) "Blausen gallery 2014" by Blausen.com staff, Wikiversity Journal of Medicine (https://commons.wikimedia.org/wiki/File:Blausen_0286_CysticFibrosis.png, accessed Jan 12, 2017). Available under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/deed.en). No changes made.

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Slide 25: "Malaria room" by YoHandy (https://www.flickr.com/photos/thefinessimo/2164822357, accessed Jan 13, 2017). Available under a Creative Commons Attribution-NonCommercial-NoDerivs 2.0 Generic License (https://creativecommons.org/licenses/by-nc-nd/2.0/). No changes made.

Slide 26: Educational purposes:
https://pubmed.ncbi.nlm.nih.gov/30905296/#:~:text=Mice%20Against%20Ticks%20is%20a,ticks%20in%20eastern%20North%20America.

Slide 27: Slide 13: "Second International Summit on Human Genome Editing, Hong Kong, Day Two, Nov. 28", by National Academy of Sciences (https://www.flickr.com/photos/nationalacademyofsciences/46085235431/, accessed Jan 15, 2019). Available under a Creative Commons Attribution-NonCommercial-ShareAlike 2.0 Generic License (https://creativecommons.org/licenses/by-nc-sa/2.0/). No changes made.

Slide 29: Burlington Free Press, October 29, 1926, p. 1. Clipping from Paul Amos Moody Papers, Box 181, Truman Allen file, University of Vermont Archives. Courtesy of Vermont Eugenics: A Documentary History (http://www.uvm.edu/~eugenics/images/hpbfp102926.html, accessed Oct 10, 2018).

Slide 30: Image: "Exhibit of work and educational campaign for juvenile mental defectives", 1906. Source: American Philosophical Society, ERO, MSC77,Ser1,Box35: Trait Files. Accessed via the Eugenics Image Archive, Dolan DNA Learning Center, Cold Spring Harbor Laboratory, ID# 348 (http://www.eugenicsarchive.org/eugenics/view_image.pl?id=348, accessed March 2, 2020). pgEd has cropped the original image.

Slide 31: "Justice Oliver Wendell Holmes," circa 1924, United States Library of Congress. (http://loc.gov/pictures/resource/npcc.26412/, accessed Feb 1, 2016).

Slide 32: Image: "Family-stock of a woman sterilized by the state of Maine", circa 1935. Source: The Harry H. Laughlin Papers, Truman State University, Lantern Slides, IBM Box,Box 10. Accessed via the Eugenics Image Archive, Dolan DNA Learning Center, Cold Spring Harbor Laboratory, ID# 958 (http://www.eugenicsarchive.org/eugenics/view_image.pl?id=958, accessed March 2, 2020).

Image credits

Slide 36: Image (top-left): "Cassava root 2" by Neil Palmer, accessed February 05, 2020 (https://www.flickr.com/photos/ciat/4627298692/in/photostream/). Available under a Creative Commons Attribution-ShareAlike 2.0 Generic license (https://creativecommons.org/licenses/by-sa/2.0/).

Image (top-right): Public domain picture, accessed February 05, 2020. (https://www.pxfuel.com/en/free-photo-xaizx)

Image (middle): "'I'iwi - Vestiaria coccinea" by USFWS - Pacific Region, accessed February 05, 2020 (https://www.flickr.com/photos/usfwspacific/36474996884/in/photolist-npj4sr-agb8jE-iVSK5i-QTfSa9-bsZRZr-XzaTNC-Yymcbo-YymaNd-wUE7m-4Wh3K5-4WgVnf-dvuz71-agb8hj-4Warst-4WeEo3-4Waswx-4WgEiL-ag8n28-4WeHBL-DVaASc-4WapjV-4Wh2Wo-4WhaKN-8WFCfh-ag8m1r-9V1gHh-29L7nri-MQqdKq). Available under a Creative Commons Attribution-NonCommercial 2.0 Generic license (https://creativecommons.org/licenses/by-nc/2.0/).

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Slide 38: Image (left): "NP Cassava processing 6" by Neil Palmer, accessed February 05, 2020 (https://www.flickr.com/photos/ciat/5867707606). Available under a Creative Commons Attribution-ShareAlike 2.0 Generic license (https://creativecommons.org/licenses/by-sa/2.0/).

Image (middle): "A group work to peel the cassava for processing" by IFPRI -IMAGES, accessed February 05, 2020 (https://www.flickr.com/photos/ifpri/14664017485). Available under a Creative Commons Attribution-NonCommercial-NoDerivs 2.0 Generic license (https://creativecommons.org/licenses/by-nc-nd/2.0/).

Image (right): "Vietnam cassava processing 16" by Neil Palmer, accessed February 05, 2020 (https://www.flickr.com/photos/ciat/4071072936/in/photostream/). Available under a Creative Commons Attribution-ShareAlike 2.0 Generic license (https://creativecommons.org/licenses/by-sa/2.0/).

Slide 39: Image: "Peeled cassava soaked in a tub for fermentation" by IITA, accessed February 05, 2020 (https://www.flickr.com/photos/iita-media-library/4535105072/in/photolist-qQQiDy-6W2ghP-2dtKUFA-2cseyvw-PN3p7H-2ejmsZY-28TApDd-ZAvhkT-DP5tJQ-24vtKGg-7UKAJL-2aXhHqx-qtAA6u-cKbhwY-mUj5QZ-mUm62q-mUj5vk-mUj5ka-rpnyA6-bQaEP8-mUm5uJ-mUm423-pRZGJ-71WUAa-qtAtnj-SfQqju-RmEqek-SYQEnY-23Mvrvz-7gH4B1-HWUtWG-8r2Lq7-PawwES-t7EXys-9z7Fxn). Available under a Creative Commons Attribution-NonCommercial-ShareAlike 2.0 Generic license (https://creativecommons.org/licenses/by-nc-sa/2.0/).

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Slide 41: Image: "Cassava root 2" by Neil Palmer, accessed February 05, 2020 (https://www.flickr.com/photos/ciat/4627298692/in/photostream/). Available under a Creative Commons Attribution-Sharealike 2.0 Generic license (https://creativecommons.org/licenses/by-sa/2.0/).

Slide 42: Educational purposes only. Via IGI. https://www.technologyreview.com/2022/06/14/1053843/carbon-capture-crispr-crops/

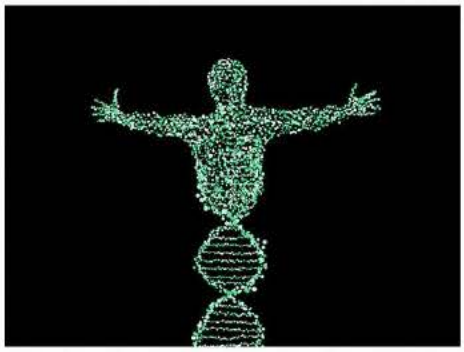
Slide 43: https://www.nature.com/articles/s41438-020-00428-4

Slide 44: https://www.frontiersin.org/articles/10.3389/fsufs.2021.685801/full and

Slide 45: pgEd

Genome editing and CRISPR

What is a gene?
What are germ cells, somatic cells, and stem cells?
How are CRISPR therapies delivered?

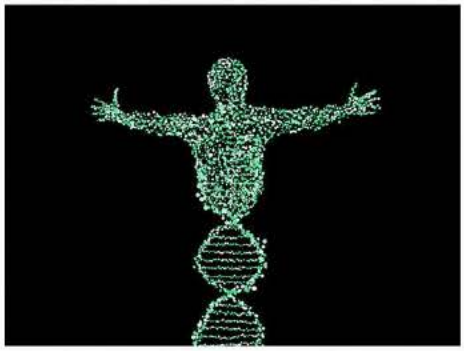


ACTGTAGCCATAGAATAGTCT
GTAATAGCTCGATGCTCGGTA
GATCTTAGACAGACAGTATCG
GCTTTAGACAGATAGTCTCGA
CGCTGACGCTTCTGATACGCT
GATAGACAGTCTCGTGACAG
ACGACAATAGACGCTCGTCG
CAATCGGC

DNA is the 'Recipe book of Life'

and

DNA can be found in virtually every cell of the body

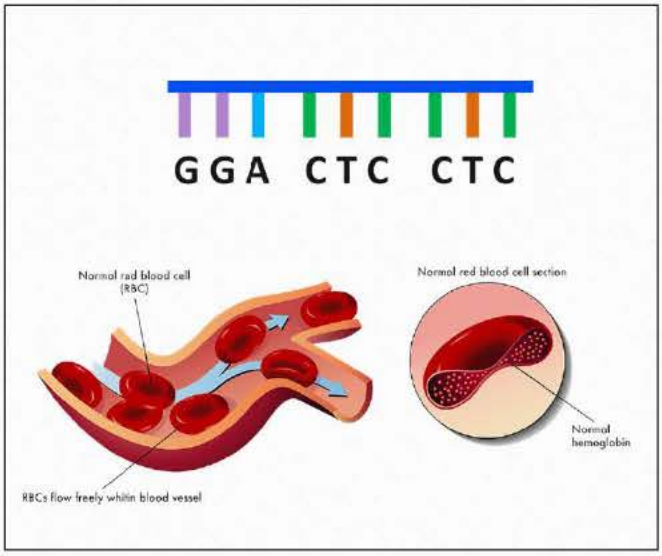


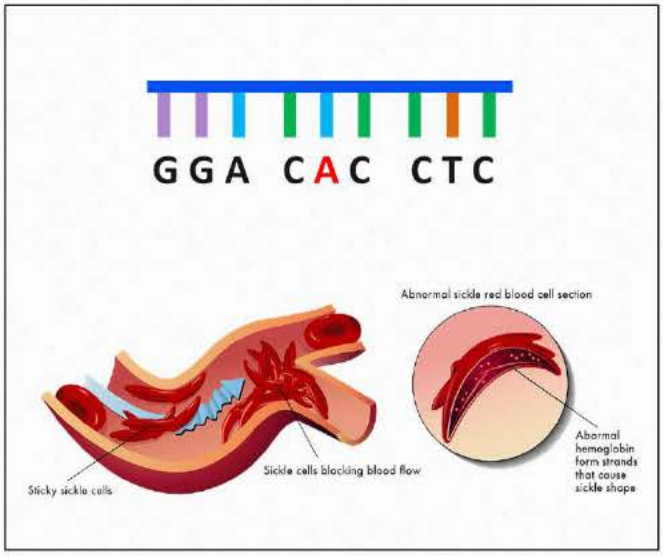
ACTGTAGCCATAGAATAGTCT
GTAATAGCTCGATGCTCGGTA
GATCTTAGACAGACAGTATAA
AAAATAGACAGATAGTCTCGA
CGCTGACGCTTCTGATACGCT
GATAGACAGTCTCGTGACAG
ACGACAATAGACGCTCGTCG
CAATCGGC

Changes in the DNA code create variation

some of which can be detrimental to human health

Sickle Cell





Cystic Fibrosis

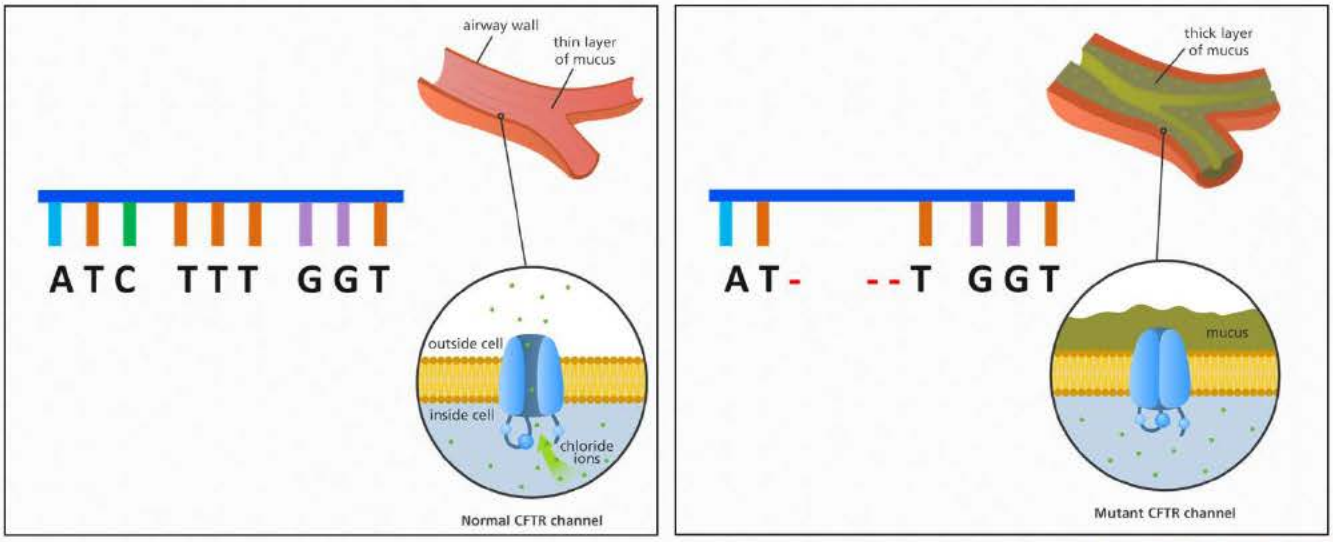
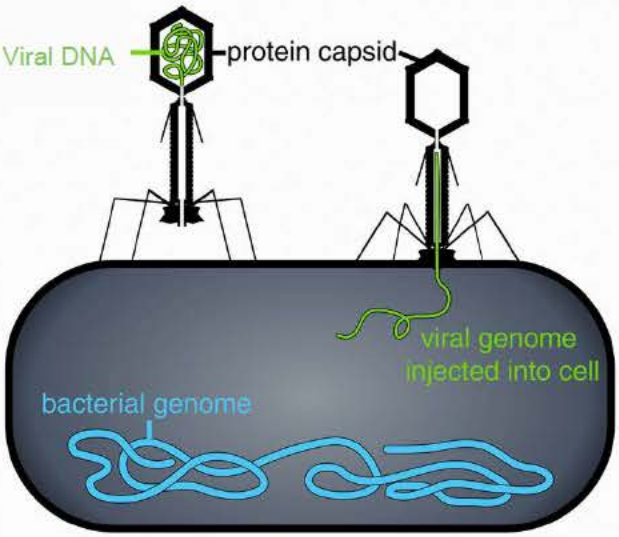
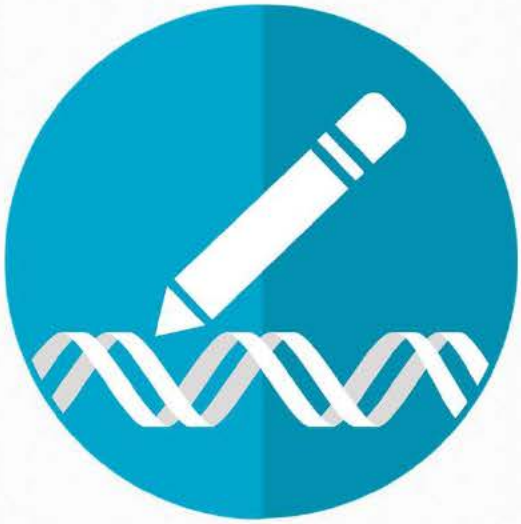


Image Credit: Genome Research Limited



CRISPR

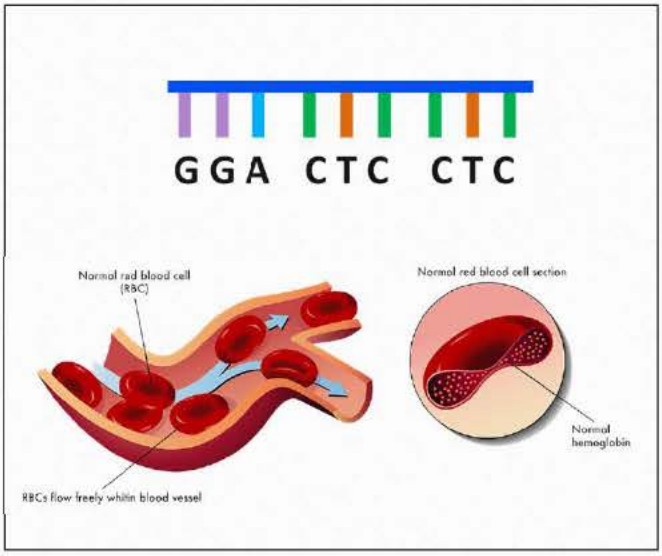
- Bacterial 'immune system'
- Recognizes specific DNA sequence
- Changes DNA

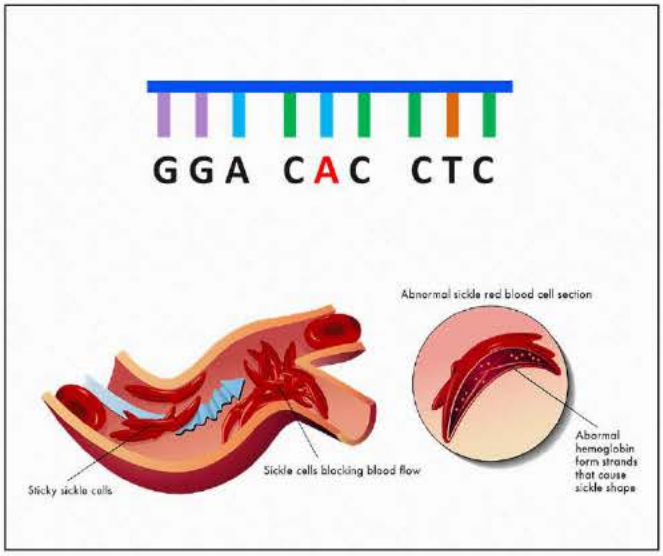


CRISPR

- Bacterial 'immune system'
- Recognizes specific DNA sequence
- Changes DNA
- Adapted as genetic tool in human cell culture (2013)

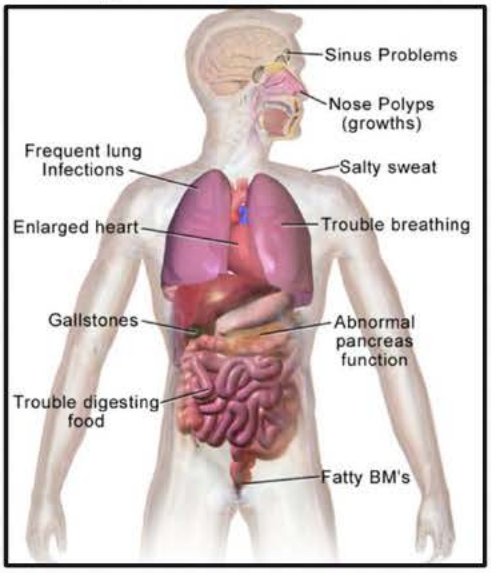
Sickle Cell





Blood cells can be treated outside the body

Cystic Fibrosis



Need to target CRISPR to specific organ systems

CRISPR

- Genetic tool used in scientific research
- Under development
- Some early clinical trials to use CRISPR as a medical treatment

Layla Richards (2015)
the first success of genome editing-based gene therapy

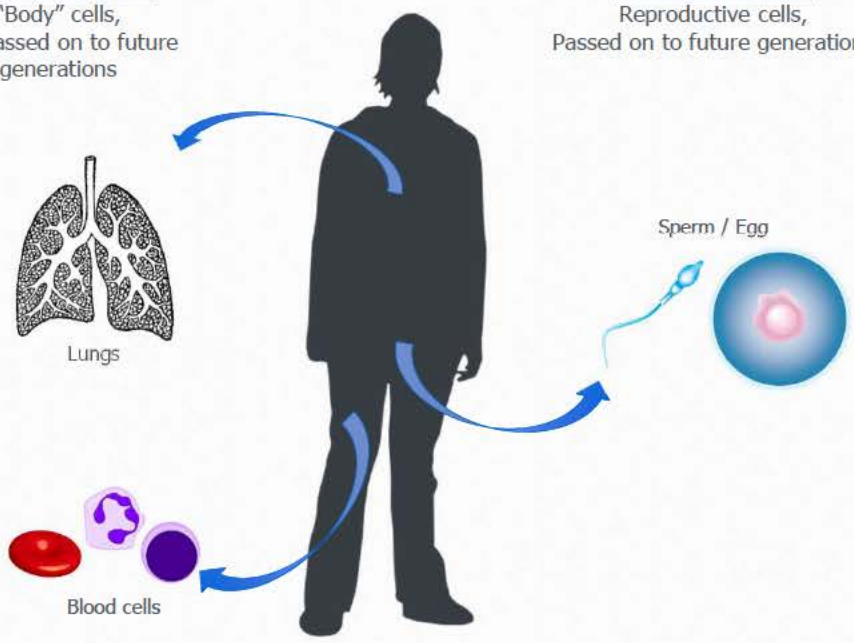
Great Ormond Street Hospital

Image: Maidiel1, CC BY-SA 4.0

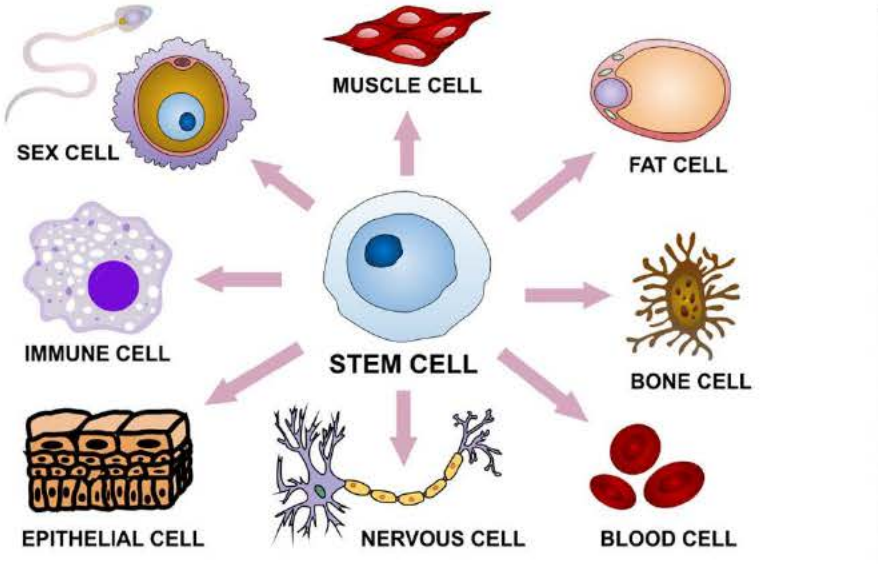
Might genome editing one day lead to a solution to the global shortage of organs?

Somatic cells
"Body" cells,
Not passed on to future generations

Germline cells
Reproductive cells,
Passed on to future generations



Stem cells



https://commons.wikimedia.org/wiki/File:Stem_cell_differentiation.svg

CRISPR is moving fast, but are we?

2015: A research group used CRISPR to make genetic changes in non-viable human embryos

2018: The birth of CRISPR edited twins

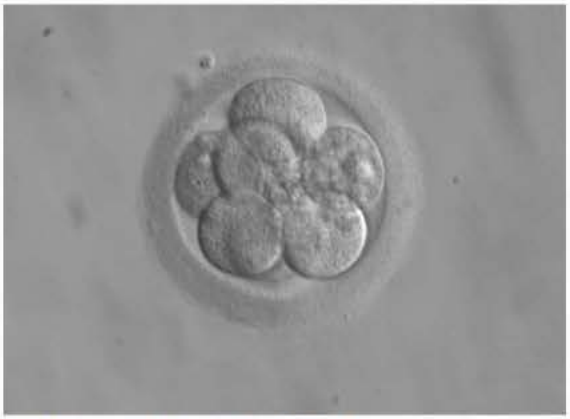


Image: ekem (courtesy: RWJMS IVF Program), public domain

APPENDIX E

Gene Editing in Health and Bioscience (presenter materials)

- Laura Reinholdt, Ph.D., Associate Professor and co-Director, Genetic Resource Sciences, The Jackson Laboratory
- Jonathan Zuckerman, M.D., Director, Adult Cystic Fibrosis Program, Maine Medical Center

August 17, 2022

Presentation before the ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY TO THE CITIZENS OF THE STATE

Submitted by Laura Reinholdt, Ph.D., Associate Professor, The Jackson Laboratory

Good afternoon, Senator Claxton, Representative Zager and members of the advisory panel, my name is Laura Reinholdt and I am Associate Professor of genetics at The Jackson Laboratory. The Jackson Laboratory is an international genetics and genomics research institution, headquartered in Bar Harbor, with other Maine-based facilities including in Augusta and Ellsworth.

I'm pleased to have the opportunity to speak to you today and would like to thank the panel for their service and interest in learning more about gene editing.

Public policy and ethical discussions of scientific technology and its potential impact on society should include and be informed by, scientists, policy makers, and the general public. Scientific and societal consensus should be the goal, and it should be an on-going discussion as technologies and our knowledge about them evolves.

For these reasons, I applaud the foresight of the Maine legislature who voted to establish this advisory committee, and congratulate co-chairs Senator Claxton and Representative Zager, for sponsoring the legislation.

In this presentation, I was asked to answer the following two-part question. "What should the State of Maine do regarding gene editing within your field of expertise in order to best benefit Mainers in the next five years and subsequently, over the next generation?."

In answering these questions, I offer my perspective on the positive, transformational impact of gene editing technology in biomedical and clinical research broadly, and locally, here in Maine.

I have spent the majority of my scientific career here in Maine, having moved here for a post-doctoral fellowship opportunity in 2001. I became a scientist because I was always fascinated by the natural world, and when I came to understand genetics, I recognized it as the biochemical thread connecting us all, dictating patterns in nature, and across generations. I knew I wanted to be as close to that work as possible and really didn't dream that I would eventually be where I am today. I'm incredibly grateful to all of the mentors that helped get me here, many of whom established their careers here in Maine.

In addition to my personal background, my presentation also reflects the collective experience of my colleagues at The Jackson Laboratory, a non-profit institution at the forefront of biomedical research in Maine. The laboratory holds over 100 active NIH grants and employs over 1,800 people at three locations: the headquarters campus in Bar Harbor, the Maine Cancer Genomics Initiative in Augusta, and at an innovative production facility in Ellsworth, constructed with matching, competitive funding from the Maine Technology Institute. The Laboratory invests substantial capital every year in research tools used by scientists at each of these locations in our mission to discover precise genomic solutions for human disease. This work is vital to enhancing our quality of life through better health and high-quality jobs. Life sciences research and development is essential to Maine's innovation economy and is highlighted in numerous recent reports including the Maine Economic Development Strategy 10-year plan and reports from the Maine Development Foundation, Maine State Chamber of Commerce, and Educate Maine. Maine's ability to sustain and grow its innovation economy is related to our continued access to critical technology including gene editing, the focus of today's discussion.

During my career, I experienced two technological inflection points – these were next generation sequencing technologies and CRISPR/cas9 based genetic engineering.

Next generation sequencing technologies have allowed us to move from sequencing a single genome for $2.7 billion dollars in 13 years to sequencing a single genome in under a day for around $1,000.

We call these technologies disruptive because they open up completely new industries and fields of research. And that has certainly been true for genome sequencing. The results are tens to hundreds of thousands of genomes revealing incredible genetic variation across humans and across all other species. As scientists could begin to ask which of these variants cause disease, which of them variants make us susceptible or resistant to certain environmental exposures, infection, which of them determine if a drug for some and not others, but we would need significant innovation in genetic engineering technologies to begin to tackle these questions.

The next technological inflection point that occurred during my career was gene editing – particularly CRISPR based genome engineering. This was the disruptive technology that would allow us to functionalize the billions of genetic variants revealed by next generation sequencing technologies. Not only would be able to know what to engineer, we had the technology to accomplish that engineering at scale.

Considering these watershed advancements, my peers in the scientific community quickly recognized the potential societal impact of 'easy' genetic engineering if it were to be applied to engineering of sperm or eggs – these "germ cells" across all species carry our genomes to the next generation.

For example, one of the first therapeutic applications of gene editing was the correction of the single mutation that causes Sickle Cell Disease in the red blood cells of a patient. Editing a patient's red blood cells effects only the patient; editing the same patient's sperm or egg cells would pass the modification on to the patient's children and to subsequent generations. This kind of gene editing - also known as "germline editing" quickly became a topic of scientific debate.

Ultimately, scientific organizations like the National Academy of Medicine, National Academy of Sciences, NIH and the World Health Organization have articulated a moratorium on germ line editing. It was, in fact, the inventors and users of the technology who were the first to self-regulate. Later, government regulation in some countries would follow suit. For example, the US Food and Drug Administration will not approve a gene therapy where there is risk of introducing heritable changes to the DNA.

With oversight including from within the scientific community and at the federal level, gene editing is a state of the art tool that is now used extensively in biomedical research. I'd like to offer three examples of how my colleagues and I use this technology in our labs at The Jackson Laboratory:

- *Discovery* (*Which genetic variants are important?*): High throughput gene editing in cell lines (which are cells grown and maintained outside of an organism) and in simple model organisms like mice allows us to ascertain function for the millions of genetic variants that have been discovered by genome sequencing projects. This simply could not be done efficiently prior to CRISPR-Cas9 and other gene editing technologies. In this application, CRISPR allows us to identify the most important, impactful genetic variants by editing them and studying the resulting physiological consequences.

- *Disease modeling* (*Which interventions / therapies are most effective in curing a genetic disease?*): Editing the genomes of mice and other model organisms to introduce the genetic variants that cause disease in people gives us an experimental system where we can test interventions in a model carrying the same disease-causing mutation. This is what we mean by "precision modeling". The specific mutation in the patient can be engineered into the mouse. At JAX we have the Center for Precision Genetics as well as the Rare Disease Translational Center – both are focused on building these important disease models, which are then distributed throughout the scientific community for pre-clinical research.
  - The number of new CRISPR-generated mouse models of human disease stewarded by The Jackson Laboratory has grown by two orders of magnitude over the last 5 years.

- *Therapy* (we can use gene editing in vivo, in cells and tissues of the human body to 'correct' a disease-causing variant or replace the affected gene product. These approaches are extensively tested in animal models, that are often CRISPR-engineered themselves. In, the laboratory mouse is critical in this pre-clinical research because like humans, they are mammals, we can manipulate their genomes, we can control their genetics as well as their environment. At JAX we have the Somatic Cell Genome Editing center that is NIH funded, completely focused on advancing methods for somatic gene editing as therapy and the requisite mouse models.
  - The next step in the process of developing gene therapy is to use this preclinical knowledge for further testing in primates or direct investigational new drug applications / clinical trials in human patients as we advance cures for genetic disease.

In these examples, gene editing is being used to discover gene variants that protect or cause disease, gene editing is being used to model these genetics in model organisms, and gene editing is being used to develop potential therapies. All of this is happening at The Jackson

Laboratory, where gene editing technology is helping us advance our mission to discover precise genomic solutions for human disease.

Coming back to the original questions – “What should the State of Maine do regarding gene editing within your field of expertise in order to best benefit Mainers in the next five years and subsequently, over the next generation?”

Within the next five years, and in concurrence with Dr. Ben King’s presentation, The State of Maine should promote awareness and education in life sciences in both schools and community organizations. To build on Dr. King’s recommendations, one way the state can do more to invest in K12 education is to support organizations and programs that are already working to support teachers and schools, and usually bringing federal dollars into the state to do so. Existing programs such as The Jackson Laboratory’s Teaching the Genome Generation, which has reached over 9,000 students at 61 Maine high schools; or, the Personal Genetics Education Program’s Faith Partnerships, which engages faith communities on how we make collective decisions about whether and how to proceed with gene editing, can be expanded to reach more students, more schools, and more community organizations in the state.

In my view, most Maine citizens are not well informed about biomedical technology or have adequate resources to learn more or engage in conversations about biomedical research, let alone specific technology like gene editing. In the near term, this advisory committee should be confident in recommending policy that enhances education and awareness, knowing that stringent federal regulations limiting the use of gene editing technology already exist.

Also in the short term, I suggest the state build and sustain an environment where discussions and panels like this become the norm, and not the exception. For example, my colleagues and I are excited to see that Maine will establish a Rare Disease Advisory Council to discuss and help solve issues that impact patients and caregivers of people with rare disease (usually children). I think in the long term, we’ll see an intersection of the gene editing technology discussed in the context of this panel with the interests of the rare disease community.

Finally, over the long term, Maine should invest in medical research talent and infrastructure such that patients are not prevented from accessing future genomic treatments due to lack of proximity to a major research hub, such as Cambridge or Boston. I suggest Maine make it a state priority to bring these medical centers closer to patients by investing in an environment where medical research can be performed, and clinical trials delivered closer to home.

Thank you for the opportunity to present before you today. I again want to thank you for your service and for bringing this important conversation into the public sphere.

Cystic fibrosis (CF) is the most common life-shortening genetic disease in the white population, affecting approximately 1 in 2500 live births (the carrier state for this autosomal recessive condition is about 1:25 in white people)**. In the State of Maine, there are currently approximately 250 children and adults with this disease.**

People with CF experience pulmonary complications resulting from the production of thick secretions in their lungs. All of the secretions cannot be cleared from their airways, which results in complications such as impaired gas exchange, bacterial infections and scar tissue formation. Bacterial infections cause exacerbations of the disease requiring inhaled antibiotics and intravenous antibiotic treatment. Each exacerbation causes further irreversible damage to the lung tissue, and progressive lung disease is currently the cause of death in approximately 85% of people with CF. To avoid these complications, affected individuals have traditionally required multiple sessions of aggressive daily airway clearance therapy, treatment with inhaled medications and increased nutritional support, all of which may require 2-4 hours per day (and more during an exacerbation).

In recent years biotechnology has transformed the treatment—and the lives—of most people with CF. A new class of medications called highly effective modulator therapy (HEMT) is now available for up to 90% of people with CF. These oral medication cocktails (developed through the screening of large compound libraries) are easy to take, improve lung function, reduce the frequency of hospitalizations and dramatically improve the quality of life of affected individuals. Early indicators point to marked improvement in life expectancy with these medications as well.

However, we are faced with a dilemma. Like all medications, HEMT is not a panacea for every person with CF. Approximately 10% of patients do not have genotypes responsive to HEMT. Others are not able to tolerate HEMT due to side effects. Furthermore, HEMT does not appear to reverse fixed injuries that develop early in life (such as male infertility and pancreatic insufficiency). Therefore, there is great interest among people in the CF community to look for more therapeutic options to address these gaps and shortcomings of HEMT.

Gene repair or replacement therapy, while still outside the scope of our current armamentarium, holds great promise as a strategy to treat people with CF disabled, for example, by nonsense mutations. More generally, treatment of genetic targets could change the trajectory of this disease with one-time ("one and done") or less frequent dosing starting at the earliest stages of life. **That would be the equivalent, in the minds of many, of changing the meaning of CF from "cystic fibrosis" to "cure found". Thus, there is great interest in the CF community to develop therapies (that is, gene-based, "mutation agnostic" therapies) that are effective for all people with the disease.**

A number of strategies (for example, RNA based treatments, DNA-based gene editing and gene replacement) are in relatively early stages of development and each carries a set of potential advantages and concerns, including durability of effect and whether benefits or harms could be passed along to offspring. However, we are right on the cusp of seeing such treatments for CF. Laying the groundwork for genetic therapies requires careful planning and preclinical testing, particularly for diseases like CF that for most can currently be in treated quite effectively. Perhaps more importantly, exploration of these novel therapies reveals important ethical and legal questions that entwine our humanity and that demand address by a cross section of society. For example, how do we intend to authorize and regulate *in utero* and/or germ cell line treatments for diseases that typically bring additional burden to daily living but do not lead to early childhood death? At this stage, a strong argument can be made to establish a

formal process by which interdisciplinary panels representing the spheres of religion, law, science, and public policy/public health review together information emerging from preclinical studies in advance of in-human trials.

Jonathan Zuckerman, M.D.
Director, Adult Cystic Fibrosis Program
Maine Medical Center

Associate Clinical Professor of Medicine
Tufts University

Research Experience and Potential Conflicts:

Grant Title: Gene therapy for CF (SCOR) Project III: Safety and efficacy of recombinant adenoviruses in the human lung
Funding Agency: National Institutes of Health
Period: 1997-99
Role: Principal Investigator

Grant Title: A phase 3, randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy and safety of lumacaftor in combination with ivacaftor in subjects aged 12 years and older with cystic fibrosis, homozygous for the *F508del-CFTR* mutation
Funding Agency: Vertex Pharmaceuticals, Inc.
Period: 2013-14
Role: Site, Principal Investigator

Grant Title: A phase 3, rollover study to evaluate the safety and efficacy of long term treatment with lumacaftor in combination with ivacaftor in subjects aged 12 years and older with cystic fibrosis, homozygous or heterozygous for the *F508del-CFTR* mutation
Funding Agency: Vertex Pharmaceuticals, Inc.
Period: 2014-16
Role: Site, Principal Investigator

Grant Title: A phase 2a, randomized, double-blind, placebo-controlled study to evaluate multiple doses of GLPG2222 in subjects with cystic fibrosis homozygous for the F508del mutation (FLAMINGO)
Funding Agency: Galapagos/AbbVie

Period: 2017-2018
Role: Site, Sub-Investigator

Grant Title: A Phase 1-2, randomized, double-blind, placebo-controlled, combined single and multiple ascending dose study evaluating the safety, tolerability, and biological activity of MRT5005 (CO-hCFTR mRNA/ICE LNP) administered by nebulization to adult subjects with cystic fibrosis (RESTORE-CF)
Funding Agency: Translate Bio MA, Inc.
Period: 2018-2021
Role: Site, Principal Investigator

Grant Title: A Phase 3, randomized, double-blind, controlled study evaluating the efficacy and safety of VX-121 combination therapy in subjects with cystic fibrosis who are homozygous for F508del, heterozygous for F508del and a gating (F/G) or residual function (F/RF) mutation, or have at least 1 other triple combination responsive *CFTR* mutation and no F508del mutation.
Funding Agency: Vertex Pharmaceuticals, Inc.
Period: 2021-present
Role: Site, Sub-investigator

APPENDIX F

Gene Editing in Health and Bioscience (related materials)

- Presentation by Frank Chessa, Ph.D., MA, HEC-C, Director of Clinical Ethics at Maine Medical Center: *Regulatory Guardrails for Human Gene Editing*
- Staff memorandum on Maine's genetic counselor workforce
- Public comment on genetic counselor licensing from Lisa Harvey-McPherson, RN, MBA, MPPM, Vice President Government Relations, Northern Light Health
- Information on genetic counselor workforce issues from Katherine Lafferty, MS, CGC, Senior Clinical Genomic Variant Analyst, Broad Institute
- Information on MaineCare coverage from Molly Bogart, Director of Government Relations, Maine Department of Health and Human Services
- Public comments from Kent H. Redford, Ph.D., Archipelago Consulting

Regulatory Guardrails for Human Gene Editing

September 21, 2022

Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Augusta, Maine

Frank Chessa, Ph.D., MA, HEC-C
Director, Clinical Ethics, MaineHealth
Assistant Professor, Tufts University School of Medicine

I have no conflicts of interest related to this material.

This presentation is supported by a grant from the National Institutes of Health, Center of Biomedical Research Excellence in Acute Care Research and Rural Disparities, FAIN P20GM139745

Outline:

1. United States – Federal
   A. Human Subjects Research – Institutional Review Boards
   B. Gene editing laws and regulations
2. United States – State Statutes
3. International

Distinction

Somatic Human

- Edited genes not passed to offspring
- Numerous disease directed clinical and preclinical trials
- Tech rapidly advancing, e.g., base editing, prime editing
- Ethical issues of human subjects research

Heritable (Germline) **Human**

- Edited genes passed to offspring
- In-vitro fertilization, typically
- Embryo cells edited, different risks to human subject
- Off target effects have longer reach

- **Further Distinction:**
  - Germline for research
  - Germline for reproduction

1.A Institutional Review Boards

- History
- Current Practice
- Jesse Gelsinger

Nuremberg Code -- Background

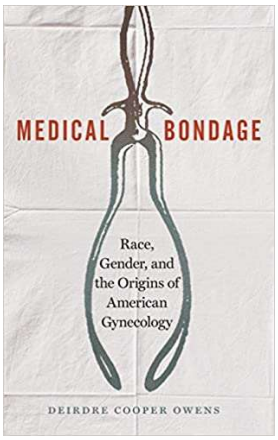
- Nazi atrocities included experimentation on concentration camp inmates
- Defense at the Nuremberg trials include the claims that German research practices were not substantially different than practices in other countries and that there is no published standard to follow
- The Nuremberg Code, written by Leo Alexander (Tufts University), was included in the tribunal's decision give presented the standard protections of human subjects
- The Nuremberg Code survives as an important document which states the ethical principles underlying the protection of human subjects

Nuremberg Code - Principles

- The voluntary consent of human subjects is absolutely essential
- The experiment should…yield fruitful results for the good of society
- Conducted so as to avoid all unnecessary physical and mental suffering
- No experiment will be conducted…where it is likely that death or disabling injury will occur…
- During the experiment …the subject should be at liberty to bring the experiment to an end…

Anarcha, Betsy and Lucy and vesicovaginal fistula, 1845

- J. Marion Sims, 1813-1883, South Carolina, Alabama, New York, Europe
- Sims speculum, Sims sigmoid catheter, Sims' positon, silver wire as suture. James Garfield, Woman's Hospital in NYC
- 1845-1849, experimental surgery on 8 to 12 women who were enslaved. Repeated surgeries (30 for Anarcha)
  - Sought women with condition from owners of slaves; paid owners to rent them; consent from owners.
  - White medical assistants/apprentices quit after a time; trained enslaved women to assist
  - Anesthesia not used (myths about pain sensitivity of persons with African ancestory; newness of anesthesia)

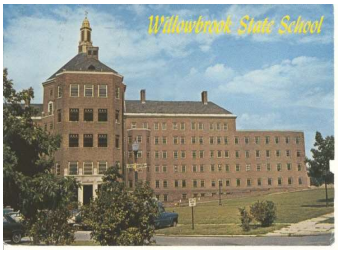


Dr. Cooper Owens Lecture: youtube.com/watch?v=op12iUfBFXo

Tuskegee Syphilis Study

- 1930 until 1972
- US Public Health Service
- Poor, African-American men in Macon County, Alabama
- "Study in nature" of syphilis
- Prevented subjects from seeking treatment in order to study untreated syphilis
- Little disclosure; deceptive language

Willowbrook Hepatitis Research, 1950-70



- 60 children (potentially an undercount) intentionally infected with Hepatitis to study effects of potential therapeutic agent.
- Saul Krugman, MD, well known for
  - Identification of Hepatitis A and B
  - Immunoglobulins confer passive immunity
- During some periods, children denied admission to Willowbrook unless they consented to the research study
- Disclosure about the study was misleading
- Some defend research: although children were intentionally infected, they probably would have been infected anyway, and they received good clinical care because they were part of the study

Research Ethics Documents

- Nuremberg Code, 1947
- Declaration of Helsinki, 1964
- National Research Act, 1974
- Belmont Report, 1978
- Common Rule, 1991
- Code of Federal Regulations (CFR)

Belmont Report, 1978

- Respect for Persons: Potential subjects decide whether to participate in research
- Beneficence: Researchers must protect the welfare of subjects
- **Justice: No group has preferential access to benefits of research; no group disproportionately burdened by research**

Institutional Review Boards

- Established by National Research Act, 1974
- 45 CFR 46, Common Rule, 1991
- Charged with ethical review of human subject research
- Membership must be diverse and community specific: scientist, nonscientist, community person
- Local boards familiar with local norms

IRB Responsibilities

- Informed consent
- Study design
- Subject selection
- Safety monitoring
- Confidentiality

Informed Consent – required disclosures

- Subjects know they are involved in research
- Right to decline participation
- Nature of research
- Risks and discomforts
- Benefits
- For therapeutic trials, alternatives to participating in study
- Right to withdraw

Study Design

- Study must make a contribution to knowledge
- Balance risks to subjects against knowledge gained
- IRB evaluates study design
  - Is the topic important?
  - Is the research design adequate?

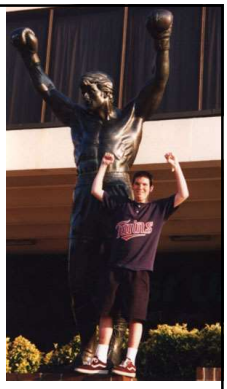
Subject Selection

- Fairness
  - No group disproportionately bears the burdens of research
  - Benefits of research open to all (No group disproportionately receives benefits of research)
- Vulnerable populations protections
  - Children
  - Mentally ill
  - Incarcerated

Shifts in Clinical Research

- **Increase in number**
  - In 2006, 59,000 clinical trials (50% increase from 2000)
- **Shift in sponsorship**
  - In 1991, 80% sponsored by federal government or nonprofits
  - In 2008, more than 50% sponsored by industry
- **Shift in who is running trials**
  - Away from academic medical centers
  - Toward for profit companies
  - Managed by Contract Research Organizations (CROs): 28% in 1993, 64% in 2003
  - Data resides in central office (often a for-profit company)
- **Shift in IRB approval of trials**
  - Away from university IRBs
  - Toward for-profit IRBs
  - Western IRB reviews more than half of FDA drug trials
  - NIH requires a single IRB for multisite trials

Jesse Gelsinger



- 18 y.o. with Ornithine Transcarbamylase Deficiency (OTC) who died after participating in gene therapy research at U Penn, 1999.
- OTC is a rare X-linked genetic disorder resulting in disruption of the urea cycle. OTC results in excess ammonia after ingesting protein.
- Edited genes were delivered by an adenovirus vector, which likely triggered a harmful immune response.
- Irregularities with consent
  - Family thought trial was for treatment, not safety
  - Informed consent omitted data on animal deaths
  - Previous adverse reactions not reported to FDA by Penn and others
  - At time of trial, Jesse's elevated LFT's (and perhaps fever) should have disqualified him
- Financial ties
  - James Wilson directed **Institute for Human Gene Therapy** at Penn
  - James Wilson founder of **Genovo**, private company, which had a financial interest in the therapy
  - Genovo contributes a quarter of IHGT's 22 million dollar budget
- Death and subsequent investigation led to near moratorium on further gene editing research.

Therapeutic Misconception

- The tendency to overestimate the benefits of an experimental therapy (patients, families and researchers). For example, a parent's belief that an agent in a phase 1 toxicity trial has a good chance of curing a child's advanced cancer.
- Further, patients and families may ignore the fact that research imposes burdens not present in clinical medicine, and that some aspects of a study might not be in their best interest (e.g., randomization).
- Therapeutic misconception also occurs when subjects inaccurately believe that the research protocol involves individualized treatments selected primarily for their benefit.
- Generally speaking, therapeutic misconception may undermine a subject's ability to provide informed consent, a necessary condition for trial participation.

Kimmelman J. The therapeutic misconception at 25: treatment, research, and confusion. Hastings Cent Rep. 2007 Nov-Dec;37(6):36-42.

1.B Federal Laws

Cloning

- There is no Federal law prohibiting cloning.
  - Multiple bills introduced since Dolly the sheep was cloned in 1997
  - General disagreement whether to ban cloning to produce a human being and also cloning for biomedical research.
- FDA used its regulatory power to require that "cloning technology to create a human being" apply to the agency for permission, The FDA made it clear that "there are major unresolved safety questions" such that they would turn down any application.
- Theoretically, a private company (not using Federal funds) could perform cloning experiments, but they would not be able to market therapies given need for FDA approval.

Cloning, State Laws

- Arizona, Arkansas, Michigan, North Dakota, Oklahoma, South Dakota, and Virginia prohibit both cloning to produce children and cloning for biomedical research.
- California, Connecticut, Illinois, Iowa, Maryland, Massachusetts, Missouri, Montana, New Jersey, Rhode Island prohibit cloning-to-produce-children while permitting cloning-for-biomedical-research.
- Minnesota appears to prohibit cloning for research, but is silent on cloning to produce children.
- Maine, silent on cloning, but prohibits research on intrauterine or extrauterine fetuses. Maine Revised Statutes Title 22 §1593, (2003)

Heritable (Germ Line) Gene Editing, Federal

- 1995, Dickey-Wicker amendment (appropriations rider) prohibits use of HHS funds for the creation of human embryos for research or for research in which human embryos are destroyed (H.R. 2880, Sec. 128).
- 2015: NIH (Francis Collins statement) says it will not fund any use of gene-editing technologies in human embryos, citing
  - serious and unquantifiable safety issues,
  - ethical issues presented by altering the germline in a way that affects the next generation without their consent
  - current lack of compelling medical applications justifying the use of CRISPR/Cas9 in embryos.
- 2016: Congress bars FDA (in an appropriations rider) from approving clinical trials "in which a human embryo is intentionally created or modified to include a heritable genetic modification"
- 2020: Language briefly removed by Democrats, who thought the prohibition was too broad, potentially banning mitochondrial research. Ban eventually restored.

NIH Statement https //www.nih.gov/about-nih/who-we-are/nih-director/statements/statement-n h-funding-research-using-gene-editing-technologies-human_embryos# ~ text However%2C%20NIH%20will%20not%20fund that%20should%20not%20be%20crossed.
Downloaded Sept 2022

3. International

laws, agreements, reports

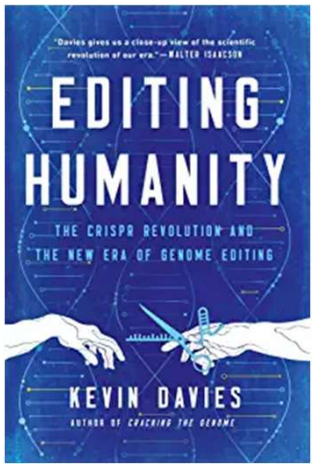
Cloning International

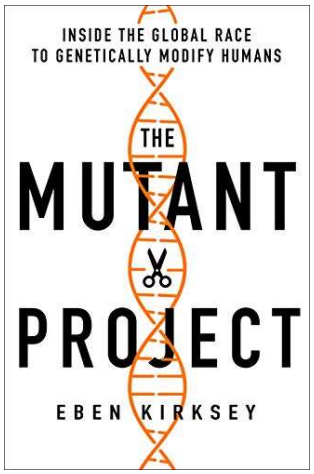
- 1997, Council of Europe *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine* (the Oviedo Convention) Banned cloning and germline gene editing. Eventually ratified by 29 countries.
- 2002, Germany bans "as a matter of principle, the importation and utilization of embryonic stem cells" as well as the derivation of stem cells.
- 2004, Canada, "No person shall knowingly create a human clone by using any technique," and barred payment to providers of sperm, eggs, or embryos.
- 2004, Italy, illegal to create human embryos for research.
- By 2005 approximately thirty countries banned human cloning.
- 2005, United Nations General Assembly adopted a declaration calling member nations to "prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life." Eventually ratified by 84 countries, including the United States. Countries to vote against the measure included the United Kingdom, India, and South Korea.

United Nations General Assembly, Fifty-ninth session, Resolution 59/280
"United Nations Declaration on Human Cloning" (March 8, 2005)

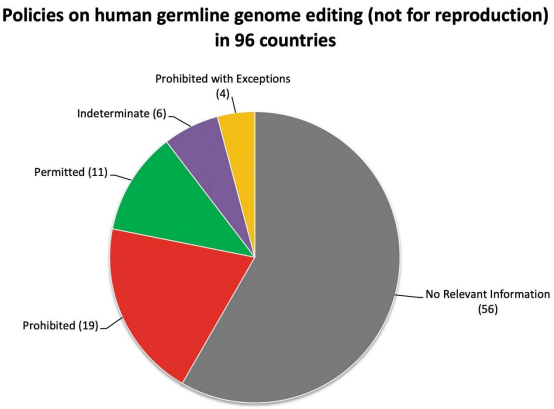
Dr. He Jiankui

- 2018 Clinical Trial
- Aimed at conferring immunity to HIV
- 3 live births
- 2 born prematurely at 31 weeks
- Trial reported by MIT tech review, prior to formal announcement/publication
- Dr. He announced/defended his trial at conference the next day
- Criticized by scientific community
- Imprisoned in China (3 year sentence)



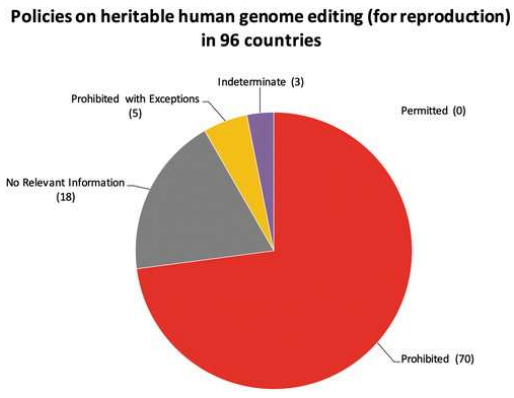


International – Gene Editing Research



Françoise Baylis, Marcy Darnovsky, Katie Hasson, and Timothy M. Krahn. Human Germline and Heritable Genome Editing: The Global Policy Landscape. *The CRISPR Journal*. Oct 2020.365-377.http://doi.org/10.1089/crispr.2020.0082

International – Gene Editing Reproduction



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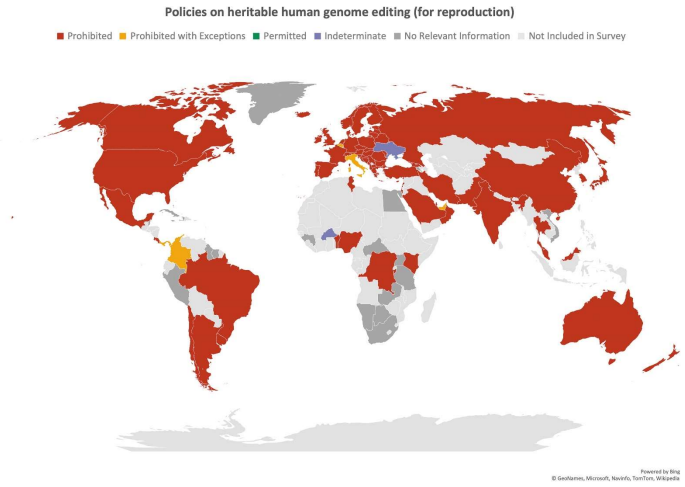

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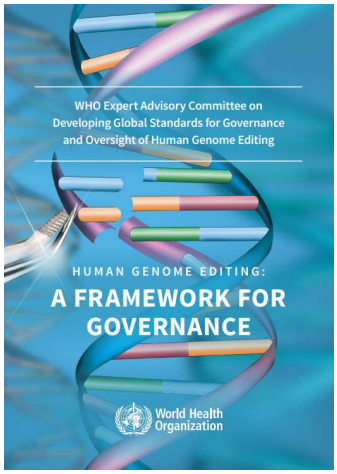
WHO Human Gene Editing Reports 2021

- 3 Reports: Human Recommendations; Position Paper; A Framework for Governance
- Somatic and Human Heritable
- "it would be irresponsible at this time for anyone to proceed with clinical applications of human germline genome editing."
- 9 process and governance recommendations

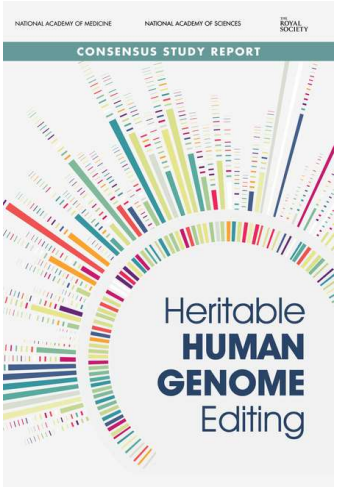


Recommendations of the Committee on the governance and oversight of human genome editing

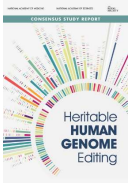
1. Leadership by the WHO and its Director-General
2. International collaboration for effective governance and oversight
3. Human genome editing registries
4. International research and medical travel
5. Illegal, unregistered, unethical or unsafe research and other activities
6. Intellectual property
7. Education, engagement and empowerment
8. Ethical values and principles for use by WHO
9. Review of the recommendations (within 3 years)

National Academy of Medicine, National Academy of Sciences, Royal Society, 2020

- Heritable Human Only
- 11 recommendations
- **Recommendation 1**: No attempt to establish a pregnancy with a human embryo that has undergone genome editing should proceed unless and until it has been clearly established that it is possible to efficiently and reliably make precise genomic changes without undesired changes in human embryos. These criteria have not yet been met, and further research and review would be necessary to meet them.



Recommendations 2-4



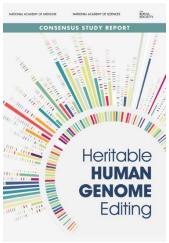
2: Extensive societal dialogue should be undertaken ….

3: It is not possible to define a responsible translational pathway applicable across all possible uses of HHGE… Clinical use of HHGE should proceed incrementally.

4: Initial uses of HHGE …should…meet all of the following criteria:

a) the use of HHGE is limited to serious monogenic diseases; …
b) the use of HHGE is limited to changing a pathogenic genetic variant known to be responsible for the serious monogenic disease …
c) no embryos without the disease-causing genotype will be subjected to the process of genome editing…; and
d) the use of HHGE is limited to situations in which prospective parents (i) have no option for having a genetically-related child that does not have the serious monogenic disease… or (ii) have extremely poor options, because the expected proportion of unaffected embryos would be unusually low, … and have attempted at least one cycle of preimplantation genetic testing without success.

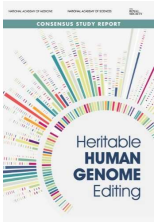
Recommendations 5-6



5: Before any attempt to establish a pregnancy with an embryo that has undergone genome editing, preclinical evidence must demonstrate that HHGE can be performed with sufficiently high efficiency and precision to be clinically useful. …

6: Any proposal for initial clinical use of HHGE should meet the criteria for preclinical evidence set forth in Recommendation 5. …

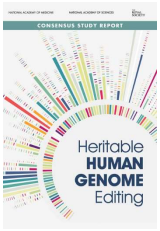
Recommendations 7-8



7: Research should continue into the development of methods to produce functional human gametes from cultured stem cells. …However, the use of such in vitro–derived gametes in reproductive medicine raises distinct medical, ethical, and societal issues that must be carefully evaluated…

8: Any country in which the clinical use of HHGE is being considered should have mechanisms and competent regulatory bodies to ensure that all of the following conditions are met...

Recommendations 9-11
(International Panels)



9: An International Scientific Advisory Panel (ISAP) should be established with clear roles and responsibilities before any clinical use of heritable human genome editing (HHGE). …

10: In order to proceed with applications of HHGE that go beyond the translational pathway … an international body with appropriate standing and diverse expertise and experience should evaluate and make recommendations concerning any proposed new class of use.

Recommendation 11: An international mechanism should be established by which concerns about research or conduct of heritable human genome editing that deviates from established guidelines or recommended standards can be received, transmitted to relevant national authorities, and publicly disclosed.

Thank You

frank.chessa@mainehealth.org

MEMORANDUM

To: Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

From: Office of Policy and Legal Analysis Staff

Date: September 21, 2022

Re: **Genetic Counselor Workforce Information**

At the second Advisory Panel meeting on September 7, 2022, members inquired whether a standard has been established for the recommended number of genetic counselors for a given population and, if so, whether this standard has been met in the State of Maine.

Workforce Research

The U.S. Government Accountability Office reported in 2020 that, "guidelines for determining the appropriate number of genetic counselors per population" have not yet been established."[1]

In 2015, the Genetic Counselor Workforce Working Group—formed by the American Board of Genetic Counseling, the Accreditation Council for Genetic Counseling, the Association of Genetic Counseling Program Directors, the American Society of Human Genetics and the National Society of Genetic Counselors—commissioned a formal workforce study to project the supply of and demand for certified genetic counselors in the United States through 2026. The working group's 2017 report[2] noted the "absence of U.S. data or guidelines indicating the appropriate ratio of [clinical genetic counselors] per population and the many variables, known and unknown, that affect demand" including: "awareness, referral patterns, reimbursement [and changes to payer coverage], geographic location, and the potential availability of genetic tests in the future that may increase demand significantly." It concluded that the then-existing shortage of genetic counselors engaged in direct patient care would be satisfied between 2024 and 2029 depending on which of two potential demand ratios was employed:

- The one full-time clinical genetic counselor per 100,000 in population recommendation from the Association of Genetic Nurses and Counsellors in the United Kingdom and Ireland; or
- The one full-time clinical genetic counselor per 75,000 in population rate "attributed to a large U.S. heath system."

The workforce study recommended "conducting additional research to assess whether the assumptions of one FTE [clinical genetic counselor] per 100,000 or one per 75,000 population are indeed appropriate to meet current or future demand in the clinical setting in the U.S."

Genetic Counselor Workforce in Maine

It is difficult to determine the number of genetic counselors in the State. The Maine Department of Labor's Center for Workforce Research and Information estimates, based on multiple sampling

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[1] U.S.GAO, *Genetic Services: Information on Genetic Counselor and Medical Geneticist Workforces*, GAO-20-593 at 14 (July 2020), *at* https://www.gao.gov/assets/gao-20-593.pdf.

[2] *See* Jennifer M. Hoskovec et al., *Projecting the Supply and Demand for Certified Genetic Counselors: a Workforce Study*, 27 J. of Genetic Counseling 16 (2018), *available at* https://pubmed ncbi nlm nih.gov/29052810/.

surveys of employers in the State, that there were approximately 10 genetic counselors employed in Maine in 2021:[3]

Lookup | Table | Graph | Wage Range | Descriptions | Tips

Filter Major Groups: Detailed Occupations Only
Select Occupational Group: (All)
Select Occupation(s): Genetic Counselors

Wage Type: Hourly / Annual
Geography: Statewide / County / Balance of State / Metropolitan Stati... / Workforce Invest...
Area Name: (All) / Maine

2021 Hourly Occupational Employment
Geography: **Statewide**
Occupational Group: ***Healthcare Practitioners and Technical***

Area Name	Occupation Title	Estimated Employment	Average Wage	25th Percentile	Median Wage	75th Percentile
Maine	Genetic Counselors	10	$37.63	$37.52	$37.66	$37.66

Blank cells indicate that an estimate is not available. Certain estimates are suppressed from publication to meet confidentiality or data quality requirements. Wage estimates above the processing limits of the statistical software are also blank. Only annual wages are provided for teaching occupations and certain others, resulting in blank cells in the hourly wage type.
Note: Data for Maine (Statewide), the metropolitan areas of Bangor, Lewiston-Auburn, Portland-South Portland, Portsmouth NH-ME, Dover-Durham NH-ME, and the Balance of State Areas, are derived from the May 2021 Occupational Employment Statistics survey. County-level estimates are locally developed using the same OES methodology but have not been reviewed by the U.S. Bureau of Labor Statistics.
Source: Maine Department of Labor, Center for Workforce Research and Information.

Display Summary Report for Occupation - select from table above (link opens in new window)

Occupation Title	SOC Code	ONET URL
Genetic Counselors	29-9092	http://online.onetcenter.org/link/summary/29-9092.00

The U.S. Census Bureau estimates that, as of July 1, 2021, the State of Maine had a population of 1,372,247 individuals.[4]

Based on the Center for Workforce Research and Information's 2021 estimated number of genetic counselors and the U.S. Census Bureau's July 1, 2021 population estimate, Maine had approximately 1 genetic counselor per 137,000 people in 2021.

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[3] *See* Maine Department of Labor (MDOL), Center for Workforce Research and Information (CWRI), *Occupational Employment and Wage Estimates*, *2021, at* https://www maine.gov/labor/cwri/oes1.html. The Occupational Employment Statistics (OES) Program "is a federal-state cooperative program between the United States Bureau of Labor Statistics (USBLS) and state agencies. Surveyed employers are asked about the number of wage and salary workers in detailed occupations and about the wage distribution for those workers. OES survey samples are drawn from the universe of non-farm employers covered by the Unemployment Insurance (UI) system." *See* MDOL, CWRI, Occupational Employment and Wages, https://www.maine.gov/labor/cwri/oes html. According to email correspondence with the Center's Director, Mark McInerney, the Center's 2021 Occupational Employment and Wage Estimates are "based on survey responses collected over multiple survey panels." For each panel, the Center's staff "classifies jobs into occupations [including the "genetic counselor" occupation] based primarily on the job title and any description of that job provided by the employer."

[4] *See* U.S. Census Bureau, QuickFacts: Maine, *at* https://www.census.gov/quickfacts/fact/table/ME/POP010220.

Stocco, Janet

From: Harvey-McPherson, Lisa <lmcpherson@northernlight.org>
Sent: Tuesday, September 20, 2022 8:58 AM
To: Claxton, Ned; Stocco, Janet; Zager, Sam; Hymanson, Patricia
Cc: Olson, Rachel
Subject: Public Comment Summary - Licensing Genetic Counselors

During the September 7th Genome-Editing Technology Advisory Panel meeting, members expressed interest in information on the number of genetic counselors in Maine. I am glad to see member interest in genetic counselors and am reaching out regarding licensing genetic counselors. Many states license genetic counselors (including New Hampshire, Massachusetts and Connecticut). Maine does not have licensing standards.

In my role as Vice President of Government Relations for Northern Light Health I have been asked to advocate that Maine establish licensing standards for genetic counselors. Given the increasing role of genetics in health care, the service provided by the counselors has significant value to the patients and families in need of this information. Licensure establishes a standard of qualification that the public (and referring providers) can rely upon when seeking this service. For example, New Hampshire licensure requires that the individual to have a currently valid certificate issued by the American Board of Genetic Counseling or the American Board of Medical Genetics.

Licensure is not a guarantee of insurance payment, but lack of licensure is a barrier to insurance coverage for genetic counseling services. Insured individuals would benefit from insurers covering the service provided by a licensed counselor.

The National Society of Genetic Counselors has excellent information on the status of state licensure. You will note that the site lists Maine status as in progress. From my research this is not accurate, I reached out to the Society regarding their source and I haven't received a response yet.

States Issuing Licenses (nsgc.org)

Thank you for the opportunity to provide comment to the Advisory Panel

Lisa Harvey-McPherson, RN, MBA, MPPM
Vice President Government Relations

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Waterville, ME 04901
Office 207-861-3282
Cell 207-356-9921
lmcpherson@northernlight.org

Stocco, Janet

From: Katherine Lafferty <klaffert@broadinstitute.org>
Sent: Wednesday, October 5, 2022 11:16 AM
To: Huang-Saad, Aileen
Cc: Stocco, Janet; Olson, Rachel
Subject: Re: Follow up on Genetic Counselor Question
Attachments: Dobson DaVanzo Report to NSGC_Final Report 9-6-16 formatted2.pdf

Hi all,

I am so sorry for taking so long to get back to you but I needed to track down some additional information to best answer your questions. Thank you for taking the time to ask these questions in the first place and please see my responses below. Happy to help clarify anything further.

- How the 1 genetic counselor per 75,000 people recommendation was developed / the source of this workforce need estimate- I have attached the workforce study here that references this number. They describe two scenarios of GCs to population ratios: 1:100,000 and 1:75,000. The 1:100,000 came out of a recommendation from a UK based genetic counseling group study. The 1:75,000 has been suggested as a better model in the US given our larger health care system, but it is, admittedly, an anecdotal suggestion. More information about this is on report page 17 of the attached document. One thing this study does mention that I forgot to factor in is the emphasis on this being clinical genetic counselors, which only makes up a portion of the genetic counseling workforce. As I layed out in my next response, there are approximately 15 FTE clinical (direct patient care) genetic counselors serving patients in Maine. If we use our population as 1.341 million then we are approximately 1 clinical genetic counselor for every 90,000 Mainers.
- How many genetic counselors are in Maine (if you know or can estimate)- In Maine we have a mix of genetic counselors that work clinically with direct patient care and a number that either do not provide direct patient care or are remotely working in patient care serving another state. In addition to better recognition for our clinical genetic counselors in Maine, if Maine was a state that licensed their genetic counselors, those who work out of state can be licensed in the state they reside, increasing the number of licensed genetic counselors for Maine.

Clinical Genetic Counselors:
MMC Cancer (also serves MaineGeneral)- 5.5 FTE
MMC Prenatal- 2 FTE
MMP Pediatrics- 4 FTE
New England Cancer Specialists (Private practice- also serves CMMC, Portsmouth, and some Mercy/Northern Lights)- 2.5 FTE
NorthernLights/EMMC- 1 FTE

Remote/Non-clinical Genetic Counselors Living in Maine:
Jackson Laboratory- 1 FTE
Invitae (CA-based)- 2 FTE
Ambry Genetics (CA- based)- 1 FTE
Broad Institute (MA-based)- 1 FTE
InformDNA (national telehealth services)- 0.5 FTE* this number may have varied due to recent layoffs
Clinical GC but working remotely for NY hospital- 1 FTE

- Whether the geographic distribution of genetic counseling services is sufficient to ensure equitable access to such counseling services for Maine's rural population (to the extent you are aware of where current genetic counselors are located). Is telehealth sufficient to remedy any in-person inequities in this regard?
  As you can see above, the vast majority of clinical genetic counselors in Maine are within the greater Portland area. We have a very underserved rural population as a result of this. I can speak to my previous experiences as part of the MMC Cancer team where we utilized telehealth services, even prior to the pandemic, to serve sites in Augusta and Belfast. Even then, clinics were sometimes only once or twice a month with up to year long wait times and geographically, this still does not reach enough Mainers. With the pandemic, many of our genetic counseling in Maine did pivot to telehealth out of necessity, but now there is a mix of who is continuing to offer this service model. For example, the NECS GCs are all still completely telehealth, the Pediatric GCs are back to only in-person, and the MMC Cancer team is a hybrid of both. While this telehealth has helped reach more Mainers, our reach is still not wide enough and often there is push back from institutions to support telehealth services for financial reasons. A huge barrier to telehealth for genetic counseling in this state is that genetic counselors cannot bill for a telehealth visit. We then have to offer this service for free, which does not support growth of genetic counseling programs and salaries for genetic counselors. Even when a genetic counselor sees a patient in-person, they still have to bill everything under a provider, sometimes requiring a physician or APP who is untrained in genetics to take time to meet with the patient as part of the visit, just so a bill can be dropped for the genetic counseling. This is an inefficient use of patient and provider time. Initiatives to support Medicare recognition of genetic counseling services and Maine specific licensure will ensure reimbursement for genetic counseling services as a whole, both in-person and virtually, so that we can continue to grow and serve our population. Until then, clinics struggle to find funding for genetic counselors and understandably, our smaller community hospitals cannot take on those salaries in their budgets the same way the larger hospitals can when they are not getting reimbursed for the services. If genetic counselors could support their own salaries with reimbursement, then both in-person and virtual services can grow across our state. Lastly, having licensure in Maine allows genetic counselors to practice at the top of their scope. When neighboring states like MA and NH license their genetic counselors, it can make it harder to recruit and retain genetic counselors in Maine. This is already a competitive job market and these are the things that may make a job in Maine appear less competitive. There were several times we had a genetic counseling position open when I was in clinic and it would take us over a year to hire.

Best regards,
Kat

On Wed, Sep 14, 2022 at 6:30 PM Huang-Saad, Aileen <a.huang-saad@northeastern.edu> wrote:

> So glad that the information was helpful
>
> I, of course, will defer this to Katherine as she is the expert in this area.
>
> Best
> aileen
>
> --
> **Aileen Huang-Saad, PhD, MBA**
> Director of Life Sciences and Engineering Programs
> Associate Professor of Bioengineering
> Northeastern University
> The Roux Institute
> 1.207.553.3925 (VoIP)
>
> Website: *https://teel.sites.northeastern.edu/*
> To make an appointment click here
> Linkedin Twitter

Stocco, Janet

From: Bogart, Molly <Molly.Bogart@maine.gov>
Sent: Wednesday, October 5, 2022 10:50 AM
To: Olson, Rachel
Cc: Stocco, Janet
Subject: RE: Another Request for Information for the Genome-editing Technology Advisory Panel

Hi Rachel –

No problem. Here you go:

1. Does MaineCare cover the cost of enrolling a patient in an out-of-state clinical trial? And, if so, under what circumstances?
    a. MaineCare does not cover the cost of enrolling a patient in an out-of-state clinical trial. However, MaineCare does cover routine patient costs associated with those trials.
2. Does MaineCare cover the cost of genetic testing? If so, under what circumstances?
    a. MaineCare does cover some genetic testing that is deemed medically necessary and approved through a prior authorization process.
3. Does MaineCare cover services/consultation with a genetic counselor in Maine? If not, would adoption of a mandatory licensing program or voluntary registration program (that checks eligibility requirements) make any difference as to whether MaineCare covers genetic counselor services?
    a. MaineCare does not currently have a mechanism for enrolling and reimbursing genetic counselors. In general, validation and/or credentials for services makes it more likely that it is possible to cover services through Medicaid.

Let me know if you have any additional questions. Thanks!

Take care,
m

Molly Bogart, Director of Government Relations
Department of Health and Human Services
Phone: (207) 592-4361 (call/text)
Email: molly.bogart@maine.gov
Pronouns: she/her

Who we serve. What we do. Who we are.

Comment related to First Advisory Panel Meeting on August 17, 2022

August 18, 2022

I would like to offer the following points to complement the presentations made during the Advisory Panel's work regarding the "Implications of genome-editing technology for the citizens of the State."

1. In Ms Waring Bateman's presentation on CRISPR she gave a brief overview of a number of elements. On one important point she did not fully portray the accuracy of CRISPR. There has been a significant literature showing a number of 'off target' effects of the technology (https://www.nature.com/articles/s41467-022-28244-5) and this is a major concern raised by people opposed to the technology. There are a number of new and ever evolving ways of making precise changes to DNA with CRISPR Cas-9 being only one and the Committee should be aware of the concerns and the rapidly evolving nature of the technology. Some of this came up in later presentations but only incidentally
2. Left undiscussed was the presence of community labs practicing DIY synthetic biology (https://neo.life/2022/04/the-synthetic-biology-community-builder/). There is a big push – including from institutions in Massachusetts – to democratize the technology. The Committee's deliberations should be informed by these efforts and consideration of ways of encouraging in Maine research in non-traditional university, research labs, and companies.
3. Related to this and treated only incidentally by the Committee in the first meeting is the rise of teaching of synthetic biology in public schools (https://www.bu.edu/articles/2021/jump-starting-biotechnology-careers-for-boston-high-school-students/). Not only are there serious curricula but there is also an international competition for high school to university students for the best application of synthetic biology to address real-world problems (https://igem.org). These and other initiatives might be worth consideration by the Committee to help position Maine in a more competitive position.
4. Ms Waring Bateman made only passing observations about synthetic biology applications for environmental outcomes and for treatment of diseases like malaria. Both of these topic have a rich literature and important lessons (e.g.: https://www.iucn.org/news/secretariat/201905/rewriting-genes-could-have-broad-knock-effects-nature-iucn-report and https://targetmalaria.org) for the Committee and I hope you will cover them in your next meeting.

Sincerely

Kent H. Redford

APPENDIX G

Gene Editing in the Natural World (presenter materials)

- Christopher Okonkwo, Ph.D., Assistant Professor of Biotechnology, The Roux Institute: *Genome Editing in the Natural Environment*
- Melody N. Neely, Ph.D., Associate Professor of Molecular and Biomedical Sciences, the University of Maine
- Hillary Peterson, Ph.D., Integrated Pest Management Specialist, Maine Department of Agriculture, Conservation and Forestry: *Gene Editing as a Tool in the Integrated Pest Management Toolbox for the State of Maine*
- Kent H. Redford, Ph.D., Archipelago Consulting
- Anne Langston Noll, Ph.D., Project Director, Maine Aquaculture Innovation Center

09.07.22

Genome Editing in the Natural Environment

Christopher Okonkwo, PhD
Assistant Professor, Biotechnology
The Roux Institute, Northeastern University
Portland, Maine
c.okonkwo@northeastern.edu

Genome editing can impact Maine's heritage industries

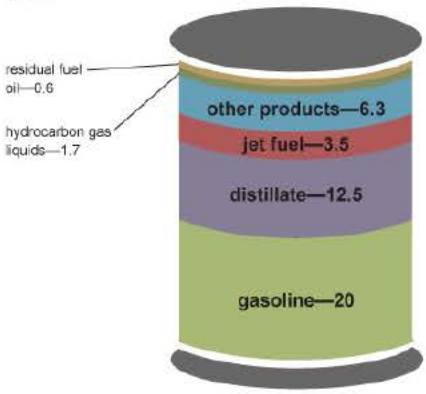
The Roux Institute
Northeastern University

Forestry Sustainable Energy

The Problem

- What will happen when the world runs out of oil?
- How will we replace the over 6,000 products made from petroleum?
- How can we mitigate the impact of fossil energy on climate?
- Are there alternative ways to produce petro-derived products?

Petroleum products made from a barrel of crude oil, 2021



Source: U.S. Energy Information Administration, *Petroleum Supply Monthly*, March 2022, preliminary data
Note: A 42-gallon (U.S.) barrel of crude oil yields about 45 gallons of petroleum products because of refinery processing gain. The sum of the product amounts in the image may not equal 45 because of independent rounding.

https://www.eia.gov/energyexplained/oil-and-petroleum-products/#tab1

The Roux Institute
Northeastern University

Forestry Sustainable Energy

The Genome Editing Solution

Exploit forest/agricultural residues as substrates for bioenergy

Edit the genomes of industrial microbial strains for efficient biofuels and biochemicals production

- Bioethanol → transportation fuel
- 2,3-Butanediol → feedstock for synthetic rubber
- 2,5-Furandicarboxylic acid → bioplastics and resins

Edit microbial genomes for carbon dioxide utilization

- Carbon dioxide conversion to bioethanol, biobutanol, etc.
- Reduction in global warming

https://www.istockphoto.com/photo/ecologist-on-fieldwork-forester-examines-trees-in-their-natural-condition-in-the-gm1323675815-409650968?phrase=forestry%20worker

Marine Plastic Bioremediation

The Problem

- It takes 50 – 450 years for plastics to decompose in the natural world
- Plastics degrade into microplastics, resulting in health consequences

The Genome Editing Solution

- With biotechnology, we can identify microorganisms that have the capacity to remove this waste and then use genome editing to improve the efficiency and capacity of plastic degradation pathways.

https://www.forbes.com/sites/rrapier/2021/09/30/the-plastic-pollution-crisis/?sh=6080985f78a5

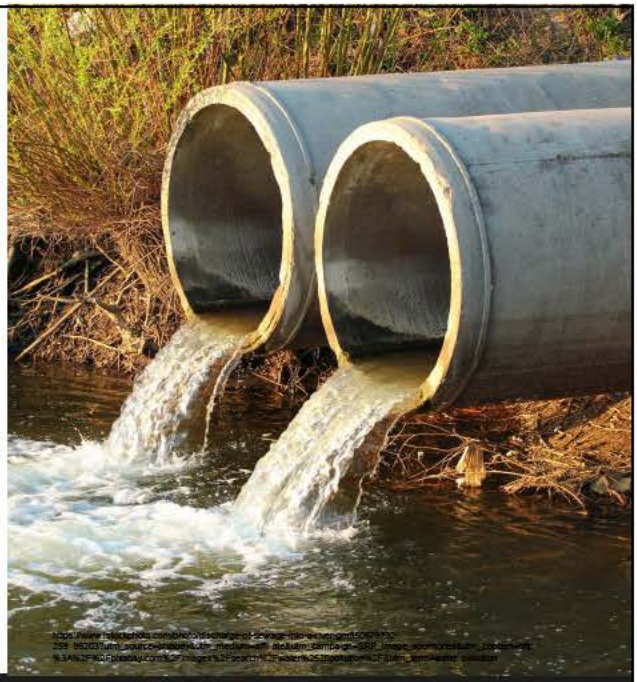
Marine Wastewater Bioremediation

The Problem

- The wastewater from anaerobic digestion results in high concentrations of ammonia, phosphorous, and heavy metals, which are environmental pollutants.

The Genome Editing Solution

- Using genomic editing, we can identify microorganisms that can remove these pollutants from the waste and make the waste safer to be released into the environment.



Ujor, V. C., Okonkwo, C. C., Rush, B. B., McCrea, G. E., & Ezeji, T. C. (2020). Harnessing the residual nutrients in anaerobic digestate for ethanol fermentation and digestate remediation using Saccharomyces cerevisiae. Fermentation, 6(2), 52.

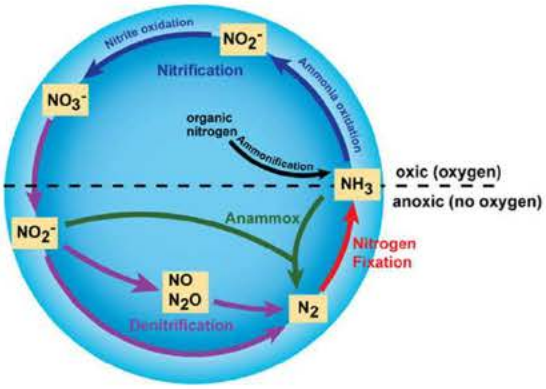
Genome editing as a solution for biological treatment of municipal/industrial wastewater

Anammox Bacteria

- Can convert organic nitrogen to atmospheric nitrogen
- Doubling time takes weeks

Saccharomyces cerevisiae **(Baker's yeast)**

- Doubling time is approximately 90 min
- Can remove phosphorus and heavy metals
- Cannot convert organic nitrogen to atmospheric nitrogen



https://www.nature.com/scitable/knowledge/library/the-n trogen-cycle-processes-players-and-human-15644632/

Agriculture Crop Resilience

The Problem

- The impact of climate change on crops, diseases, and pests results in low yield.

The Genome Editing Solution

- With genome editing, it is possible to help plants resist drought, control the impact of pests, and reduce disease, thus, increasing crop yields and productivity.

https://www.the-scientist.com/news-opinion/gene-edited-soybean-oil-makes-restaurant-debut-65590

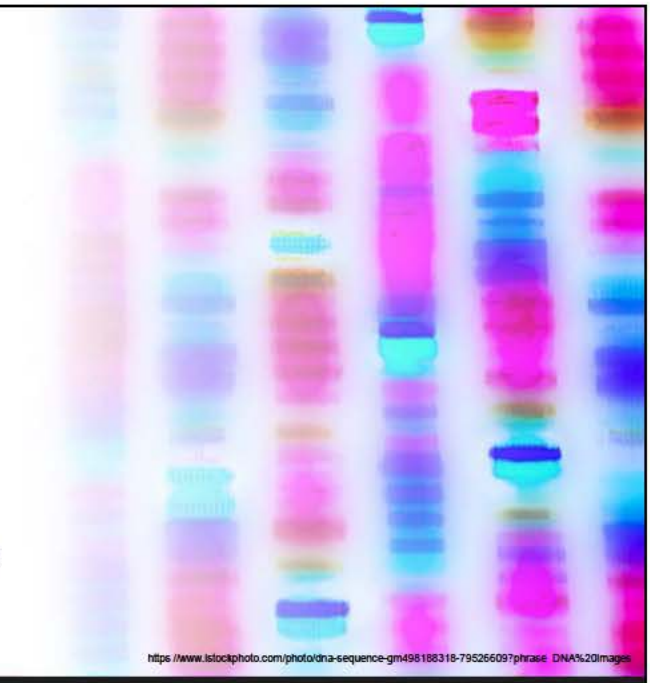
Opportunities

For society, gene editing will:

- Mitigate global warming
- Create value for forest residues in Maine
- Increase food security

For Maine, investing in genome editing will result in:

- Increased collaborations between industry and academia
- Spin-off biotech companies
- A Maine biotech hub
- Multiple future industries
- Workforce opportunities for individuals at all levels (high school diploma, Associates, Bachelors, Masters, and Doctorates)



https://www.istockphoto.com/photo/dna-sequence-gm498188318-79526609?phrase=DNA%20Images


LVX
VERITAS
VIRTVS
The Roux Institute
Northeastern University
N

Gene editing examples to benefit Maine industry

Potatoes

CRISPR/Cas Genome Editing in Potato: Current Status and Future Perspectives, Jagesh Kumar Tiwari1 et al Front Genet 13:827808

Blueberries

Blueberry fooled into flowering. Surridge, C., Nat. Plants 5, 910 (2019). https://doi org/10 1038/s41477-019-0520-y

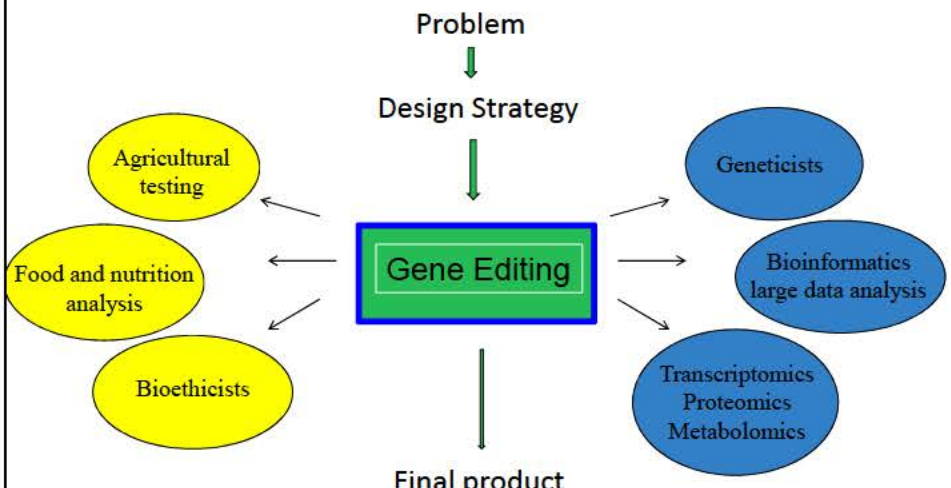
Zebrafish

Aquaculture

A Sterile Solution: How CRISPR Could Protect Wild Salmon, https://research ncsu edu/ges/2021/07/a-sterile-solution-how-crispr-could-protect-wild-salmon/

THE UNIVERSITY OF MAINE

Multidisciplinary Research Consortium



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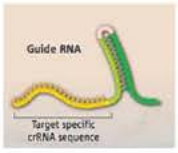
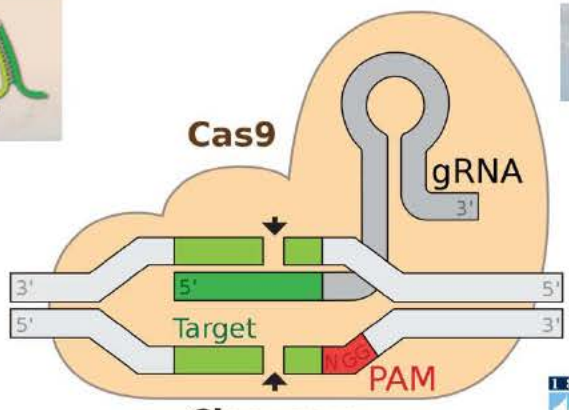
Gene editing using CRISPR

clustered regularly insterspaced short palindromic repeats



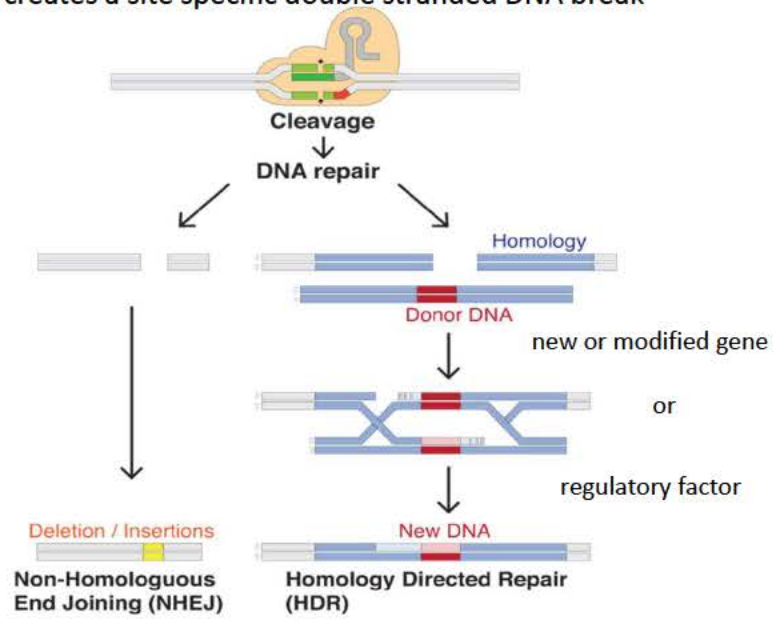


Cleavage

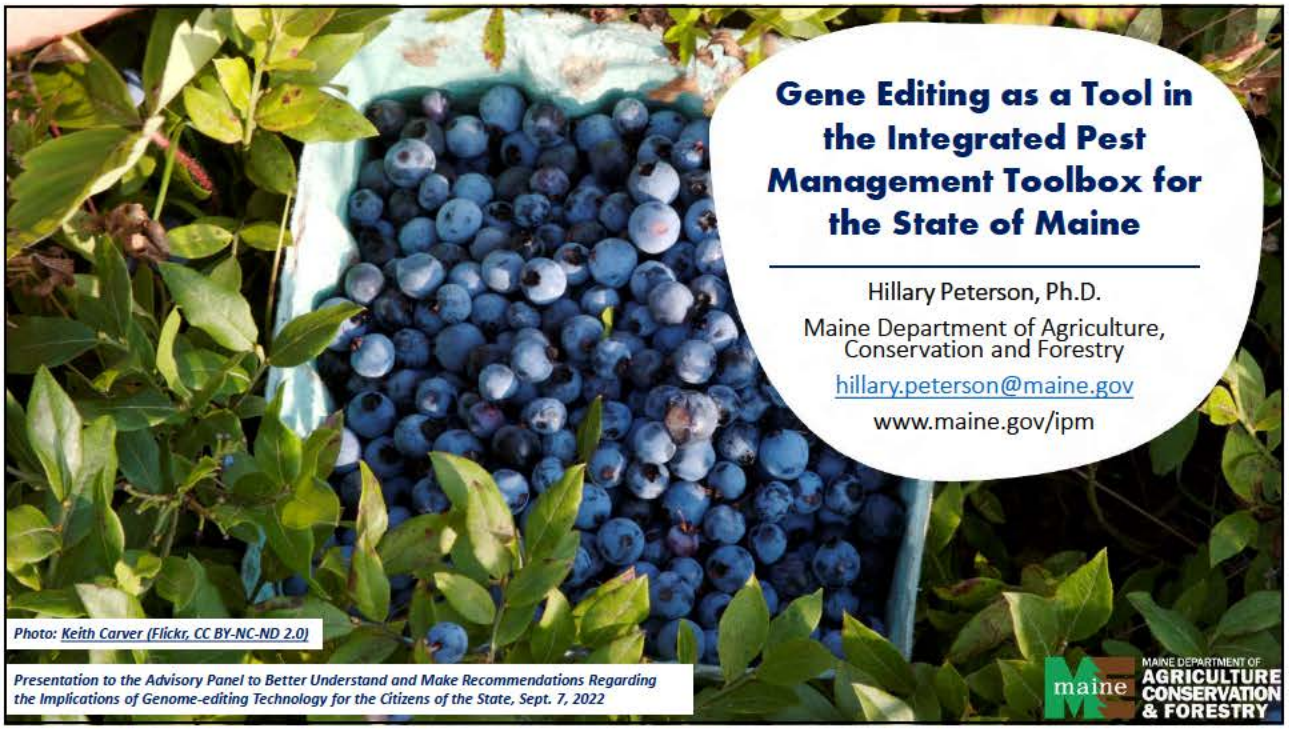
Cas enzyme – site directed nuclease
creates a site specific double stranded DNA break

https://en wikipedia org/wiki/CRISPR_gene_editing

Cas enzyme – site directed nuclease
creates a site specific double stranded DNA break



https://commons wikimedia org/w/index php?curid=103390868



Gene Editing as a Tool in the Integrated Pest Management Toolbox for the State of Maine

Hillary Peterson, Ph.D.
Maine Department of Agriculture, Conservation and Forestry
hillary.peterson@maine.gov
www.maine.gov/ipm

Photo: Keith Carver (Flickr, CC BY-NC-ND 2.0)

Presentation to the Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, Sept. 7, 2022

maine MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Integrated Pest Management (IPM)

maine MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Integrated Pest Management

Gene editing can fit within the many pieces of an integrated pest management program, which aids in the reduction of pesticide use

There is no set policy or position within ME DACF.

What is Integrated Pest Management (IPM)

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Maine Wild Blueberries

- Predictable Pests, Pathogens & Weeds
- Invasive Species
- Growth Conditions
- Pollination
- Pruning
- Harvest & Sanitation

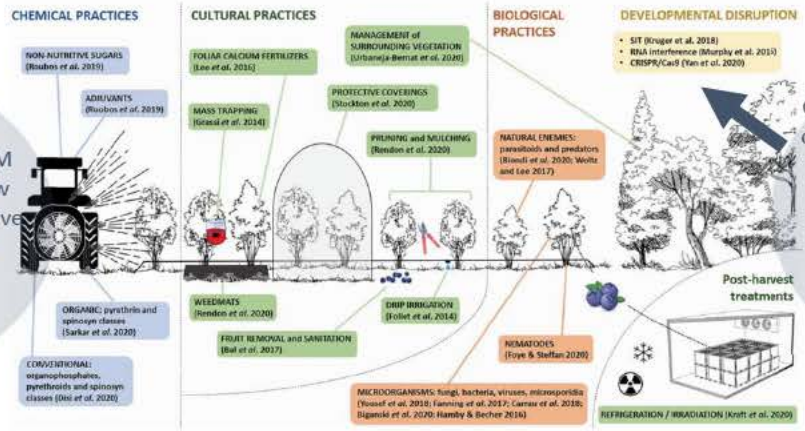
Integrated Pest Management

A system that combines several methods to prevent and mitigate pest related problems in an integrated and biologically based manner.

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Gene editing fits within the many pieces of an integrated pest management program

Recent drafted IPM plan from a review paper on the invasive spotted winged drosophila



CRISPR/Cas9 mediated disruption of the white gene leads to pigmentation deficiency and copulation failure in *Drosophila suzukii*

Figure: Tait et al. 2021 (Open Access Review Paper)

The IPM Toolbox

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

1. Set plants up for success with ideal growth conditions

Traditionally – soil conditions, plant cultivars, moisture, pH, pruning, sanitation, mulching, irrigation

2. Monitor for pests and disease and keep records

Traditionally – visual scouting, photos, notebooks or spreadsheets, calendars

3. Properly identify pests and disease before treating

Traditionally – trapping and using guides, working with taxonomists and extension experts, pest control companies

4. Mitigate pesticide use through other means

Traditionally – biological control, natural enemies, mass trapping, repelling, physical barriers; preventing with step #1

How can gene editing fit into the IPM toolbox?

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

1. Set plants up for success with ideal growth conditions

2. Monitor for pests and disease and keep records

3. Properly identify pests and disease before treating

4. Mitigate pesticide use through other means

Gene Editing & Plant Growth Conditions

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Set plants up for success with ideal growth conditions

Traditionally:
soil conditions, plant cultivars, moisture, pH, pruning, sanitation, mulching, irrigation

Photosynthesis hack boosts soybean yield 20%

RIPE researchers prove bioengineering better photosynthesis in for the first time ever

PUBLISHED ON AUGUST 25, 2022

CRISPR–Cas9-based genetic engineering for crop improvement under drought stress

Abdul Sami, Zhao Xue, Saheera Tazein, Ayesha Arshad, Zong He Zhu, Ya Ping Chen, Yue Hong, Xiao Tian Zhu & Ke Jin Zhou

Application of Gene Editing for Climate Change in Agriculture

Review Article | Open Access | Published: 15 June 2019

CRISPR technology is revolutionizing the improvement of tomato and other fruit crops

Tian Wang, Hongyan Zhang & Hongliang Zhu

Horticulture Research 6, Article number: 77 (2019) | Cite this article

The Cold-Regulated Genes of Blueberry and Their Response to Overexpression of *VcDDF1* in Several Tissues

Aaron Walworth and Guo-qing Song*

Author information • Article notes • Copyright and License information Disclaimer

Genome Editing in Potato with CRISPR/Cas9

Satya Swathi Nadakuduti [1], Colby G Starker [2], Daniel F Voytas [2], C Robin Buell [3 4 5], David S Douches [6 4]

Gene Editing & Mitigating Pests

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Mitigate pesticide use through other means

Traditionally:
biological control, natural enemies, mass trapping, repelling, physical barriers

CRISPR/Cas9 mediated genome engineering in Drosophila

Andrew Bassett [1], Ji-Long Liu [2]

CRISPR/Cas9 mediated disruption of the *white* gene leads to pigmentation deficiency and copulation failure in *Drosophila suzukii*

Ying Yan [a, b], Judith Ziemek [a], Marc F. Schetelig [a, b]

Temperature-dependent sex-reversal by a *transformer-2* gene-edited mutation in the spotted wing drosophila, *Drosophila suzukii*

Jianwei Li & Alfred M. Handler

RESEARCH ARTICLE | Open Access

Resilin* is needed for wing posture in *Drosophila suzukii

Steven Lerch, Yang Yang, Justin Flaven-Pouchon, Nicole Gehring, Bernard Moussian

Oral RNAi to control *Drosophila suzukii*: laboratory testing against larval and adult stages

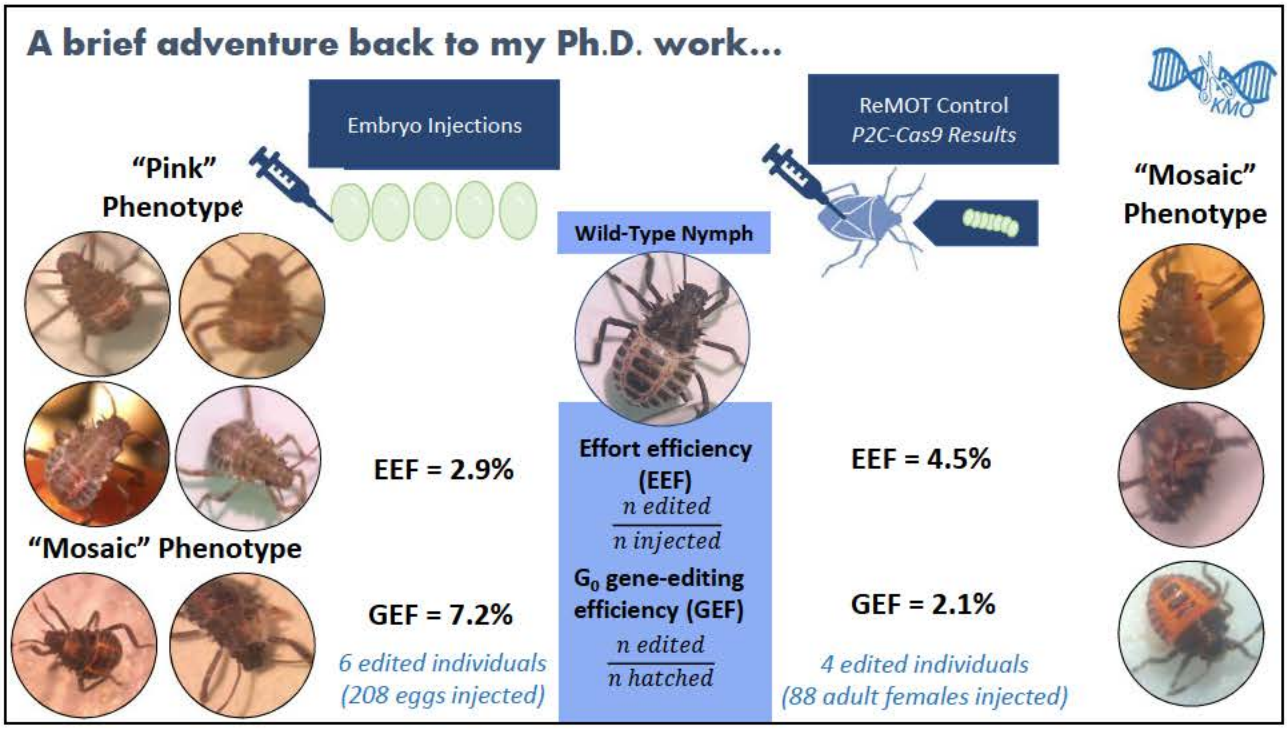
Clauvis Nji Tizi Taning, Olivier Christiaens, Nick Berkvens, Hans Casteels, Martine Maes & Guy Smagghe

(not just CRISPR!)

Gene editing can fit within the many pieces of an integrated pest management program...

...including collaboration and ease of initial proof of concept testing within species...

A brief adventure back to my Ph.D. work...



How can Maine prepare?

MAINE DEPARTMENT OF AGRICULTURE CONSERVATION & FORESTRY

Remember gene-editing technology remains **one** piece of the toolbox

Support research in agriculture

Increase awareness and education while respecting many perspectives

Photo: Keith Carver (Flickr, CC BY-NC-ND 2.0)

Testimony for Topic 2: Gene-editing in the Natural World

Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Testimony of Kent H. Redford
Archipelago Consulting
Portland, Maine
September 1, 2022

1. Brief background of relevant experience

I have a PhD in ecology and have spent 40 years in conservation, based in a university, NGOS (TNC and WCS) and most recently as an independent practitioner and consultant[1]. I have spent the last ten years working on the intersection between conservation and synthetic biology. The first major effort was a meeting in Cambridge, UK that for the first time brought together people from both of these two areas.[2] I was then asked by the International Union for Conservation of Nature (IUCN) to chair and put together a working group to examine the intersection of conservation and synthetic biology that resulted in a Technical Assessment[3], several international presentations and a resolution voted on at the World Conservation Congress in France last year. Most recently, with my colleague Bill Adams we published a book on the topic, "Strange Natures. Conservation in the era of synthetic biology."[4]

2. Key Messages from International Union for Conservation of Nature's Task Force on Synthetic Biology and Biodiversity Conservation (edited by KHR)[5]

Part of the IUCN Task Force work referred to above was production of a set of key messages for policy makers. I include an edited version of these as part of my testimony as they were written for policy makers and provide an appropriate summary of the work of the group as well as providing important background material for the Committee's deliberations.

1. Conservation implications

Synthetic biology has important implications for the conservation and sustainable use of biological diversity that are both direct and indirect. While most synthetic biology products are not designed as conservation applications, some of these will nonetheless have substantial impacts on conservation practices and outcomes.

2. New tools

New tools are needed for effective conservation and sustainable use of biological diversity. In recent years, global, regional and national measures promoting biodiversity

[1] Archipelago Consulting: https://archipelagoconsulting.com
[2] https://www.cambridge.org/core/journals/oryx/article/synthetic-biology-and-the-conservation-of-biodiversity/3FADF2D127D8F61389946FD3BBC3CA4C
[3] https://portals.iucn.org/library/node/48408
[4] https://yalebooks.yale.edu/book/9780300230970/strange-natures/
[5] https://portals.iucn.org/library/sites/library/files/documents/2019-012-En-Syn_0.pdf

conservation have resulted in some successes, but biodiversity continues to decline globally. Biodiversity conservation requires the continued application of proven approaches but scaling these efforts up to the level necessary to reverse the declines will continue to be a major challenge, given the seemingly intractable nature of some of the threats. Some synthetic biology applications, if appropriately designed and targeted, could enhance biodiversity conservation, for example, by mitigating threats and increasing species' resilience to them.

3. Rapid growth
The practice of synthetic biology is increasing rapidly, with major developments being promised and some delivered across multiple sectors. Over the last 15 years there has been a five-fold growth in companies with public and private investment approaching US$ 10 billion over this period. Synthetic biology labs are found throughout the world in academic, corporate and non-traditional spaces like community biotech labs; increasingly young people are being taught to use these technologies. The distributed nature of access to synthetic biology techniques presents both opportunities and challenges for the conservation community.

4. Beneficial conservation impacts
Synthetic biology may be beneficial to conservation and sustainable use of biodiversity. For example, by protecting threatened species against disease or climate threats, eradicating invasive species, increasing genetic diversity in small populations of threatened species, restoring a proxy of an extinct species, remediating degraded ecosystems, or product replacement.

5. Detrimental conservation impacts
Synthetic biology may be detrimental to conservation and sustainable use of biodiversity. Detrimental effects may stem from the movement of genes, or escape of engineered gene-drive-carrying organisms, impacting non-target populations or species, changes to ecological roles played by target organisms, broader ecosystem effects, product replacement that exacerbates a conservation problem, socio-economic effects of product replacement on livelihoods and on production and consumption patterns, distracting funding from other conservation approaches, and moral hazard reducing the urgency and importance of biodiversity conservation

6. Values and worldview
Values, worldviews, and lived experiences influence the development, assessment and governance of synthetic biology. Thus, to produce evidence for conservation-relevant decision making, scientific methods and norms operate within contexts defined by the framing of problems and solutions, the integration of multiple perspectives and types of expertise, and who is trusted to produce credible knowledge Community and stakeholder engagement have been proposed to help navigate this complexity.

7. Indigenous and local communities
Indigenous and local communities are key actors in research, governance and decisions around synthetic biology for conservation. Synthetic biology has potentially significant positive and negative impacts on local and indigenous communities, which manage,

govern, reside in or depend on a large part of the world's biodiversity. Historically there has been limited engagement with indigenous and local communities at both the project and global level. Recently there have been calls for recognition of the rights of indigenous and local communities in decision making around synthetic biology and engineered gene drive. There have been some attempts to involve them in synthetic biology initiatives

8. Governance
Multiple existing governance structures are relevant to synthetic biology, but synthetic biology and engineered gene drive raise questions and challenges for these frameworks. Relevant governance frameworks include international, regional and national legal frameworks as well as religious, customary and indigenous governance systems, and scientific norms and practices. Challenges relate to the extent to which current and future synthetic biology and gene drive applications are covered by existing regulations, norms and processes, implementation and enforcement in the context of accessibility of parts and tools, different levels of governance capacity among jurisdictions, mechanisms to address environmental harm, particularly transboundary impacts, and the ability of governance frameworks to keep up with the rapid pace of technological innovation

3. "What should the State of Maine do regarding gene editing within your field in order to best benefit Mainers in the next 5 years?

I would suggest that the Committee consider the following as loci of action within the next 5 years:

1. Create training experiences for students in middle and high school. Numerous curricula exist and public schools in other states (perhaps Maine as well?) are actively involved in teaching students[6]. These courses would not be just about the technology itself but also about the important governance and ethical issues surrounding potential uses of synthetic biology.
2. Create incentives, if they do not exist, to create teams for high schools and colleges to field iGEM teams to participate in regional, national and global iGEM jamborees[7].
3. Create or incentivize a network of business in the State using synthetic biology and publicize their work to draw other businesses to Maine.
4. Look into the USDA's pending decision on whether to allow genetically altered chestnuts to be planted outside of experimental plots in order to recreate native chestnut forests[8]. If approved, there is work going on at UNE by Professor Klak that might facilitate planting of chestnuts in Maine. Consider if this is something that the Penobscot might want to consider on their lands.
5. Conduct a State-wide poll that uses carefully developed educational materials to assess the citizens' opinions and concerns about possible uses of synthetic biology.[9]

[6] See for example: https://biobuilder.org/education/for-teachers/
[7] https://jamboree.igem.org
[8] https://allianceforscience.cornell.edu/blog/2020/08/usda-to-decide-fate-of-american-chestnut-restoration/
[9] For example see: https://www.liebertpub.com/doi/full/10.1089/genbio.2022.0024

6. Create a citizen panel to evaluate possible uses of synthetic biology applications in agriculture and conservation.
7. Create incentives for development and deployment of industrial uses of synthetic biology – perhaps involving a retooling of parts of the forestry industry.

4. "What should the State of Maine do regarding gene editing within your field in order to best benefit Mainers over the next generation?"

I would suggest that the Committee consider the following as loci of action within the next generation:

1. Continue with the previous 7 suggestions.
2. Create and fund an active research program that would examine the potential of synthetic biology to help in nature-based solutions[10] including carbon sequestration.

Thank you for the opportunity to make this contribution and I stand ready to provide additional information to the Committee if useful.

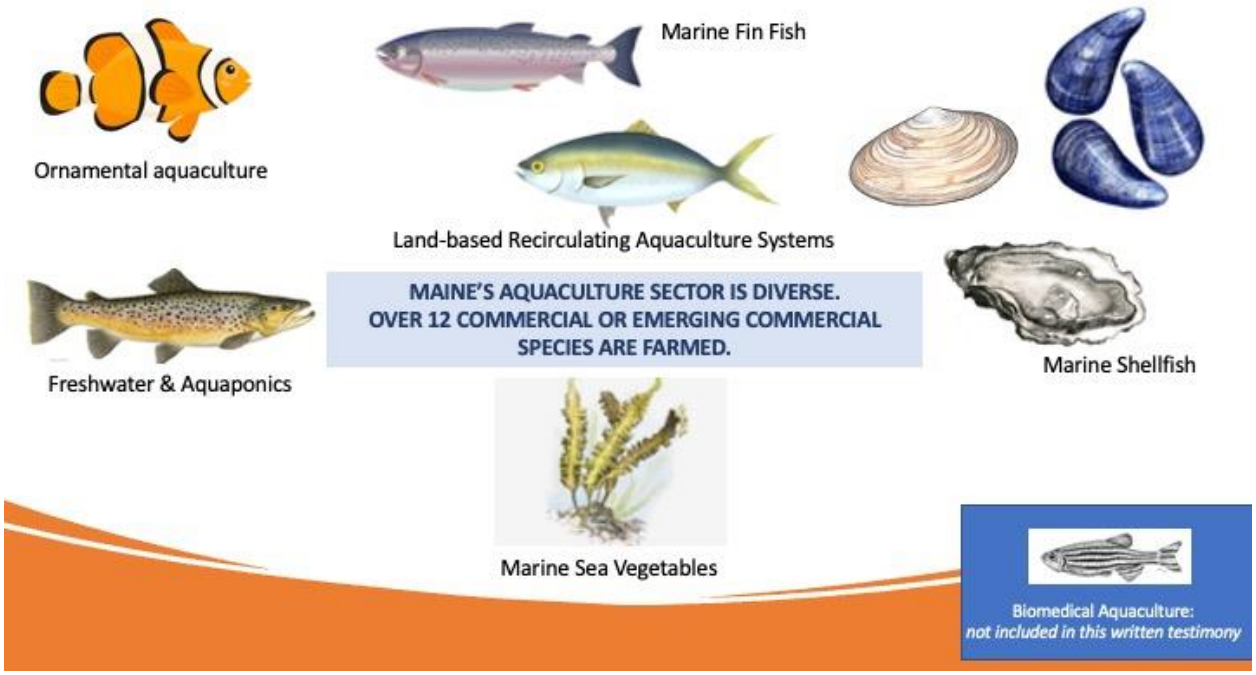
[10] https://www.iucn.org/our-work/nature-based-solutions

Written Testimony to the *Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State* from the Maine Aquaculture Innovation Center.

September 13, 2022

Prepared by: Anne Langston Noll, PhD, Project Director, Maine Aquaculture Innovation Center (MAIC)

MAINE'S AQUACULTURE SECTOR



POTENTIAL RISKS AND CONCERNS FOR MAINE'S AQUACULTURE SECTOR

Concerns currently outweigh enthusiasm for genome-editing technology in Maine's aquaculture sector (no matter whether that is cisgenic - DNA only from the same species - or transgenic - DNA from other species - genome-editing). It is currently illegal to commercially culture any transgenic aquatic animals in Maine.

Perceived, or potential risks may include:

- Unintended, off-target effects (pleiotropic effects),
- Non-clarification of trait-related genes,
- Negative public perception,
- The negative impact genome-editing technology could have on the reputation of Maine's seafood acceptance.

POTENTIAL OPPORTUNITIES FOR MAINE'S AQUACULTURE SECTOR

Important research tool: Even if never deployed into commercial practice, genome-editing technology has a very important role to play in aquaculture research. The technology will be revolutionary for advancing knowledge of the biology of our farmed aquaculture species, diseases and pests, impacts of climate change, and much more.

An alternative to selective breeding: Classical, selective breeding is a key component of domestication of farmed species. The selection for improved growth rates, disease resistance and increased quality have been important for Maines aquaculture sector. Selective breeding has been successful in Maine for responding to disease challenges (oysters and salmon) selecting strains that grow well in cold-water (oysters and salmon), and selecting strains that are of high value (ornamental fish).

In certain cases there may be limitations to what selective breeding can achieve; for example it is limited by the heritability of the trait we are attempting to select for, the generation interval of the species and the genetic variation which exists within farmed stocks. However, genome editing does offer the potential to expedite the selective breeding process and select for traits beyond yield and disease resistance. Genome-editing could accelerate our ability to select for traits that allow farmers to :

- Increase aquaculture productivity to meet increasing demands for high quality protein,
- combating pest and disease pressures,
- improving animal welfare,
- adapting to climate change, and
- Reduce potential environmental impact.

Sterility: Genome-editing technology has the potential for producing sterile plants and animals.

WHAT SHOULD THE STATE OF MAINE DO REGARDING GENOME-EDITING WITHIN AQUACULTURE IN ORDER TO BEST BENEFIT MAINERS IN THE NEXT 5 YEARS?

Commission a study to fully understand the current state of the science around the use of genome editing in aquatic animal and plant species. This study should include a review of the techniques, their benefits and potential risks, and the policies and regulations other jurisdictions are currently using to manage these benefits and potential risks.

SUGGESTED REFERENCES FOR FURTHER INFORMATION

- Gratacap et al. 2019. Potential of genome editing to improve aquaculture breeding and production. *Trends in Genetics*. Vol. 35; No. 9
- NASCO 2006, The Williamsburg Resolution: A Resolution by the Parties to the Convention for the Conservation of Salmon in the North Atlantic Ocean To Minimise Impacts from Aquaculture, Introductions and Transfers, and Transgenics on the Wild Salmon Stocks. Adopted in 2003, latest amendment 2006
- Okoli et al. 2022, Sustainable use of CRISPR/Cas in fish aquaculture: the biosafety perspective. *Transgenic Research*. 31:1-21
- United Nations FAO. 2022. *Gene editing in aquaculture*. Bangkok.
- Wray-Cahen et al. 2022. Advancing genome editing to improve the sustainability and resiliency of animal agriculture. *CABI Agriculture & Bioscience*. 3:21
- Yang et al. 2022. Genome editing and its implications in genetic improvement in aquaculture. *Reviews in Aquaculture*. 14: 178-191

APPENDIX H

Gene Editing in the Natural World (related materials)

- Staff memorandum on genetic engineering and organic farming and processing

MEMORANDUM

To: Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

From: Office of Policy and Legal Analysis Staff

Date: September 21, 2022

Re: **Types of genetic engineering prohibited in organic farming and processing**

At the second Advisory Panel meeting on September 7, 2022, members inquired about the types of gene-editing technologies prohibited in organic farming under applicable federal regulations.

Regulations promulgated by the U.S. Department of Agriculture's National Organic Program (NOP) direct that "To be sold or labeled as '100 percent organic,' 'organic,' or 'made with organic (specified ingredients or food group(s)),' a product must be produced and handled without the use of . . . (2) Excluded methods, except for vaccines: Provided, That, the vaccines are approved in accordance with § 205.600(a) . . .." 7 C.F.R. § 205.105(e).[1] NOP regulations define "excluded methods" as:

> A variety of methods used to genetically modify organisms or influence their growth and development by means that are not possible under natural conditions or processes and are not considered compatible with organic production. Such methods include cell fusion, microencapsulation and macroencapsulation, and recombinant DNA technology (including gene deletion, gene doubling, introducing a foreign gene, and changing the positions of genes when achieved by recombinant DNA technology). Such methods do not include the use of traditional breeding, conjugation, fermentation, hybridization, in vitro fertilization, or tissue culture.

7 C.F.R. §205.2. In 2011, the NOP issued a Policy Memorandum regarding genetically modified organisms (*attached*), explaining that inadvertent cross-contamination does not constitute a violation of the excluded methods regulations if organic producers and processers "have verifiable practices in place to avoid contact with GMOs."[2] In addition, a NOP Policy Memorandum from 2013 regarding cell fusion techniques used in seed production (*attached*) demonstrates the complexity of differentiating between emerging technologies the NOP concludes "are not possible under natural conditions" (ex: cell fusion where the donor cells are from different taxonomic plant families) and technologies the NOP concludes are permissible because they have "been a part of traditional breeding programs for many years without being considered genetic engineering" (ex: in vitro fertilization and fusion of cells from the same taxonomic plant family)."[3]

The National Organic Standards Board (NOSB), which is comprised of organic farmers and processors, scientific experts and other industry stakeholders, was established by federal law "to assist . . . in the development of standards for substances to be used in organic production." 7 U.S.C. §6518 (2022). In November 2016, the NOSB recommended that the NOP "develop a formal guidance document for the determination and listing of excluded methods." This recommendation, which has been refined several times but has not been adopted by the NOP, establishes four criteria to determine whether specific methods should be included in a table of excluded methods developed by the NOSB. The most recent NOSB recommendations (from April 28, 2022) regarding its proposed excluded methods table are attached.[4]

---

[1] *See also* 7 C.F.R. § 205.301(f) ("All products labeled as "100 percent organic" or "organic" and all ingredients identified as "organic" in the ingredient statement of any product must not: (1) Be produced using excluded methods . . .."); 7 C.F.R. § 205.670(b) (If there "is reason to believe that [an] agricultural input or product has come into contact with a prohibited substance or has been produced using excluded methods," "preharvest or post harvest testing" may be required).

[2] *Available at* https://www.ams.usda.gov/sites/default/files/media/OrganicGMOPolicy.pdf.

[3] *Available at* https://www.ams.usda.gov/sites/default/files/media/NOP-PM-13-1-CellFusion.pdf.

[4] *Available at* https://www.ams.usda.gov/sites/default/files/media/MSExcludedMethodsFinalRecApril2022.pdf.

APPENDIX I

Gene Editing and the Humanities (presenter materials)

- Kate McBrien, Maine State Archivist*: Malaga Island & Eugenics*

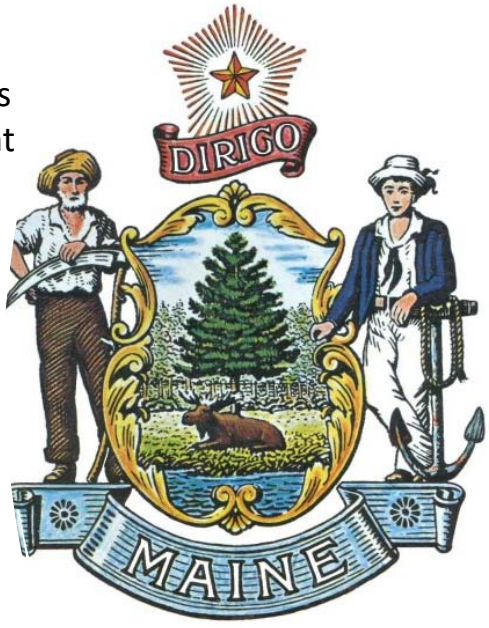
Malaga Island & Eugenics

Kate McBrien
Maine State Archivist

1

The Maine State Archives is **critical** to a transparent State Government.

Archives document the critical functions of government, protect citizens' rights, enhance civic engagement, improve cultural knowledge and understanding, and ensure transparency and accountability of public officials.



2

Malaga Island,
Phippsburg, ME

3

A small fishing community of multi-race families lived on Malaga Island from around 1863 until 1912, when the State of Maine evicted them from their homes.

4

A PICTURESQUE HARBOR and home of "Ex-King" McKinney on Malaga Island, which is now owned by the State of Maine. (See other side.) A 699

5

6

Missionaries operated a school on Malaga Island in 1906.
The State opened a school building on the island in 1908.

7

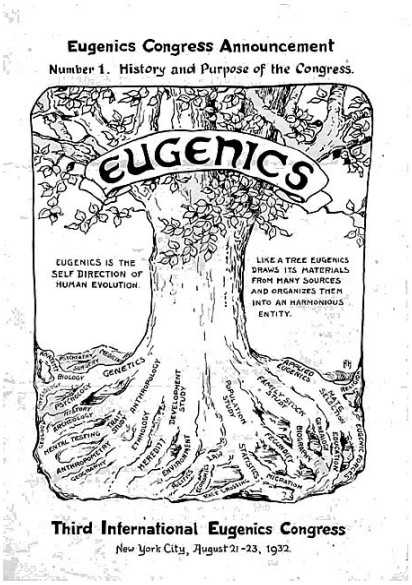
Executive Council report 1911-1912

After viewing conditions it was decided at a Council meeting shortly after, that the good of the State and the cause of humanity demanded that the colony be broken up and the people segregated. The inhabitants then numbered about 56, a large part of whom were State paupers. It was decided that to rid the Island of its population, and to prevent further squatting that the State should hold a title to the property. The owners of the Island had endeavored to rid it of its inhabitants, and after an expenditure of $71, abandoned the idea.

8

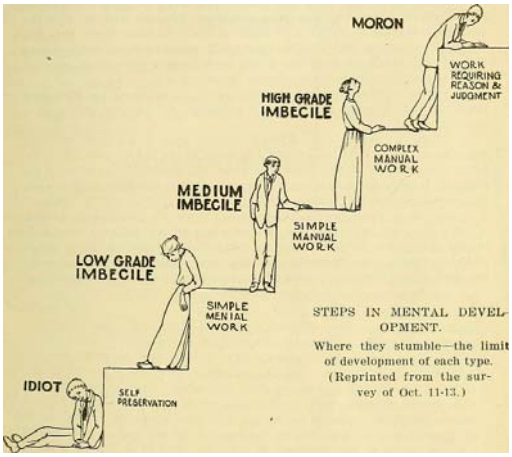
What is Eugenics?

Eugenics is the study of how to arrange reproduction within a human population to increase the occurrence of heritable characteristics regarded as desirable.



9

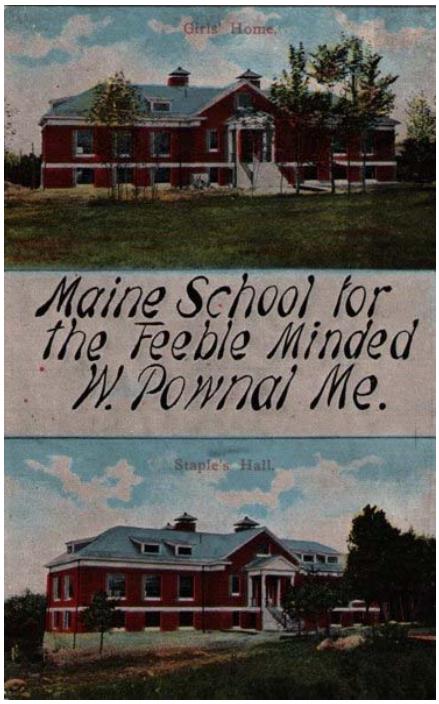
Feeble-Minded



In many states, including Maine, the application of Eugenics focused on the control of those individuals deemed "feeble minded".

10

- **1903:** Maine State Legislature appointed a committee to look into the "advisability of establishing a Home for the Feeble-minded of the State"
- **1908:** Maine School for the Feeble Minded opened, modeled after the Massachusetts School for the Feeble-Minded in Waverly, MA
- **1911**: residents of Malaga Island institutionalized in the Maine School for the Feeble Minded



11

Report of the Maine Commission for the Study of the Feebleminded, 1917-1918

- Appointed by Governor Carl E. Milliken 1917
- "Whereas, a study and survey of the conditions and needs would materially assist a future Legislature in determining a policy to be pursued in the matter"
- Conducted a survey of potential feebleminded individuals in the State
- Included 10 case studies of Maine families

12

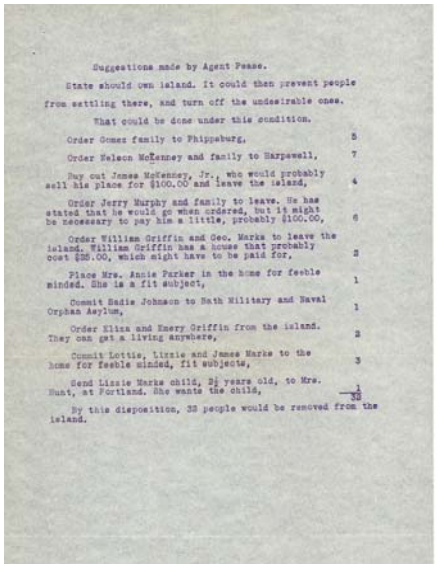
Commission recommendations:

"Broadly stated, the sociological need of the inhabitants of Maine is that her well equipped citizens work together to formulate and attack certain definite social and economic problems. The intellectual and moral standards of the State's inhabitants as a whole may be advanced faster and their efficiency be increased by seeking to humanly diminish the burden of feeblemindedness."

You can view the entire report on the Internet Archive here: https://archive.org/details/reportofmainecom00nati/page/n7/mode/2up

13

Executive Council reports, 1911



Suggestions made by Agent Pease.

State should own island. It could then prevent people from settling there, and turn off the undesirable ones.

What could be done under this condition.

Order Gomez family to Phippsburg, 5

Order Nelson McKenney and family to Harpswell, 7

Buy out James McKenney, Jr., who would probably sell his place for $100.00 and leave the island, 4

Order Jerry Murphy and family to leave. He has stated that he would go when ordered, but it might be necessary to pay him a little, probably $100.00, 6

Order William Griffin and Geo. Marks to leave the island. William Griffin has a house that probably cost $35.00, which might have to be paid for, 2

Place Mrs. Annie Parker in the home for feeble minded. She is a fit subject, 1

Commit Sadie Johnson to Bath Military and Naval Orphan Asylum, 1

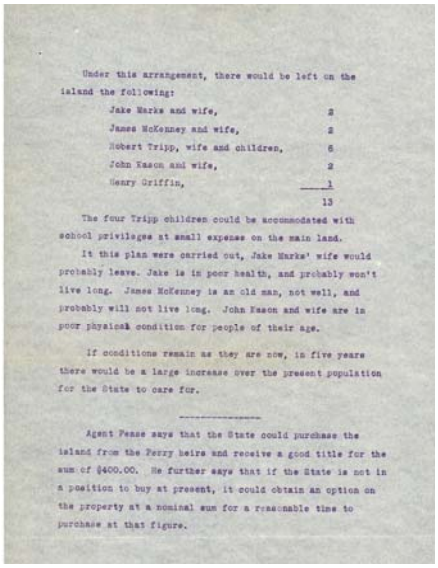
Order Eliza and Emery Griffin from the island. They can get a living anywhere, 2

Commit Lottie, Lizzie and James Marks to the home for feeble minded, fit subjects, 3

Send Lizzie Marks child, 2½ years old, to Mrs. Hunt, at Portland. She wants the child, 1

13

By this disposition, 33 people would be removed from the island.



Under this arrangement, there would be left on the island the following:

Jake Marks and wife,	2
James McKenney and wife,	2
Robert Tripp, wife and children,	6
John Kason and wife,	2
Henry Griffin,	1
	13

The four Tripp children could be accommodated with school privileges at small expense on the main land.

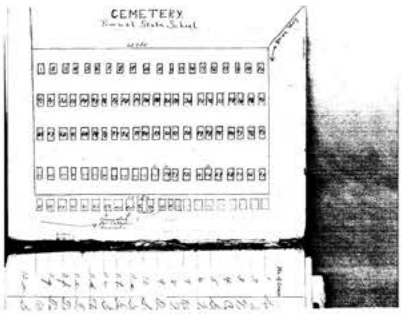
If this plan were carried out, Jake Marks' wife would probably leave. Jake is in poor health, and probably won't live long. James McKenney is an old man, not well, and probably will not live long. John Kason and wife are in poor physical condition for people of their age.

If conditions remain as they are now, in five years there would be a large increase over the present population for the State to care for.

Agent Pease says that the State could purchase the island from the Perry heirs and receive a good title for the sum of $400.00. He further says that if the State is not in a position to buy at present, it could obtain an option on the property at a nominal sum for a reasonable time to purchase at that figure.

14

Pineland Cemetery



Removed from Malaga buried Nov. 1912

- 11a Rufus G ff n
- 11b Ha y G ff n
- 11c T my G ff n
- 11d Th ee Easton ch ld en (Names unknown)
- 11e Calv n T pp (ch ld en of Lau a T pp)
- 11f Lau a T pp (ch ld en of Lau a T pp)
- 11g Two G ff n ch ld en (no names)
- (fathe , Hen y G ff n)
- 12a Roxanna G ff n
- 12b Ellen G ff n
- 12c Lucy G ff n Johnson
- 13 El zabeth Da l ng
- 14 Hannah Ma ks
- 15a Geo ge G ff n
- 15b Ha old Mu phy

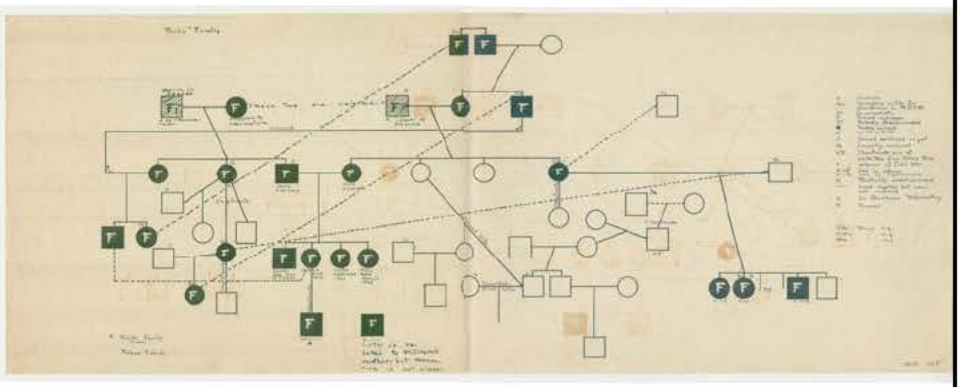
6. Jake Ma ks	Jan. 1912
8. James Ma ks	May 25, 1912
18. Ann e Pa ke	May 30, 1916
39. W l am Gomez	Nov. 17, 1919
41. L zz e Ma ks	Dec. 15, 1921
64. Etta Ma ks	Jan. 26, 1925
80. W l am A. Ma ks	Ap l 13, 1928

15

Marks family, Malaga Island

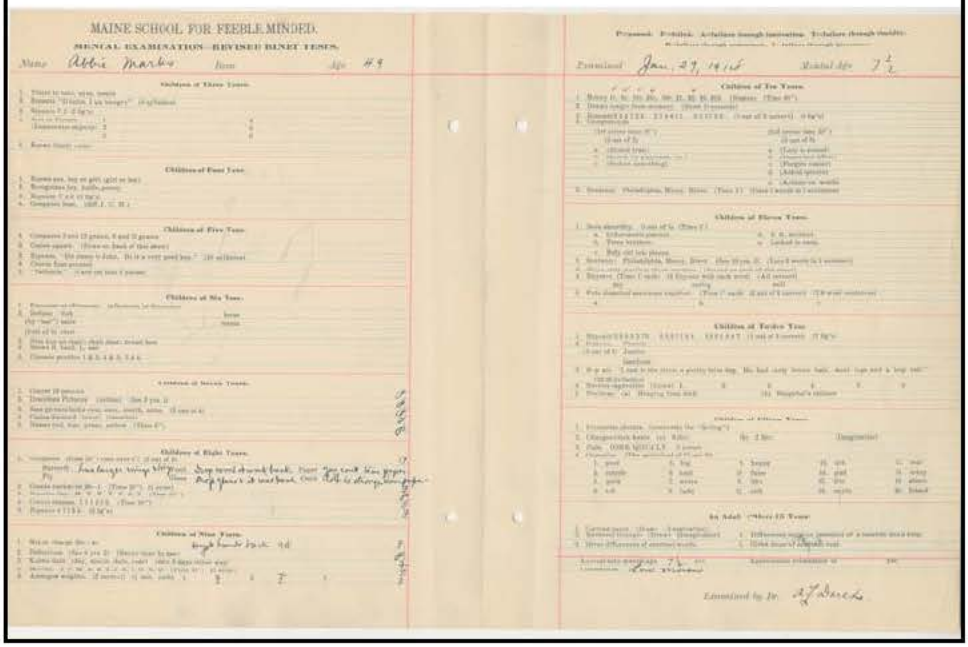
16

Eugenics chart for Marks family



17

Medical classification for Abbie Marks: "Low Moron"


MAINE SCHOOL FOR FEEBLE-MINDED.

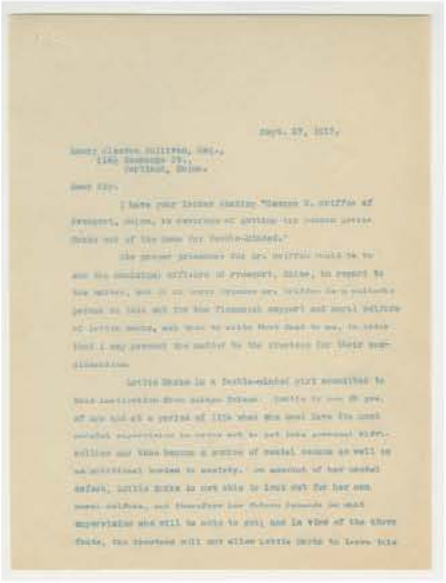
MENTAL EXAMINATION—REVISED BINET TESTS.

Name Abbie Marks Item Age 19

Examined Jan. 29, 1916 Mental Age 7 2

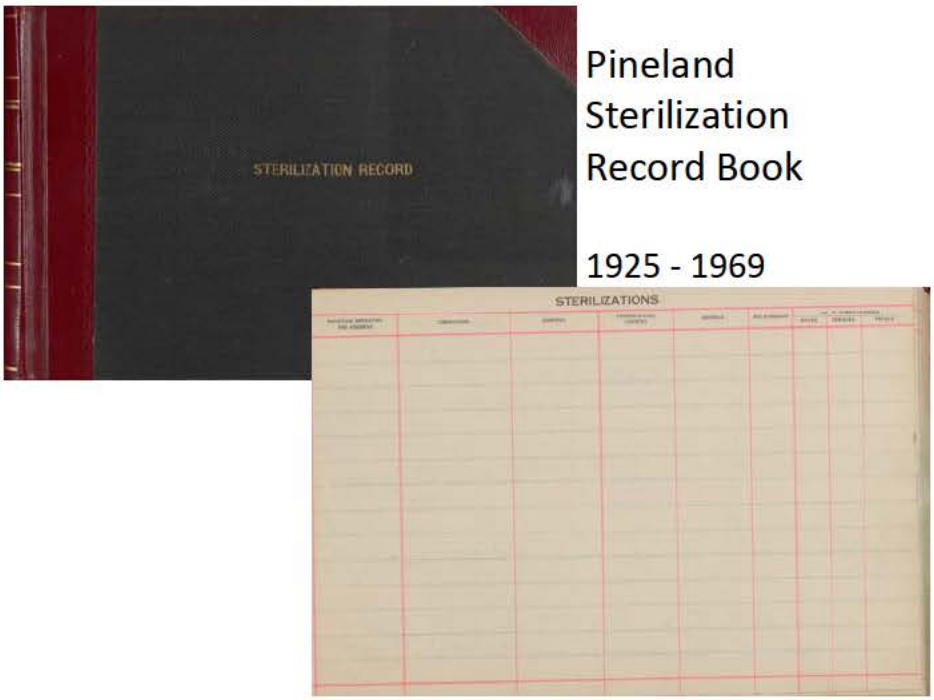
Examined by Dr. A. J. Beck

18



"Dear Sir:
... Lottie Marks is a feeble-minded girl committed to this institution from Malaga Island. Lottie is now 23 yrs. Of age and at a period of life when she must have the most careful supervision in order not to get into personal difficulties and thus become a burden to society. On account of her mental defect, Lottie Marks is not able to look out for her own moral welfare, and therefore her future depends on what supervision she will be able to get..."

19



Pineland Sterilization Record Book

1925 - 1969

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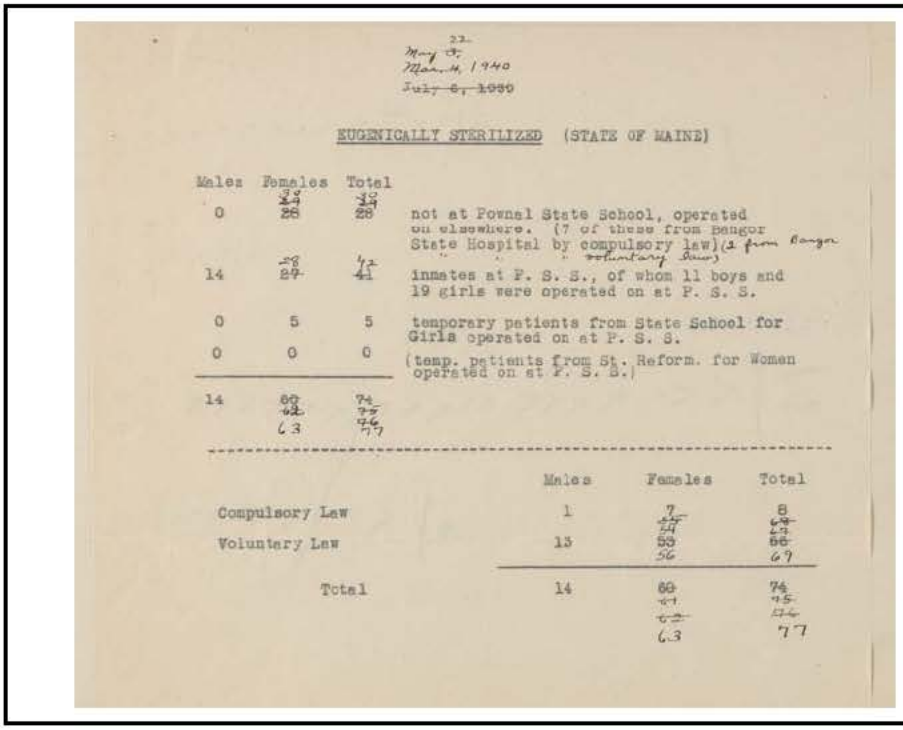


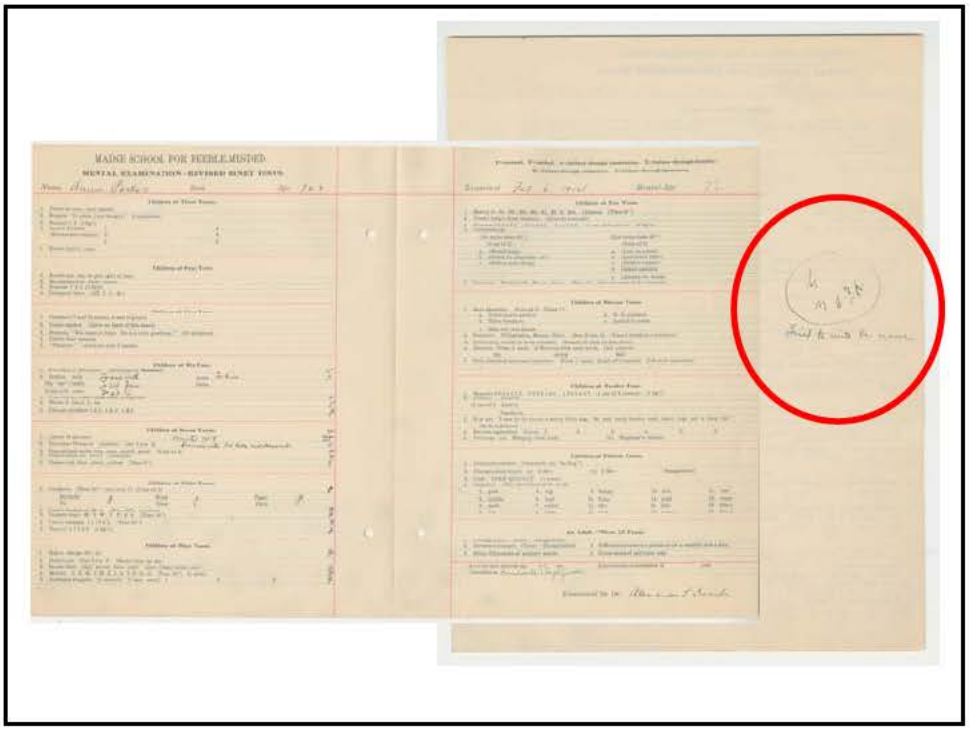
22.
May 6,
March 1, 1940
July 6, 1939

EUGENICALLY STERILIZED (STATE OF MAINE)

Males	Females	Total	
0	~~26~~ 25	~~29~~ 25	not at Pownal State School, operated on elsewhere. (7 of these from Bangor State Hospital by compulsory law)(2 from Bangor voluntary laws)
14	~~28~~ 27	~~42~~ 41	inmates at P. S. S., of whom 11 boys and 19 girls were operated on at P. S. S.
0	5	5	temporary patients from State School for Girls operated on at P. S. S.
0	0	0	(temp. patients from St. Reform. for Women operated on at P. S. S.)
14	~~60~~ ~~62~~ 63	~~74~~ ~~75~~ ~~76~~ 77	

	Males	Females	Total
Compulsory Law	1	~~7~~ ~~5~~ ~~4~~	~~8~~ ~~6~~ ~~7~~
Voluntary Law	13	~~53~~ 56	~~66~~ 69
Total	14	~~60~~ ~~61~~ ~~62~~ 63	~~74~~ ~~75~~ ~~76~~ 77

21



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APPENDIX J

Gene Editing and the Humanities
(related materials)

- Staff memorandum on the Malaga Island legislative apology and scholarship fund

MEMORANDUM

To: Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

From: Office of Policy and Legal Analysis Staff

Date: October 19, 2022

Re: **Malaga Island Legislative Apology and Scholarship Fund Information**

At the third Advisory Panel meeting on September 21, 2022 members inquired whether the State of Maine had issued an apology for the actions surrounding the expulsion of the residents of Malaga Island, Maine. Additionally, members expressed an interest in learning more about the scholarship fund for descendants of Malaga Island residents that was mentioned during the presentation by Kate McBrien.

Governor John Baldacci offered an apology to the descendants of Malaga on September 12, 2010. In 2017 Governor Paul LePage joined others in dedicating a memorial in honor of the community of Malaga Island.

The 124th Maine Legislature adopted H.P. 1327, *Joint Resolution Recognizing the Tragic Expulsion of the Residents of Malaga Island, Maine in 1912 and Rededicating Ourselves to the Maine Ideals of Tolerance, Independence and Equality for All Peoples* on April 7, 2010, setting forth legislative findings related to the history of Malaga Island including the forced eviction of all Malaga Island residents by the State of Maine in 1912 and forcible relocation of many islanders to the Maine School for the Feeble Minded as well as the forced sterilization under state law of many residents of the Maine School for the Feeble Minded in 1925, and resolving:

> That We, the Members of the One Hundred and Twenty-fourth Legislature now assembled in the Second Regular Session, on behalf of the people we represent, do recognize with profound regret the tragic displacement of the Malaga islanders in 1912, in the name of the disgraced Eugenics Movement, with its overtones of prejudice against poverty, racism and stereotyping; and, while rebuking this past, rededicate the future to the ideals of tolerance, independence and equality of all peoples in our ever-changing world, which are the birthright and heritage of all proud Mainers; and rededicate ourselves as lawmakers to the social and economic justice that is the right of all peoples[.][1]

The Malaga 1912 Scholarship Fund was established in Public Law 2013, chapter 368, *An Act Making Unified Appropriations and Allocation for the Expenditures of State Government, General fund and Other Funds and Changing Certain Provisions of the Law Necessary to the Proper Operations of State Government for the Fiscal Years Ending June 30, 2014 and June 30, 2015*. (See page 204 of the PDF version of the enacted law). The initial proposal, as submitted by Governor LePage, was for "one-time funding" of $500,000 "for scholarships for descendants of former residents of Malaga Island," with the Commissioner of Education directed to award the funds to a nonprofit entity to administer the scholarship program. Prior to enactment of the budget bill, the total funding was reduced to $300,000 by the Legislature. After enactment, the Commissioner of Education selected the Maine Community Foundation to manage the scholarship program.

[1] An official copy of the text of this Joint Resolution can be found on pages S-1819 to S-1820 of the Senate Legislative Record for the Second Regular Session of the 124th Legislature, which is available at http://lldc mainelegislature.org/Open/LegRec/124/Senate/LegRec_2010-04-07_SD_pS1785-1830.pdf.

APPENDIX K

Gene Editing in Systems and Institutions (presentation materials)

- Brian Whitney, President, Maine Technology Institute
- Joan Ferrini-Mundy, Ph.D., University of Maine System Vice Chancellor for Research & Innovation and President of the University of Maine and the University of Maine at Machias: *University of Maine System Education & Research Perspective on Fostering a Vibrant Biotechnology Sector in the State*
- Dana O'Brien, President, FocusMaine
- Lon Cardon, Ph.D., FMedSci, President and CEO, The Jackson Laboratory

Maine Technology Institute
Investing in Innovation

Good morning.

Senator Claxton, Representative Zager, and esteemed members of the Advisory Panel, my name is Brian Whitney and I am the President of the Maine Technology Institute, our state's unique, public-private partnership that helps catalyze innovation in Maine.

Working with partners across the State, MTI focuses its efforts on helping to diversify and grow our economy within Maine's targeted technology sectors. Those sectors include Biotechnology, Composites & Advanced Materials, Environmental Technology, Forestry & Agriculture, Information Technology, Marine & Aquaculture, and Precision Manufacturing.

Since its creation in 1999, MTI has disbursed over $300 million across more than 3,000 distinct projects and leveraged over $1 billion in private sector matching funds. MTI remains the state's only source of private-sector-focused, R&D financing leading to new products and services, job creation and other economic benefits.

As I noted, Biotech is one of the seven targeted technology sectors in which we focus our attention. A recent report issued by the Bioscience Association of Maine demonstrated why a focus on this sector is warranted and strategic. The association's 2022 State of the Industry report revealed some wonderful sector-related data about the strengths of Maine's life sciences sector.

For example, you may or may not be aware that there are approximately 500 establishments engaged in the life sciences sector in Maine and those entities employ nearly 10,000 people. Some of the largest employers include: Idexx, Jackson Labs, Puritan Medical Products, Abbott Labs, Corning, and Covetrus. Many of these enterprises gained global recognition during the coronavirus pandemic and established Maine's life sciences sector as a key responder to the public health crisis.

Not coincidentally, the pandemic also contributed to dramatic job increases in the sector. Life science jobs in Maine grew by 42% over the last five years, outpacing total job growth in Maine.

Perhaps most surprisingly, given that Massachusetts is one of the pre-eminent hubs of life sciences activity, life science jobs in Maine grew at the fastest pace of ALL New England States over the past decade. And, average annual earnings for jobs in this sector in Maine were just under $109,000.

Maine has also been able to attract interest from federal research granting institutions, as well as private equity investors. Over the past five years, Maine has secured more than $14 million

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MAINETECHNOLOGY.ORG

in awards from the National Science Foundation (NSF) with our state's R1 top tier research university, the University of Maine, leading the way. The National Institutes of Health (NIH) has directed more than half a billion in funding to Maine during that same period, with 70% of that funding going to research efforts at the Jackson Laboratory. And, finally, Maine's life sciences companies raised nearly $267 million from 2017 – 2021 with much of that going to MTI portfolio companies like Covetrus and RockStep Solutions.

While overall the data was incredibly impressive, it also revealed areas for improvement in several spheres including the number of life sciences patents developed in Maine and our level of spending on higher education research & development (Maine ranks last in both compared to our New England counterparts).

Back in 2019, I was honored to participate in the development of Maine's ten-year economic development strategy. It rightly focused on talent and innovation as helping to move the needle in our economy. That plan included three main goals, including raising the average annual wage by 10%, increasing the value of what we sell per worker by 10%, and attracting 75,000 people to Maine's talent pool.

It emphasized that Maine ought to continue to invest in research and development to support innovation in the private and nonprofit sectors.

It also noted that Maine ought to utilize its strengths and abundant natural resources to grow and diversify its economy by developing new and innovative ways to leverage those resources. Without question, Maine's life sciences sector can and will help Maine achieve these attainable goals through continued innovation and sustained growth.

MTI's role is to encourage a more vibrant biotech sector by utilizing our state appropriation and occasional bond funds, as well as sporadic federal funding, to fund development projects in both the public and private sectors. We have been able to offer grants, loans and equity investments to nascent biotech startups, have helped fund shared-use life sciences equipment and infrastructure at our university and at co-working spaces and incubators in different parts of Maine, and have assisted in the growth of our world-renowned research organizations like the Jackson Laboratory, Mount Desert Island Biological Labs, Bigelow Laboratory, and the Maine Medical Center Research Institute.

I also want to note that recently, MTI, in partnership with the Maine Department of Economic & Community Development, issued a request for proposals to help enable the establishment of a private sector led life sciences laboratory and incubator, where biotechnology and life sciences entrepreneurs could gain access to shared lab spaces and office infrastructure to help them start and scale their enterprises.

I am pleased to report that we have made a conditional $750,000 award to a Cambridge-based life sciences firm, specializing in genetics and genomics, that will offer companies a turnkey lab space and office space, and provides all the overhead services needed (bio-hazard waste removal,

meeting rooms, office support and amenities) as well as a very impressive list of laboratory equipment that is shared among the tenants. They expect to reach out to Maine colleges and universities to find interns and share lab space and equipment when needed. This is a potential huge development for the life sciences sector in Maine and MTI was thrilled to play a small role.

Overall, MTI's programs help innovators accelerate progress to the market, leverage additional private and public investment, and ultimately, expand their economic impact in Maine.

In addition to funding, MTI also offers other forms of support and assistance. We provide free technical assistance to Maine organizations interested in seeking a share of the $3.7 billion that the federal government makes available each year through its Small Business Innovation Research program. As you can imagine, the federal application process can be challenging so MTI deploys experts, at no-cost to the Maine applicants, so they can submit more competitive proposals.

We have an entrepreneur-in-residence program where we have a cadre of seasoned entrepreneurs and former executives that we deploy to our portfolio companies to help them overcome challenges and seize upon opportunities. Again, this is a free service.

We recently launched the Maine Entrepreneurial Resource Corps where we help provide matchmaking for small businesses seeking vetted consultants for specific short-period, high-impact projects, and MTI picks up half the cost.

We also encourage and promote interest in the sector through event sponsorships of things like the annual Maine Biological and Medical Sciences Symposium (MBMSS) - - a state-wide gathering of scientists and students from all across the state of Maine; UMaine's Annual Student Symposium, a joint undergraduate and graduate student event; the Maine Science Festival, the Bioscience Association of Maine, the TechStars and Founder Residency at the Roux Institute, and assorted business accelerators and pitch competitions.

Without question, Maine has a strong and growing life sciences sector that will help us tackle and overcome challenges to human health, our environment, and our natural resource-based industries now and in the future.

Thank you for your time and consideration. I am happy to address any questions you may have.

University of Maine System
Education & Research Perspective
on Fostering a Vibrant Biotechnology Sector in the State

October 19, 2022

Joan Ferrini-Mundy

Vice Chancellor for Research & Innovation, University of Maine System

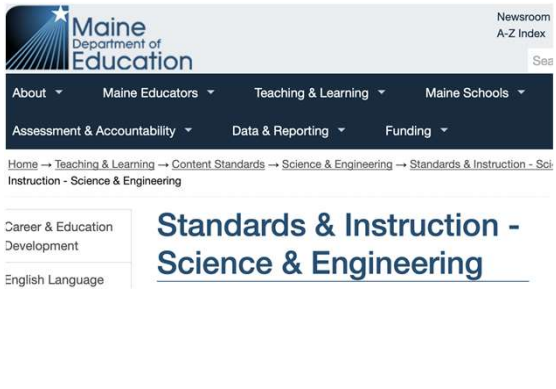
President, University of Maine and University of Maine at Machias

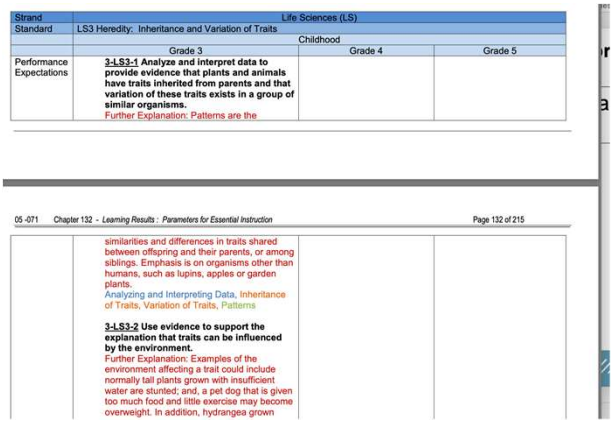
Presentation to the Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-Editing for the Citizens of the State

Maine's Public Universities
UNIVERSITY OF MAINE SYSTEM

Focus: Key Factors

Strong preparation at PK-12 in all STEM areas





Strand	Life Sciences (LS)		
Standard	LS3 Heredity: Inheritance and Variation of Traits		
	Childhood		
	Grade 3	Grade 4	Grade 5
Performance Expectations	**3-LS3-1 Analyze and interpret data to provide evidence that plants and animals have traits inherited from parents and that variation of these traits exists in a group of similar organisms.** Further Explanation: Patterns are the		

05 -071 Chapter 132 - *Learning Results : Parameters for Essential Instruction* Page 132 of 215

similarities and differences in traits shared between offspring and their parents, or among siblings. Emphasis is on organisms other than humans, such as lupins, apples or garden plants. Analyzing and Interpreting Data, Inheritance of Traits, Variation of Traits, Patterns

3-LS3-2 Use evidence to support the explanation that traits can be influenced by the environment. Further Explanation: Examples of the environment affecting a trait could include normally tall plants grown with insufficient water are stunted; and, a pet dog that is given too much food and little exercise may become overweight. In addition, hydrangea grown

Focus: Key Factors

Awareness/exposure to choices in STEM careers beginning in PK-12

ACTION A1:
Maine's Career Exploration

Research shows that heightened economic mobility for children is a result of "the connectedness, the day-to-day interactions, the diversity of people and experiences, the exposure to others, and sense of belonging."[16] We will use our neighborhood businesses and employers to enrich student learning.

Maine Career Exploration will start while students are in kindergarten and work with students until one year following graduation from high school. The mission of the program is to connect students and their families to the Maine economy, and to grow our own talent.

Maine Jobs and Recovery Plan

Contact Us | Search

Home | About the Plan | Investment Dashboard | Find a Program | News & Updates

Home → Maine Career Exploration Program

Maine Career Exploration Program

Department of Economic and Community Development

Allocation: $25,000,000

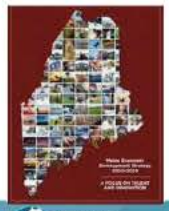
Apply Now:

- Application Portal (closed May 26, 2022): Children's Cabinet Pilot Program
- Application Portal (closed May 12, 2022): Statewide Expansion of Extended Learning Opportunity (ELO) Programming

Maine's Public Universities
UNIVERSITY OF MAINE SYSTEM

Focus: Key Factors

Options and retention in career pathways and postsecondary programs



In 2018, 44% of Maine's workforce has a work credential that goes beyond a high school diploma.[15] A "credential" is a two or four-year college degree, or a license in the trades, or a professional certificate. The goal set in Maine law to increase this proportion to 60% by 2025.[14]

THE MAINE EDUCATION FUNNEL EFFECT AND ACHIEVEMENT GAPS

	ECONOMICALLY DISADVANTAGED	NON-ECONOMICALLY DISADVANTAGED	ALL MAINE STUDENTS
ENTERING 9TH GRADE	100%	100%	100%
HIGH SCHOOL GRADUATES	79%	95%	87%
ENROLL IN COLLEGE 2017	40%	71%	55%
RETURN FOR 2ND YEAR OF COLLEGE (2018)	28%	62%	46%
EARN A 2- OR 4-YEAR DEGREE	16%	44%	30%

Maine's Public Universities
UNIVERSITY OF MAINE SYSTEM

Student Readiness for Success in STEM Fields

UMaine:

- ~90% of students who take mathematics placement exam are placed into at least College Algebra
- ~30% now meet Calculus 1 standards.
- ~75% of first-year students who take a math course in their 1st semester earn a grade above a "D"

Ongoing challenges UMS-wide:

- Needs for developmental mathematics
- Time management, study habits, how to learn
- Pandemic learning loss

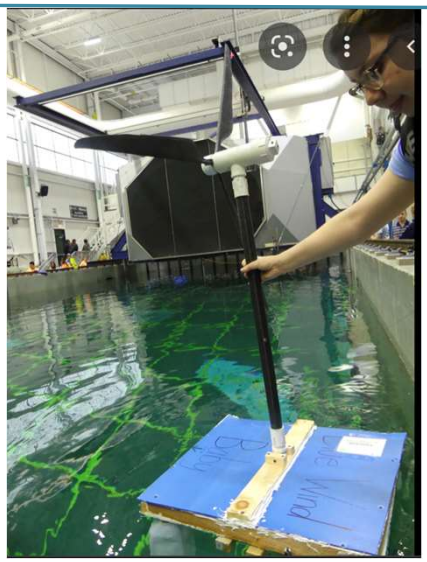
Cultivating Interest in STEM College and Careers

- **UMaine Cooperative Extension 4H school, community and camps**
- **USM Maine Robotics Camp**
- **STEM Outreach Center at UMaine**
- **Upward Bound Math Science Program**
- **UMaine Consider Engineering Program**

Expanding Your Horizons: 7th & 8th Grade Girls STEM conference

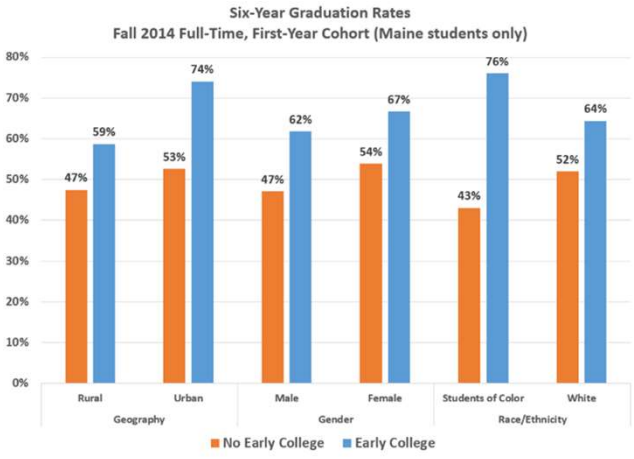
UMaine WindStorm Challenge

"I'm confident in saying that without the Windstorm Challenge, I likely would not have stayed in Maine to pursue my higher education, let alone end up working as an engineer. This competition was among the earliest experiences I had in extensive problem solving. This competition shows students what focusing on a STEM field can lead to and gets them to consider their futures at an earlier age."
-Nathan Faessler, 2011 Winner, Now UMaine ASCC Engineer



Improving STEM Readiness Through UMS Early College

- Allows students to take college credit-bearing courses at their high school, at UMS university or through UMS online at no cost to them
- Raises college aspirations, high school and college degree attainment, and college and career readiness while reducing student debt
- +/- 4,000 students enrolled annual, limited funding limits growth
- Many STEM-specific pathways



A Transformative Investment in the Future of Maine

Engineering, Computing & Info Science
$75m support + $75m challenge

Student Success & Retention
$20m support + $25m challenge

Graduate & Professional Center –
$55m support + $50m challenge

Harold Alfond FOUNDATION

UMS TRANSFORMS Student Success and Retention

Research Learning Experiences

Gateways to Success

Pathways to Careers

Belonging, Agency, & Purpose

We want interventions that start with the student perspective & increase those who believe:

1. **I belong here**
2. **I have something to contribute**
3. **I can tolerate and overcome challenges**
4. **What I do matters**

UMS TRANSFORMS: Research Learning Experiences (RLES)

- Small cohort, credit-bearing courses that establish connections early that can last throughout their time at the university
- Engagement in authentic, open-ended research and scholarship, where the student shapes the narrative, and the product has meaning outside of the classroom
- Near-peer mentoring that provides achievable developmental examples and relatable student support
- Formal assessment to inform next steps

UMS TRANSFORMS: RLE Bridge Week

Required RLE for Incoming Microbiology, Molecular and Cellular Biology and Biochemistry Majors

Hunt for Viruses: Learn about the structure of DNA in genomes, with a particular focus on the role of viral genomes and their role in bacterial virulence. Develop skills in the extraction of nucleic acids from bacterial cultures and sequencing isolated DNA. Assemble bacterial genomes and hunt for viral/phage genomes that potentially contribute to bacterial pathogenesis.
These bioinformatic analyses will be conducted in the fall.

UMS TRANSFORMS: RLE Bridge Week

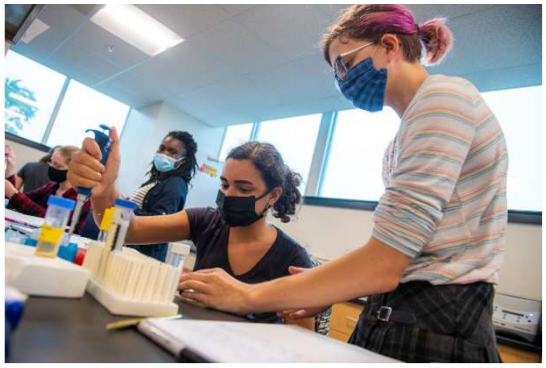
"When I started college last year, my goals were to simply obtain a degree and maybe get a soul-destroying desk job by the end of it. Now, especially after this week, I feel like my engines are revving. I want to get the highest grades I can, and more importantly ***I want to learn enough to be able to make scientific contributions****."*

"This small snippet of the course has already piqued my curiosity, and I cannot wait to learn more, and do more, and ask more questions, and get the answers to those, and then ***have even more questions****."*

"I think the coolest learning experience was the hands-on lab component - not a specific experiment, but just the whole process! ***It was super exciting to actually DO things****! Lab work usually feels so tedious but this helped to show me what genuine exploration and experimentation felt like - it was THRILLING!"*

UMaine Phage Genomics Course

- Phage Genomics year-long , hands-on research course for first-year students
- Partnership between UMaine Honors College and Dept. of Molecular and Biomedical Sciences, Howard Hughes Medical Institute
- Students learn how to handle large data sets, and more importantly, *how to learn*
- Students publish in the genomics discipline and provide new genomic sequencing data to the scientific community
- 96% of MBMS grads employed in biomedical sciences or healthcare, or con't education



Maine IDeA Network of Biomedical Research Excellence (INBRE)

- Collaborative network of Maine educational and research institutions led by MDI Bio Labs and sponsored by National Institute of General Medical Sciences within NIH
- Within UMS, includes UMaine and Universities of Maine at Farmington, Fort Kent, Machias and Presque Isle
- Through Maine INBRE, UMaine will offer honors students "Molecular Mechanisms of Human Disease" in 2023 that will be taught by Dr. Ben King and include intensive week at MDIBL and spring semester UMaine course in lab and bioinformatics methods

Strengthening Maine's PK-12 STEM Educator Workforce

Maine Center for Research in STEM Education (RiSE Center) at UMaine conducts research, leads graduate education and professional development, and builds community partnerships to improve evidence-based STEM education in Maine and beyond

- Through Maine STEM Partnership, a statewide preK–16+ STEM education improvement network with 160+ Maine schools, 700+ teachers, 29,000+ students, the RiSE Center provides research-guided professional development from events to intensive fellowships, and classroom instructional materials
- STEM Education Research with recent projects focused on integrating computing into science teaching and learning, improving STEM teacher recruitment and retention, and building data literacy and career competency through coastal science education.

Maine Education Policy Research Institute (MEPRI) provides policymakers objective data, policy research and evaluation

Recommendations to Foster Vibrant Biotech Sector

- Support investments in UMS
  - High-impact research learning (MEIF)
  - Paid internships that lead to Maine careers
  - World-class faculty
  - Modern infrastructure
- Maintain rigorous standards for PK-12 Maine students and educator certification
- Invest in hands-on PK-12 learning opportunities including extended learning opportunities with community partners, facilities/equipment, public early college and educator professional development

Your Questions

Advisory Panel to Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Testimony of Dana O'Brien, President of FocusMaine
October 19, 2022

Good morning, Senator Claxton, Representative Zager, and members of the advisory panel. My name is Dana O'Brien, and I am the President of FocusMaine.

About FocusMaine

FocusMaine is a private sector led economic development organization that seeks to accelerate the growth of Maine's highest potential industries. We are a catalyst and collaborator. We are an impactful partner. We are a funder. We marshal the best assets across the state to enrich strategies and ultimately deliver wins for the people of Maine – in the form of new jobs, businesses, and market opportunities.

FocusMaine's work is currently centered on advancing Maine's food and agriculture, aquaculture, and biotechnology industries, as well as promoting workforce opportunity across all industries.

We invest in workforce development, business development, and market development. We co-create initiatives with partners. Our resources come from charitable foundations, businesses, and state & federal government grants, as well as individual giving.

Innovation sits at the intersection of our current signature industries, as does plentiful opportunity for Maine to lead. It is this theme of opportunity that I want to discuss with you today and ultimately challenge you to embrace as you think about the workflow coming out of this advisory panel.

I will focus less on genome editing as a specific biological tool and more on Maine's opportunity to enrich itself on the foundation of life science progress and economic growth.

Opportunity to Confront Big Challenges Through Science

Society is confronted by monumental challenges – to our planet, our health and well-being, and our food systems. COVID-19 has, in many ways, magnified those challenges. But the pandemic has also shown us the value of science as an impactful tool to confront, mitigate, or even move beyond our biggest obstacles. The speed at which companies developed COVID-19 vaccines and therapeutics through biotechnology is eye popping. We must embrace science, educate the public about science, and enhance workforce and business opportunities centered on science to meet these urgent societal needs.

Opportunity to Understand and Position Biotechnology as a Solution

It's important to remember that genome editing is one of many biotechnologies in use today. Biotechnology is a rich set of tools that play a big role in our lives. We benefit from biotechnology regularly – and may not even know it.

Some common biotechnologies include monoclonal antibody technology to diagnose and treat disease. Or bioprocessing technology that uses bacteria, yeast, or enzymes to cleanup toxic waste sites, produce food, manufacture chemicals, or produce energy from agricultural feedstocks. Other biotechnologies are used to tailor human and animal drug treatments, slow food spoilage, improve food nutritional content, produce meatless proteins, and develop biodegradable plastics, among other things.

Opportunity to Build a Competitive, Thriving Maine Bioeconomy

Investment in biotechnology and the data analytics that accompanies advances in genetics is off the charts. A McKinsey analysis showed a $35 billion venture capital investment in biotechnology companies with advanced platform technologies, between 2019 and 2021. Because this kind of scientific innovation is so central to confronting the challenges already discussed, private and government dollars are flowing toward research, development, and product development – for human and animal health, for agriculture, and for green manufacturing. A recent study published by MassBio notes that so much money is flowing into the Boston-Cambridge, Massachusetts, biotechnology epicenter that demand is outpacing the state's existing biomanufacturing infrastructure and workforce capabilities.

Maine should, and really must, take steps to capture the overflow reverberating out of Massachusetts. Doing so would mean more on-ramps for people in Maine to be part of this transformational industry and more connections across the region to strengthen innovation and economic opportunity.

Maine has quality existing life science infrastructure – at our universities and community colleges, within our top-notch scientific institutions, and in private industry. According to the 2022 BioME Industry Report, life science jobs in Maine have grown 42 percent over the past 5 years, outpacing all other industries in the state and leading the industry's job growth in New England. And the Roux Institute is injecting exciting new investment and growth opportunity in our state. FocusMaine is motivated by the early progress of the Roux Institute and counts itself as an impactful Maine partner with Northeastern University and others.

We are also motivated by the Governor's commitment to life science innovation and the promise of biotechnology as a tool to fight climate change and build a modern Maine economy – as outlined in the state's 10-year economic development plan. FocusMaine worked closely with the state as that plan was drafted and is pleased to hold a seat at the implementation table.

Our congressional delegation is also leading for us. Just yesterday, Senator Collins reinforced her already robust commitment to federal biomedical research investments that are transforming our lives. It is exciting to think about how this investment will positively impact Maine as she prepares to become the chairwoman or ranking member on the Senate Appropriations Committee.

But there is work to be done.

Turning Opportunity into Action

FocusMaine is a lead voice working to enhance the state's bioeconomy.

The focus of our work to date has centered on business and talent attraction, sector promotion, and partnering with premier research institutions like the Roux Institute and the University of Maine System to draw federal resources toward the state. We are linked to more than 50 small biotech companies in the Boston-Cambridge area, many of which have a profound interest in building business growth in Maine. Including the company Brian Whitney mentioned, which I think will draw several small biotechs to Maine if it gets rooted.

But to fully capture the opportunity just discussed and to secure Maine's place as a bioeconomy powerhouse will take focused work and the collection of valuable input from the private sector, academia, and government.

We believe there is room for the creation of a singular, all of Maine approach, or strategy, that provides our congressional delegation, Maine lawmakers and our Governor with a concise bioeconomy action plan.

We must turn opportunity into action.

We must position Maine to outcompete other states and regions working diligently to capitalize economically on massive life science investment trends. We must learn from and model other regions, including Boston-Cambridge, North Carolina's RTP, St. Louis, and so on.

There are also tremendous opportunities to leverage biotechnology for the benefit of Maine people. Maine's health care systems are integrating precision medicine tools into clinical practice. Access to cutting edge clinical trials for cancer and other diseases is expanding to reach underserved, rural communities. And federal funding for scientific research to understand gene-editing technologies like CRISPR and the ethical, legal, and social implications of genetics and genomics is a priority for the NIH.

I joined FocusMaine in June and since then have been listening and learning from leaders across the state operating in this space. There is tremendous energy to move and FocusMaine is uniquely positioned to bring people together and catalyze this energy for the good of the state and its people.

In closing – a call to action:

- Let's beat the other states and regions
- Let's organize and act
    - Invest in science
    - Invest in people
    - Invest in business development

Thank you for the opportunity to speak with you today. I would like to submit FocusMaine's 2021 annual report and the BioME annual economic report for the advisory panel's record.

I look forward to answering any questions you may have.

October 19, 2022

Presentation before the ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY TO THE CITIZENS OF THE STATE

Submitted by Lon Cardon, Ph.D., FMedSci, President and CEO,
The Jackson Laboratory

Good morning, Senator Claxton, Representative Zager and members of the advisory panel, my name is Lon Cardon and I am president and CEO of The Jackson Laboratory. The Jackson Laboratory is an international genetics and genomics research institution, headquartered in Bar Harbor, with other Maine-based facilities in Augusta and Ellsworth. I joined the Jackson Laboratory at the beginning of this year, with half of my previous career spent in academia, searching for genes that cause human disease, and the latter half in the pharmaceutical industry, trying to turn those discoveries into treatments.

I'm pleased to have the opportunity to speak to you today and would like to thank you for your service to the Legislature and people of Maine, and for bringing this important conversation to the fore.

My colleague, Dr. Laura Reinholdt, Associate Professor at our Bar Harbor campus, appeared before this panel in August. She discussed the critically important use of gene editing in research using mouse models for human disease.

My presentation will provide a bridge to take gene editing from early "pre-clinical" research studies to the human patient, focusing on three things. First, I will discuss gene editing in the development of human therapeutics. Second, I will discuss The Jackson Laboratory Rare Disease Translational Center, which is already using this technology. Finally, I will address the panel's question of what Maine can do regarding gene editing now and in the future.

First, gene editing in the therapeutic context. As described by Dr. Reinholdt, gene editing has transformed basic research. Until this technology development, the field of genetics was passive: we had to wait until some new disease or symptoms occurred and then try to find the genes that might have caused it. Many important discoveries were made this way, but they were made by chance and took months, years to discover.

Now, with gene editing, that process has changed dramatically. We can design and create such variants overnight, and even hundreds or thousands of them. This level of speed and precision is transformative for biomedical research, and the technology has advanced so rapidly that early stage scientists, even high-school students, can learn to deploy the tools productively.

If basic biology research studies of a rare disease therapeutic are successful, one next goal is to translate those findings into a drug treatment for a human patient. Toward this aim, gene editing

provides a key advance in a series of technologies that have been progressing over the past few decades. To understand the potential of gene editing in therapeutics, it is useful to understand how we got to where we are.

In rare diseases and some others, the disease emerges because of a genetic defect that doesn't let the gene make the gene product that is necessary for the healthy state. The gene is effectively 'broken.' The earliest solution to this, over 20 years ago, was for scientists to make correct versions of the gene product outside the body – literally in manufacturing factories – and then inject them into the patient. The broken gene is still in the body, but we offset that by putting in some working parts to take over the load. These are so called 'gene or enzyme replacement' therapies and drugs are approved for a number of rare diseases.

The next generation of these therapies, which are appearing today in some neurological and blood disorders, use exactly the same principle, but instead of making the unbroken product outside the body in a factory, scientists use some tricks to help the body make it itself. The broken gene is again still there, but a therapeutic gene has been delivered to sit alongside the broken one to put some properly working copies in our bodies. This and related approaches is what many people refer to as "gene therapy."

'Therapeutic gene editing' is the next generation of this type of biomedicine. This is a substantial change because in this case, the goal is not to just add some working parts alongside the broken ones, but to target the broken gene itself. Here we are trying to repair or replace that broken copy itself. In some cases, gene editing could render a permanent change at the genetic level. This is about as good as it could get, if safe and effective.

Second, JAX Rare Diseases commitment. Disease therapies based on gene editing are still rare. This panel has already heard examples of how gene editing is being used in the treatment of sickle cell disease, and I believe we are at the beginning of other treatments to come, but it is still early, and like nearly all new approaches that can transform medicine, it takes time to understand how to use them safely and to their greatest benefit.

Getting in early to lead the basic research is why, within my first year at JAX, I established the Rare Disease Translational Center, and named my colleague Dr. Cat Lutz as vice president. Dr. Lutz is a proud alumnus of The University of Maine, where she earned a Ph.D. in biochemistry. Throughout her career she has been involved in major milestones in rare disease research, including the preclinical studies of what would become Spinraza, the first FDA approved therapy for Spinal Muscular Atrophy. If this Advisory Panel is planning to make recommendations regarding the formation of the Rare Disease Advisory Council, I suggest the panel recommend the appointment of a scientist like Dr. Lutz, who not only has an internationally recognized track record of research productivity, but has demonstrated experience working closely with rare disease stakeholders including patients, patient advocacy groups, physicians, and researchers.

Since 2016, The JAX Rare Disease Translational Center has worked with dozens of rare disease foundations and their associated research teams to generate, using CRISPR/Cas9 and other gene editing methods, custom mouse models of rare conditions in order to lay the groundwork for new therapeutic interventions. Now, the Rare Disease Translational Center is expanding its focus. Under Dr. Lutz's leadership, JAX will work with hospitals from the point of diagnosis and with pharmaceutical companies to conduct pre-clinical tests of new therapeutics. I believe rare disease is an area where the expertise and scale of The Jackson Laboratory can have a major impact, and in fact, it has a natural symmetry because the Jackson Laboratory has been working on rare diseases for almost its entire 93 year existence. The ability of this Center

to realize the aspirations of the genomic revolution to treat rare disease will rely in part on gene editing.

Third and finally, this panel has accepted the difficult task of making recommendations regarding the implications of gene editing to the citizens of Maine. You've considered difficult scientific, ethical, and financial questions and have come up with a number of actionable recommendations that could make a difference in Maine. I'll leave you with two recommendations.

I agree with other presenters who recommended the state of Maine increase investments in education and teacher professional development. Most of today's students will be tomorrow's consumers of the precision therapeutics developed and implemented using gene editing technology. Some of today's students will pursue careers that put them in direct contact with gene editing: research scientists, physicians, engineers, social scientists, genetic counselors, farmers, and others. Today's students will also drive innovation and become biotech entrepreneurs, creating products and services using gene editing and creating economic opportunity in the process.
I also urge this panel to support recommendations that increase access to teacher professional development in genomics, which combines genetics and computer sciences to enable data-intensive research in one or many genomes. Increasingly, genetics research is performed using only computational methods, and there is an abundance of genomic data and an urgent need to grow this digitally-capable workforce. Any recommendation by this panel to support education or teacher professional development will advance the Maine 10-year Economic Development Strategy to *Grow Local Talent* and prepare students and teachers for the digital economy in biomedicine.

Investments in education and teacher professional development should parallel investments into the biosciences economy, specifically research; otherwise Maine's support of STEM education will increasingly benefit other states. I urge this advisory panel to consider gene editing as an example of why it is important that Maine begin to make perennial investments into bioscience research and development. As has been shown by Mr. Whitney and Maine Technology Institute, competitive grant awards made by the $45 million Maine Technology Asset Fund (MTAF) 2.0 in 2017 have so far created over 5,300 jobs and $1.4 billion in economic impact across the state.

Through MTAF 2.0, JAX was awarded $12.5 million to initiate construction of a world-class mouse vivarium in Ellsworth—an award that JAX matched with over $240 million in additional investment. The Ellsworth vivarium dramatically extends our mouse production and services capacity, including development of highly specialized mouse strains using gene editing technology. As of the first quarter of 2022, JAX can attribute 262 new jobs to MTAF 2.0, and annual salaries of over $18 million. JAX's Ellsworth expansion, catalyzed by state investment, has indisputably created indirect economic impact; look no further than private investments in housing, childcare, and other ventures that are made possible by the economic durability of the biosciences sector, which will not only grow, but will become increasingly efficient through technology improvements like gene editing. Just as the 2012 discovery of CRISPR/Cas9[1] was funded by a combination of private and public grants, so too can state funding help leverage private and federal support which collectively will grow the Maine innovation economy.

[1] https://www.science.org/doi/10.1126/science.1225829

I'll close by again thanking you for inviting me to share my experience and suggestions on what Maine should do now and in the future. Science is too often removed from the public sphere and I'm pleased to be a part of today's proceeding.

APPENDIX L

Gene Editing in Systems and Institutions (related materials)

- Information from the Maine Department of Education on Science, Technology, Engineering and Mathematics (STEM) education

Stocco, Janet

From: Belolan, Courtney <Courtney.Belolan@maine.gov>
Sent: Tuesday, September 20, 2022 3:00 PM
To: Olson, Rachel
Cc: Stocco, Janet
Subject: RE: Request for information from Maine Legislative Study Group

Hello Rachel,

I am only able to provide very general information to your questions. As a local-control state, the decisions regarding programming and curriculum are left up to local districts, and Career and Technical Education centers. As such we do not have data on the types of programs offered in the different Maine school districts.

- The current Maine Learning Results for science are the NextGen Science standards which include learning outcomes related to genetics articulated throughout the k-12 grade span. Gene-editing specifically is not noted in the standards.
- Maine schools do not offer additional endorsements or certifications on diplomas. Some students in CTE programs may earn certifications or credentials through any trade-specific opportunities that are available to them.

Please let me know if you have any further questions, or if I can support your work in any other way.

Regards,

Courtney Belolan
(she/they)
Director of Policy and Government Affairs
Maine DOE
(207) 215-7396

From: Olson, Rachel <Rachel.Olson@legislature.maine.gov>
Sent: Friday, September 16, 2022 2:25 PM
To: Belolan, Courtney <Courtney.Belolan@maine.gov>
Cc: Stocco, Janet <janet.stocco@legislature.maine.gov>
Subject: RE: Request for information from Maine Legislative Study Group

Thank you, Courtney. Let me know if you have any questions!

Rachel

From: Belolan, Courtney <Courtney.Belolan@maine.gov>
Sent: Friday, September 16, 2022 1:44 PM
To: Olson, Rachel <Rachel.Olson@legislature.maine.gov>
Cc: Stocco, Janet <Janet.Stocco@legislature.maine.gov>
Subject: RE: Request for information from Maine Legislative Study Group

Hello Rachel,

I am working on collecting information for a response and will have it to you on Tuesday.

Courtney Belolan
(she/they)
Director of Policy and Government Affairs
Maine DOE
(207) 215-7396

From: Olson, Rachel <Rachel.Olson@legislature.maine.gov>
Sent: Thursday, September 15, 2022 12:40 PM
To: Belolan, Courtney <Courtney.Belolan@maine.gov>
Cc: Stocco, Janet <janet.stocco@legislature.maine.gov>
Subject: Request for information from Maine Legislative Study Group

Dear Ms. Belolan,

Hello, my name is Rachel Olson and I am a legislative analyst with the Office of Policy and Legal Analysis. My colleague, Janet Stocco, and I are providing staff support to the *Advisory Panel To Better Understand and Make Recommendations Regarding the Implication of Genome-editing Technology for the Citizens of the State.* The study's website is here and its authorizing legislation is here.

At the most recent study meeting, held on Wednesday, September 7th, Advisory Panel members has questions about STEM programs within Maine schools, including CTE programs, and more particularly if any of these programs (or schools in general) had curriculum relevant to genetics and gene-editing.

In particular, the Advisory Panel wanted to know, and hope that you (or another person at DOE) can answer:

- How many Maine schools, including CTE programs, offer STEM specific programming? The example that was mentioned was Bangor High School's STEM Academy. So, the request is focused on similar programming and not just on single-course offerings. This could include any programs offered at CTE schools as well, but such programming should be focused on skills applicable to post-secondary schooling or careers in the field of genetics or genome-editing (human or non-human organisms).
- How many Maine high schools offer additional certifications or endorsements on their diplomas (if any?)? If any, how many of them include STEM related endorsements?

If at all possible, I would like to be able to share this information with the Advisory Panel at their meeting next Wednesday, September 21st. If that is not doable, the final meeting of the Advisory Panel is scheduled for October 19th.

Thank you in advance for any assistance you can provide. Please do not hesitate to reach out if you have any questions regarding my request.

Sincerely,

Rachel Olson
Legislative Analyst
Office of Policy and Legal Analysis
Maine State Legislature
(207) 287-1670
Rachel.Olson@legislature.maine.gov
http://legislature.maine.gov/opla

Stocco, Janet

From: Belolan, Courtney <Courtney.Belolan@maine.gov>
Sent: Tuesday, October 11, 2022 1:50 PM
To: Zager, Sam
Cc: Stocco, Janet; Olson, Rachel
Subject: RE: STEM endorsements in Maine schools?

Hello Sam,

Thank you for reaching out to clarify. The most accurate answer is that local SAUs may decide to include an endorsement, such as a STEM endorsement, however there are no regulations or rules from the DOE or Maine State Revised Statutes that outline expectations or standards for such endorsements. The decision to include an endorsement on a diploma, and what the requirements are for that endorsement, are a local decision made at the individual SAU level. In addition, the DOE does not collect information about the endorsements offered.

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(she/they)
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From: Zager, Sam <Sam.Zager@legislature.maine.gov>
Sent: Sunday, October 9, 2022 6:04 PM
To: Belolan, Courtney <Courtney.Belolan@maine.gov>
Cc: Stocco, Janet <janet.stocco@legislature.maine.gov>; Olson, Rachel <rachel.olson@legislature.maine.gov>
Subject: STEM endorsements in Maine schools?

Hi Courtney,

Thank you very much for helping us on the Gene Editing Panel (LD 1771) understand the science education landscape better.

Could you please clarify something? You wrote in your 9/20 email to Janet Stocco and Rachel Olson, "Maine schools do not offer additional endorsements or certifications on diplomas."
However, Commissioner Makin separately wrote in a 10/1 email to Rep. Brennan that "many districts do offer a STEM endorsement on their high school diploma/transcripts."

Thank you!

Sam

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Maine State Legislature
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Thank you!

Sam

APPENDIX M

Panel Correspondence

- Letter to Commissioner of Education, Chancellor of the University of Maine System and President of the Maine Community College System
- Letter to Maine's Congressional Delegation
- Letter to Commissioner of Economic & Community Development
- Letter to Commissioner of Health and Human Services
- Letter to Governor's Office regarding the Office of Affordable Health Care

STATE OF MAINE
ONE HUNDRED AND THIRTIETH LEGISLATURE

ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY FOR THE CITIZENS OF THE STATE

November 30, 2022

A. Pender Makin, Commissioner
Department of Education
23 State House Station
Augusta, ME 04333-0023

Dannel P. Malloy, Chancellor
University of Maine System
5703 Alumni Hall, Suite 200
Orono, ME 04469

Dave Daigler, President
Maine Community College System
323 State Street
Augusta, ME 04330

Dear Commissioner Makin, Chancellor Malloy and President Daigler,

We are writing to you on behalf of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, which was established by the 130th Maine Legislature through Resolve 2021, chapter 177 "to study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology."

Throughout the course of our meetings, the medical professionals, academic researchers, industry leaders, ethicists, and others who shared their expertise emphasized the importance of promoting awareness of and education regarding gene editing technologies. Maine citizens faced with personal or public health crises cannot properly evaluate potential genomic medicine and related treatment options or decide whether to avail themselves of preventative health measures developed with novel genetic technologies unless they have a strong foundational

understanding of genetics, genomics and related technologies. Nor can the State's populace engage in necessary conversations regarding whether and how society should proceed with gene editing and related technologies and grapple with the complicated bioethical and environmental issues related to these technologies without a firm foundation of scientific knowledge. Closely related, representatives from Maine's existing life sciences industries report that their growth depends on a highly educated and skilled workforce, with expertise not only in genetics but also in data science and analytics. The State will not be able to position itself as a future hub of genomic and gene-editing research unless it invests additional resources in promoting genetics, genomics and data science education at all levels, from primary school through post-secondary and graduate school programs.

Accordingly, the panel recommends that the State take a multi-pronged approach to enhancing education in gene-editing and related technologies in the State. First, the panel encourages the Department of Education to affirm the importance of primary and secondary education in genetics, genomics and related technologies by gathering, assembling and aggregating educational resources to assist in teaching these concepts and enhancing professional opportunities for primary and secondary teachers on these topics. Because gene-editing technologies lie on the cutting edge of science, many primary and secondary teachers lack an up-to-date understanding of how these technologies work or detailed knowledge about the potential benefits and detriments of these technologies. Programs like The Jackson Laboratory's Teaching the Genome Generation have helped bridge the gap in educator knowledge and more teachers should be made aware of this and similar programs. To assist in financing these opportunities, the panel has also urged Maine's congressional delegation to advocate for increased federal funding and grant opportunities to enhance professional development programs for primary and secondary school educators in genetics, genomics, data science and related technologies.

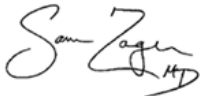
The panel further recommends that the University of Maine System, Maine Community College System and Department of Education jointly convene a genetics education summit that will allow primary and secondary school educators to tap into the expertise held by Maine's post-secondary institutions regarding genetics, genomics and related technologies. Educators at all levels have developed innovative programs designed both to spark students' interest in bioscience fields and to prepare them to enter the competitive bioscience workforce, including, for example, the innovative Phage Genomics Course for first-year students at the University of Maine and the biomedical research support program offered to high school students by the Hancock County Technical Center in part through a partnership with The Jackson Laboratory. The panel suggests that summit participants also consider whether to create new scholarship opportunities within genetics and related fields for indigenous and other populations that were disadvantaged and mistreated by unethical genetic research and eugenics policies in the past.

Finally, the panel recommends that the genetics education summit focus not only on developing resources for formal education settings but also on developing community-based education programs and resources in genetics, genomics and related technologies. As an initial step, it may be fruitful to conduct a baseline survey to assess public knowledge of and attitudes toward genetics, genomics and gene-editing technologies, including the public's view of the potential benefits of and its concerns about these emerging technologies.

Thank you in advance for considering these consensus recommendations of the panel. We would be happy to discuss them further.

Sincerely,

Senator Ned Claxton, Chair



Representative Samuel Zager, Chair

cc (*via email*):

Members, Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Courtney Belolan, Director of Policy & Governmental Affairs, Maine Department of Education

Samantha Warren, Director of Government & Community Relations, University of Maine System

Becky Smith, Director of Government & Community Relations, Maine Community College System

STATE OF MAINE
ONE HUNDRED AND THIRTIETH LEGISLATURE

ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY FOR THE CITIZENS OF THE STATE

November 30, 2022

Senator Susan Collins
413 Dirksen Senate Office Building
50 Constitution Ave. NE
Washington, DC 20510

Representative Chellie Pingree
2162 Rayburn House Office Building
45 Independence Ave. SW
Washington, DC 20515

Senator Angus King
133 Philip A. Hart Senate Office Building
120 Constitution Ave NE
Washington, DC 20510

Representative Jared Golden
1222 Longworth House Office Building
15 Independence Ave. SE
Washington, DC 20515

Dear Senator Collins, Senator King, Representative Pingree and Representative Golden,

We are writing to you on behalf of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, which was established by the 130th Maine Legislature through Resolve 2021, chapter 177 "to study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology."

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science and analytics. The State will not be able to position itself as a future hub of genomic and gene-editing research unless additional resources are invested in promoting genetics, genomics and data science education at all levels, from primary school through post-secondary and graduate school programs.

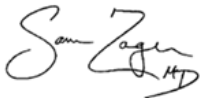
Because gene-editing technologies lie on the cutting edge of science, many primary and secondary teachers lack an up-to-date understanding of how these technologies work or detailed knowledge regarding the potential benefits and detriments of these technologies. For this reason, the panel has recommended that the Maine Department of Education affirm the importance of primary and secondary education in genetics, genomics and related technologies by gathering, assembling and aggregating educational resources to assist in teaching these concepts to primary and secondary students and by enhancing professional opportunities for primary and secondary teachers on these topics.

To assist the department in achieving these goals, the panel urges each of you to advocate for increased federal funding and grant opportunities to enhance professional development programs for primary and secondary school educators in genetics, genomics, data science and related technologies. Programs like The Jackson Laboratory's Teaching the Genome Generation, which is supported by funding from the National Institutes of General Medical Sciences within the National Institute of Health, have helped bridge the gap in educator knowledge and have provided teachers with lesson plans and laboratory materials that they can use in their classrooms to pass on that knowledge. Additional funding will be essential to ensure that primary and secondary educators across the State have access to similar professional development trainings and programs in this exciting and critically important field of study.

Thank you in advance for considering these consensus recommendations of the panel. We would be happy to discuss them further.

Sincerely,

Senator Ned Claxton, Chair



Representative Samuel Zager, Chair

cc (*via email*):

Members, Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

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ONE HUNDRED AND THIRTIETH LEGISLATURE

ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY FOR THE CITIZENS OF THE STATE

November 30, 2022

Commissioner Heather Johnson
Department of Economic & Community Development
59 State House Station
Augusta, ME 04333-0059

Dear Commissioner Johnson,

We are writing to you on behalf of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, which was established by the 130th Maine Legislature "to study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology." *See* Resolve 2021, chapter 177, §5.

During the course of its work, the panel was excited to learn about the cutting-edge genomic and gene-editing research being performed at the University of Maine, the Roux Institute, The Jackson Laboratory and other public and private institutions across the State. Existing and potential areas of future research that might be harnessed to benefit the State span a broad spectrum, from the development of genomic medicines to treat patients with rare diseases to the engineering of microorganisms that decrease the presence of phosphorous, heavy metals and other environmental pollutants in municipal and industrial wastewater. The recent *State of the Industry 2022* report from the Bioscience Association of Maine (BioME) reveals that Maine's institutions of higher education and private industry have drawn hundreds of millions of grant dollars for bioscience research from the National Science Foundation, National Institutes of Health, Small Business Innovation Research, and Small Business Technology Transfer Research programs and the State has invested millions of dollars in the biotechnology sector through the Maine Technology Institute and other innovative programs. These investments successfully catalyzed growth in the State's life sciences industry, where jobs grew by 42% in Maine over the past five years, far outpacing the State's 1% overall job growth and the growth in life sciences jobs across New England over the same time period. These occupations provide workers with significantly higher median hourly earnings than average workers in the State.

For all of these reasons, we encourage the Department of Economic and Community Development to convene a statewide conference on genomic and gene-editing research to help harness the power of existing and future research in genomic and gene-editing technologies and the benefits these technologies can bring to Maine patients, agricultural and fishery industries and economy. Based on what we learned during the course of the Advisory Panel process, we suggest the following topics for exploration by conference attendees:

- Surveying the genomic and gene-editing research currently being performed in public and private institutions of higher education and in the private sector in the State;
- Developing methods to enhance research collaborations between the State's institutions of higher education and the private sector; and
- Grappling with and making recommendations regarding the ethical, legal, and social implications of genomic and gene-editing research, including data privacy issues.

Thank you in advance for considering these consensus recommendations of the panel. We would be happy to discuss them further.

Sincerely,

Senator Ned Claxton, Chair

Representative Samuel Zager, Chair

cc (*via email*):

Members, Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Ben Goodman, Legislative Liaison, Department of Economic & Community Development

STATE OF MAINE
ONE HUNDRED AND THIRTIETH LEGISLATURE

ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY FOR THE CITIZENS OF THE STATE

November 30, 2022

Commissioner Jeanne M. Lambrew
Department of Health and Human Services
11 State House Station
Augusta, ME 04333-0011

Dear Commissioner Lambrew,

We are writing to you on behalf of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, which was established by the 130th Maine Legislature "to study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology." *See* Resolve 2021, chapter 177, §5.

The potentially high costs and extraordinary benefits of genomic medicine—including gene therapy, gene editing and related treatments—emerged as one of the primary themes during the panel's first meeting, which focused on gene editing in health and biosciences. We were excited to learn from patients and their families, medical professionals and academic researchers about the emerging field of genomic medicine through which physicians and researchers can make targeted corrections to genetic mutations carried by patients with single-gene disorders. Unfortunately, because this research is in its infancy and many of these diseases are rare, there are only small patient populations available to share the cost of developing such treatments. A revolutionary new treatment for the devastating progressive genetic motor neuron disease spinal muscular atrophy (SMA), for example, costs approximately $2 million, but can save the life of a young child with SMA. It is crucial that officials establishing policies affecting patient access to this treatment and similar types of genomic medicine weigh not only the exceedingly high cost of these treatments but also the toll that untreated disease can take on patients and their families.

The panel believes that the Rare Disease Advisory Council, recently established through Public Law 2021, chapter 740, will serve as a helpful forum for engaging in crucial policy discussions regarding patient access to and the cost of genomic medicine. The council's enabling legislation,

codified at 22 M.R.S. § 1700-B, charges the council with performing several enumerated duties, including:

> D. Identify[ing] and distribut[ing] publicly available educational resources to providers of health care in order to foster recognition of symptoms of and treatment for rare diseases among patients of those providers; [and]
>
> E. Evaluat[ing] the systems for delivery of treatment for rare diseases in place in the State and develop[ing] recommendations to improve quality of life and to provide services and reimbursement for those services for persons with rare diseases;

As it performs these duties, the panel recommends that the council specifically address the financial burdens and potential benefits of genomic medicine for Maine rare disease patients, their families and the State as a whole. The panel further recommends that, when you make your initial appointments to the council under §1700-B(2)(L) & (M), you appoint at least one adult and one parent or guardian affected by a rare disease that is the result of a single-gene disorder, with preference given to an adult with a rare disease who is eligible to participate in a clinical trial involving genomic medicine and to the parent or guardian of a child who is similarly eligible for clinical trial participation. Taken together, these steps will help ensure that issues surrounding access to genomic medicine for rare diseases are given priority in council discussions and that the voices of patients with single-gene disorders and their families form an integral part of these discussions.

Thank you in advance for considering these consensus recommendations of the panel. We would be happy to discuss them further.

Sincerely,

Ned Claxton

Senator Ned Claxton, Chair

Sam Zager MD

Representative Samuel Zager, Chair

Cc (*via email*):

Members, Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Molly Bogart, Director of Governmental Affairs, Maine Department of Health and Human Services

STATE OF MAINE
ONE HUNDRED AND THIRTIETH LEGISLATURE

ADVISORY PANEL TO BETTER UNDERSTAND AND MAKE RECOMMENDATIONS REGARDING THE IMPLICATIONS OF GENOME-EDITING TECHNOLOGY FOR THE CITIZENS OF THE STATE

November 30, 2022

Bethany Beausang, Senior Policy Advisor
Office of the Governor
1 State House Station
Augusta, ME 04333-0001

Dear Ms. Beausang,

We are writing to you on behalf of the Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State, which was established by the 130th Maine Legislature "to study the implications of genome-editing technology and the legislative, administrative or other steps that the State should take to capitalize on the potential and avoid the hazards of genome-editing technology." *See* Resolve 2021, chapter 177, §5.

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The panel believes that the Office of Affordable Health Care, recently established through Public Law 2021, chapter 459, will serve as a helpful forum for engaging in crucial policy discussions regarding patient access to and the cost of genomic medicine. Title 5, section 1322(3) of the

Maine Revised Statutes directs the office to report at least annually to both the Governor and the Legislature "on matters affecting the cost of health care in the State" after engaging in specific statutorily prescribed duties, including:

> A. Analyz[ing] health care cost growth trends and correlation to the quality of health care;
>
> B. Analyz[ing] health care spending trends by consumer categories, payer type, provider categories or any other measurement that presents available data in a manner that may assist the legislative oversight committee in understanding health care cost drivers, health care quality and utilization trends, consumer experience with the health care system or any other aspect of the health care system;
>
> C. Monitor[ing] the adoption of alternative payment methods in this State and other states that foster innovative health care delivery and payment models to reduce health care cost growth and improve the quality of health care;
>
> D. Based upon the data obtained and the analysis pursuant to paragraphs A to C, develop[ing] proposals for consideration by the legislative oversight committee on potential methods to improve the cost-efficient provision of high-quality health care to the residents of this State; [and]
>
> E. Based upon the data obtained and the analysis pursuant to paragraphs A to C, conduct[ing] a systemic review of the health care system and develop proposals to improve coordination, efficiency and quality of the health care system[.]

As it carries out these duties, the panel recommends that the office examine not only traditional drivers of health care costs but also newly emerging cost drivers including genomic medicine, which as the panel has learned may involve large up-front treatment costs but also may dramatically improve the lives of patients with rare diseases and generate long-term costs savings for both patients and insurance carriers.

It is our understanding that the Governor is currently in the process of selecting an executive director for the office, who will operate independently under the general policy direction of both the joint standing committee of the legislature with jurisdiction over health coverage matters and a newly appointed Advisory Council on Affordable Health Care. We respectfully request that, once an executive director is in place, the Governor's Office pass along the panel's recommendation to that new executive director.

Thank you in advance for considering these consensus recommendations of the panel. We would be happy to discuss them further.

Sincerely,

Ned Claxton

Senator Ned Claxton, Chair

Sam Zager MD

Representative Samuel Zager, Chair

cc (*via email*):

Members, Advisory Panel To Better Understand and Make Recommendations Regarding the Implications of Genome-editing Technology for the Citizens of the State

Members, Advisory Council on Affordable Health Care