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The Ethics of Transformative Technology

A Letter From the Cultures Editorial Staff (written by Katy Stewart)

In June 2012, Emmanuelle Charpentier and Jennifer Doudna published a seminal paper marking their groundbreaking findings regarding the ability of CRISPR-Cas9 to edit genomes. This relatively easy-to-use technology has since inspired companies and researchers around the globe to find innovative ways to harness its capabilities. Stretching the limits of what we thought was humanly possible, researchers are using the technology to transform how we think about precision medicine, organ transplantation, and the future of humanity.

As excitement flourishes around gene editing technology, artificial intelligence continues to advance, now touching nearly every corner of our daily lives. Beyond chess-playing supercomputers, researchers have found the nexus of these two transformative technologies to create precision medicine solutions for some of the medical world’s toughest challenges.

In this final issue of Cultures, we step back from the rumors and sensationalized headlines to assess what can be realistically achieved with these technologies, and the tough ethical implications we must consider.

Despite the breakneck speed at which these transformative technologies continue to advance, national and international policies and regulations surrounding both CRISPR and AI lag behind. In the summer of 2017, over 100 AI experts wrote and signed an open letter to the United Nations urging a ban on AI-operated automatic weapons in warfare. Discussions like these need to happen more often. We must ask ourselves “how much should we allow these innovative technologies to grow before we intervene and set ethically sound policies?”

As the science progresses, bioethics experts, policy gurus, and the scientists themselves must collaborate to decide what’s best for all of us. In this issue, we discuss the ethical considerations of AI with Venerable Tenzin, who believes that government entities should be involved in AI regulation, and with GoodAI’s founder and CEO, Marek Rosa, who says morality in an AI agent cannot simply be coded. In one of Cultures’ most enlightening interviews, Dr. Alta Charo shares her first-hand experience guiding CRISPR policy and ethics. In another, Dr. Luhan Yang and her team at eGenesis hope to solve the organ transplant shortage one pig at a time.

From one company using gene editing technology to create healthier specialty food ingredients to another using similar technology to fulfill its vision of no more organ shortages, this issue of Cultures continues the international discussion on how to ensure these technologies remain ethical while still fostering innovation.

Transformative technology will continue to proceed at an unfathomable speed. Understanding the ethical considerations of such technology is essential as we begin to envision what the future will look like. It is time we all get involved to shape the future we want to see.
CRISPR is a genome-editing tool that can selectively delete, modify or correct a disease-causing abnormality in a specific DNA segment. CRISPR refers to Clustered Regularly Interspaced Short Palindromic Repeats occurring in the genome of certain bacteria. CRISPR technology uses a protein-RNA complex composed of Cas9, which binds to a guide RNA (gRNA) molecule that has been designed to recognize a particular DNA sequence.

1. The Cas9 protein forms a complex with guide RNA in a cell.
2. This complex is attached to a matching genomic DNA sequence.
3. The Cas9-RNA complex cuts the double strands of the DNA.
4. A segment of DNA can be removed or revised using donor DNA.

**KEY WORDS**

**gDNA**
gDNA is a short synthetic RNA which defines the genomic target to be modified.

**Cas9**
Cas9 is an enzyme that acts as a pair of ‘molecular scissors’ to cut the two strands of DNA at a specific location in the genome so that bits of DNA can then be added or removed.
CULTURES: Tell us more about your role at the University of Wisconsin.

CHARO: I am a professor here and have been one since 1989 when I arrived. I have served in a number of positions around campus related to ethics. I was a member of the institutional review board for many years, have been on the bioethics committee, have served as the associate dean here at the law school, and done a great deal of guest lecturing or informal consultation on the science side of campus.

CULTURES: How can institutions prepare for ethical issues we may not currently be able to fathom? Should governments be more involved?

CHARO: I don't think there is an answer that one could use for each of the technologies and regulatory or ethical issues. I tend to think in terms of process. So, in the area of ethics, I think there are a few things for which are essential. The first is an absolute commitment to the scientific method, to objective analysis, and to the creation of an evidence-based policy. That requires people to enter a debate with a willingness to abandon their preexisting notions and opinions and see where the evidence goes.

The second part of the process is to have a kind of moral compass for secular and state institutions. The moral compass that has to be maintained is what I call distributive justice. How do you fairly distribute the risk and benefits of a technology? For nonreligious institutions, the moral compass has to be distributive justice. I think religious institutions are going to base their policies on the ideologies of the doctrine of their own denomination. For these groups, I think the crucial thing is that they be open about when their policies are based on their doctrine and not on evidence-based reasoning. It is really, really crucial that people who are acting out of religious doctrine not do so in a way that fundamentally imposes a limit on those who do not share their values.

CULTURES: At a time when we are seeing vast technological advances throughout the sciences, what can individual scientists do to better communicate their work and the ethical implications?

CHARO: I am a professor here and have been one since 1989 when I arrived. I have served in a number of positions around campus related to ethics. I was a member of the institutional review board for many years, have been on the bioethics committee, have served as the associate dean here at the law school, and done a great deal of guest lecturing or informal consultation on the science side of campus.
**CHARO:** I think we have to start by recognizing that most individual scientists are not necessarily interested in – or good at – a lot of the public speaking or public engagement that we associate with the policy world. But scientists can get involved with the many campus activities and professional societies related to these policy positions.

It is really crucial that scientists be willing to stop and listen long enough to hear the non-science aspect of these discussions. Think about genetically modified organisms. We all recognize that years and years of scientific research have failed to find any substantial difference between genetically engineered food and other kinds of food – safety has really not been an issue. I’ve known scientists who have become very disparaging of the opponents of genetically engineered foods. And I think it is partly because they are not hearing that, underneath the rhetoric, (some of which is disingenuous, I agree) there is a kind of spiritual objection and an emotional attachment to things that are perceived as natural.

Listening, hearing, and responding in a way that acknowledges these emotional reactions is necessary. It is important to ask, “How does one accommodate an emotional or spiritual attachment that leads to a different conclusion than what is indicated by the evidence?” How does one balance these two things? It is important to give people who are not scientists a way of feeling that they are a respected part of the discussion. In that way, scientists can make themselves more accessible and avoid the possibility that they are perceived as condescending.

**CULTURES:** How has your work in bioethics changed since the discovery of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)?

**CHARO:** Genome editing has simply accelerated our path toward engineering things in a way that I don’t think anybody really expected. My first involvement was with Jennifer Doudna’s meeting in the Napa Valley in January 2015, which she organized with David Baltimore and Paul Berg. Then I found myself involved in several different kinds of National Academies activities, including the International Summit and the consensus study. And, I have written with other people, such as Dana Carroll, and Hank Greely about non-human applications and areas where regulations don’t necessarily make sense.

I have also been lecturing on both the non-human and human aspects of CRISPR, and been in conversation in various contexts with the Department of Defense. Their biotechnology people have been very attentive to the capacity of CRISPR to change the range of things that one can do or how precisely one can do them. CRISPR has therapeutic implications for our soldiers and veterans, but it also has the potential to be diverted toward weaponization. CRISPR is really easy to do and gives you the ability to develop organisms that are more dangerous, more pathogenic, more easily transmittable, or somehow more resistant to countermeasures. The one comforting thing is that it is actually very hard to weaponize these kinds of things, because it is hard to figure out how to get these things to stay alive long enough and distribute them widely enough to actually get them to do the damage you want them to do.

**CULTURES:** You were co-chair of the National Academies report entitled “Human Genome Editing: Science, Ethics and Governance,” that determined gene editing on reproductive cells may be permitted in the future. How did you come to this conclusion? What factors did you consider?
The committee was formed with a large number of international participants representing a wide distribution of expertise across science, medicine, sociology, ethics, law, etc. We had two ways of collecting information. (1) Staff would bring key literature to everyone’s attention and identify things we all should be reading. (2) We hosted a series of public sessions where we invited speakers to come present to us. We had representatives from religious groups, scientists, and government actors.

The report is only about human applications; we didn’t talk about agriculture or crops or animals or national security. We looked separately at heritable versus non-heritable changes, and we looked at differences between therapeutic uses versus so-called enhancement.

We recognized that basic laboratory science was crucial if we were going to understand this and emphasized the need for continued, sustained laboratory science.

**Therapeutic interventions:** We tried to discuss the range of ways those might be accomplished, and we talked about how this is actually going to be the larger area of application when it comes to humans. We looked at the regulations that now govern research with human beings, as well as extra rules and advisory bodies for gene therapy, and found that they really had all the tools they would need. We found it fairly easy to distinguish most therapeutic and prevention uses from what you could call enhancement. But enhancement turns out to be a complicated term. Many enhancements are quite well accepted, whether in better nutrition or in cosmetic surgery. And indeed, when engaging in therapy, we often leave patients better off than they would have been before their illness or injury. Is that an enhancement? But nonetheless, there is great public concern about enhancements done solely to move from ordinary to extraordinary capability, and fear of uneven access and unfair advantages.

**Heritable “germline” editing:** We recognize that this is where the public focuses a lot of its attention, even though it’s the least likely area of application. There are alternatives for people who want to have genetically related children without the risk of passing on a deleterious mutation. But we were able to identify a few circumstances for people who wanted genetically related children for whom something like embryo or gamete editing would be the best option.

I think what you see in this report is a conclusion that there are some circumstances where one could imagine heritable germline editing being ethically defensible.

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**CHARO:** This committee was formed specifically to do two different things. One was to try to identify overarching goals that could guide policy development regardless of national boundaries or cultural tendencies. The second task was much more specific: it was to make precise recommendations to our federal government here in the United States, particularly with respect to whether our regulations are adequate.

I think what you see in this report is a conclusion that there are some circumstances where one could imagine heritable germline editing being ethically defensible. We chose not to base our recommendations on speculation, but looked as much as possible to evidence drawn from experience and from a good understanding of the technical limitations inherent in the technology.
CULTURES: What one piece of advice would you give an early career scientist looking to change the world with transformative technologies?

CHARO: Read science fiction. Science fiction is where you can, with the help of the authors, begin to imagine a world with a particular technological innovation, and because it is in the context of fiction, the authors give you the scope to imagine how it affects the world. You want to be able to imagine a transformative technology and to imagine whether or not it is something that you would be happy to see developed. Make sure you don't limit yourself to the dystopian vision of science, and make sure you also look at the stuff that is good. Then when you are pursuing your very careful, very incremental science, also try to imagine what it is you want the world to look like and spend a little time working toward that as well. You have to work on two tracks. You not only have to focus on your quiet, head-down bench science incremental work, but you also have to have some bigger, more dramatic outcome that you keep in mind, and try to see if your science can take you in that direction.

There are many opportunities that young scientists should be aware of. There are fellowships from the American Association for the Advancement of Science that are a phenomenal opportunity to get a job with the government, whether in legislative or executive branches, and spend one or two years contributing to the policymaking effort. A substantial percentage of the people who have done that program wind up staying in the policy world. There are shorter-term fellowships that go on for 6 to 8 weeks. There are also part-time fellowships at the National Academy of Science where you simply have a portion of your time bought out so that you can spend part of your time working with a committee at the National Academy of Science on a particular project. There are opportunities at a number of advocacy organizations, whether it's the Sierra Club type of organization for people who are interested in environmental issues or any one of the reproductive health organizations. There are opportunities to try out the policy world if that's where you want to go instead of staying tied to the bench. And, finally, I would not “diss” going into industry. Industry is crucial to how we develop our policies. Companies look at the future, decide what might be a salable commodity, and begin developing it. They are at the vanguard of developing something that really can transform society. Understanding the world of business is a way to work toward having some effect on where the science goes.

“Read science fiction. You have to work on two tracks. You not only have to focus on your quiet, head-down bench science incremental work, but you also have to have some bigger, more dramatic outcome that you keep in mind, and try to see if your science can take you in that direction.”
Alta Charo

R. Alta Charo (BA Biology, Harvard 1979; JD Law, Columbia 1982) is the Sheldon B. Lubar Distinguished Research Chair and Warren P. Knowles Professor of Law and Bioethics at the University of Wisconsin. Her previous employment includes the Congressional Office of Technology Assessment and the US Agency for International Development. She served on President Clinton’s National Bioethics Advisory Commission, and was a member of President Obama’s HHS transition team, followed by two years as a senior policy analyst at the FDA during his administration. Charo is an elected member of the National Academy of Medicine (formerly known as the IOM), where she co-chaired the committee on guidelines for embryonic stem cell research and on human genome editing. At present she co-chairs the Academies’ Regenerative Medicine Forum, and is a member of ethics advisory committees on synthetic biology, gene drive and neuroscience at DOD’s Defense Advanced Research Projects Agency (DARPA). Charo is a fan of Star Trek and Jane Austen, in equal measure.
CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) and CRISPR-associated (Cas) genes are changing the scientific world, as we know it. The technology allows researchers to edit parts of the genome by removing, adding, or altering sections of the DNA sequence. The technology is fast, cheap, and relatively easy to use, allowing researchers to reach new horizons when it comes to human genome modification projects.

Solving the Organ Donor Shortage – One Pig at a Time

Interview with Luhan Yang, Ph.D.
Written by Katy Stewart, Cultures Editor
Dr. Luhan Yang, co-founder and Chief Scientific Officer of the Cambridge, Massachusetts company eGenesis, has spent much of her scientific career focused on CRISPR-Cas9. As a student at Harvard, she co-authored one of the first published articles demonstrating how CRISPR-Cas9 could be used for human genome editing. Now she is determined to solve the international organ transplant crisis with the technology she helped to perfect. “The figures are striking,” said Dr. Yang on a recent phone call with Cultures. “In the United States alone, there are over 100,000 patients in need of organs. Only 20% [of them will] receive transplantations and that’s only the tip of the iceberg.” With organ donation numbers stagnant over the past two decades, Dr. Yang is desperately searching for an alternative solution.

She and her team at eGenesis think they’ve found it. With pigs. “Certain breeds of pigs have a similar size and pathology to human beings, which provides a gold standard model for people to try and engineer human transplantable organs,” says Yang.

For some, envisioning xenotransplantation conjures visions of Frankenstein-esque operations. But for Dr. Yang and eGenesis co-founder, Dr. George Church, it is the best solution for a dire situation.

Researchers and industry experts have attempted to use pigs for xenotransplantation for years. “The last time the scientific community took a serious look at this was in 1996, led by big pharma. It was a huge failure because of two technical issues. One was the issue of rejection, and the other was the potential for viral transmission from the pig genome to the human genome.”

Porcine endogenous retroviruses (PERVs) are microorganisms integrated into the genome of all pigs.1 Unable to be eliminated through breeding techniques, the retroviruses can infect human cells following transplantation, making previous porcine organ donations an ineffective option.

In September, researchers at eGenesis successfully “created the first generation of pigs free of the endogenous virus using CRISPR-Cas9.”2 With this development, Yang believes xenotransplantation can be reconsidered as a viable option for those in need of a new organ.

“The beauty of CRISPR-Cas9, compared to prior gene editing techniques,’ she told Cultures, ‘is the multiplex ability, meaning it can tackle many genetic targets in a cell at once. Using such a capacity, we can address these two issues. On the one hand, we can modify large portions of the genome to enhance compatibility and on the other hand, we can eradicate those viral elements.”

Three of the 37 piglets created by eGenesis, born without PERVs.
There are many ethical questions about the use of CRISPR-Cas9. But for Dr. Yang, none prevent her from pursuing successful pig xenotransplantation. “There was a survey in the 1990s when the industry first used [xenotransplantation] for human therapy. Survey results showed that regardless of region, religion, or background, human life is held to the highest regard, so it is quite acceptable to do xenotransplantation to save a human life, especially if there is a patient waiting for an organ.” Seventy-one percent of the public in 1999 said that they would consider xenotransplantation for a family member, if no human organ match were available.³

Dr. Yang is frank about the efforts of eGenesis takes to consider the bioethics of their work, every step of the way. “At eGenesis, we prioritize our energy to first address the safety issues, to ensure the medicine and/or therapy poses no harm. We are very open and proactive, and engage the community and public”. Through publicly available, peer-reviewed publications, Dr. Yang hopes to promote transparency about her mission with the public. Hopefully, she says, people will “watch, debate, listen and form their own opinion” about xenotransplantation.

Dr. Yang knows there are hurdles to overcome. While CRISPR-Cas9 has allowed her to do the unthinkable – reconstruct a pig’s genome and successfully breed PERV-free piglets – she also understands the technology is new, and limited. “[CRISPR-
eGenesis successfully addressed two of the largest obstacles to xenotransplantation using CRISPR technology:

1. immunological incompatibility
2. viral transmission

Cas9 is good at cutting the genome to break the gene but when it comes to inserting a gene, the capacity is limited. If you want to insert 1,000 base pairs using CRISPR-Cas9 into a specific location in the genome, the efficiency is in the single digits. If we want to engineer a pathway or confirm novel functionality, we are talking about hundreds of thousands of basepairs, and CRISPR is not ready for that.

Despite these limitations, eGenesis is set on making history to engineer pigs perfected for human donor transplantation. Dr. Yang plays the long game and passionately keeps her eye on the goal. “eGenesis’ mission is to create a world where there is no organ shortage. We understand it is an audacious mission, but it gives us pride and a sense of purpose. While we are still at the early stages of our journey, we are dedicated to translating this mountain of information on this new technology, while using additional innovation to provide solutions for patients in need. And that’s what excites me the most.”

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1. Gene that carries endogenous virus is removed in somatic cell.
2. Cells are used to reconstruct pig embryo (free of endogenous virus).
3. Resulting pig is free from endogenous virus and can be used for transplant.
4. Xenotransplanted organ is compatible with human immune system.

Gene Editing and Xenotransplantation

SOURCE
Luhan Yang, Ph.D.

Dr. Yang is leading the scientific strategies and efforts at eGenesis. She previously developed the highly programmable genome-engineering tool, CRISPR-Cas9, for use in mammalian cells, and pioneered the first isogenic human stem cell lines to model human diseases at the tissue level. She was named among the “30 Under 30” in Science and Healthcare by Forbes Magazine (2014), was a laureate of the “Young Entrepreneur Initiative” competition (2014) and “Young Global Leader” by World Economic Forum. Dr. Yang holds B.S. degrees in Biology and Psychology from Peking University and a Ph.D. in Human Biology and Translational Medicine from Harvard Medical School.
Two summers ago, I was sitting in the waiting room of my doctor's office, scanning the magazines displayed on their bookshelf when I saw the latest issue of The Economist. The cover struck me. A healthy baby surrounded with arrows and phrases like “High IQ,” “Sprinter,” and “20/20 vision.” The title read, “Editing Humanity.” This was the latest in a string of sensational headlines following the first use of the gene editing technology, CRISPR, in human embryos. A few months prior, the cover of MIT Technology Review had displayed a similar image – a doll-like baby with blond hair and unusually large blue eyes. It read, “We can now engineer the human race”. As a Ph.D. student in Molecular and Cell Biology studying CRISPR’s key component, Cas9, these images really bothered me. They say, “designer babies’ are here and you should be afraid.” It’s no surprise that one of today’s biggest public misconceptions about CRISPR is assuming that designer babies are around the corner.
These dystopian fears are not new. Concerns over designer babies rose to the public consciousness decades ago when recombinant DNA technology and in vitro fertilization (IVF) were being developed, and again when Dolly the sheep was cloned[1-3]. In the years since, many countries have passed laws or embraced guidelines that regulate the scientific use of human embryos. A majority of countries with advanced research programs have laws or guidelines in place that either ban or restrict genetic modification of human embryos for reproductive purposes[4]. Even the first two countries to use CRISPR in human embryos for research purposes, China and the UK, explicitly prohibit initiating a pregnancy with genetically modified human embryos*.

In the US, the regulatory landscape is unique. Rather than ban any practices outright, Congress has instead tied the federal purse strings. In 1996, Congress passed an appropriations bill with a rider attached known as the Dickey-Wicker Amendment, which effectively prevents the use of federal funds to conduct research on human embryos[5,6]. Perhaps you’re thinking, “But I heard that human embryos were edited in the US this summer.” You’re right. Shoukhrat Mitalipov’s lab at Oregon Health & Science University used CRISPR in human embryos to fix a mutation that causes a type of heart disease[7] (though the molecular mechanism is being debated). This work received private funding and was performed for research purposes, aimed at curing a genetic disease, not at creating a super baby[8]. If similar work was to be brought to the clinic, it would need approval by the FDA, regardless of the source of funding. To prevent any such application from coming to market, Congress added a stipulation to appropriated funds that prevents the FDA from considering any applications that involve editing human embryos[9]. So, for now at least, genetically engineered babies will not be made in the US any time soon, no matter the motivation.

Changing these laws would likely require broad societal consensus. While a survey published in Science this summer suggests that public opinions about genome engineering have shifted when it comes to genetic disease, by-in-large the public remains strongly opposed to genetic ‘enhancements’ associated with designer babies[10-13]. Even among scientists and policy groups, genetic germline enhancements are strongly cautioned against. None of the statements or guidelines published in the last few years by major ethics groups or important research and medical academies recommend any forays into germline enhancements[14].

Not only is the regulatory landscape unfavorable for creating a super baby, the biology makes it difficult. The reality is that most human traits are extremely complex. The characteristics people tend to associate with designer babies – intelligence, height, and athletic ability – are not controlled by one or even a few genes. Take the seemingly simple trait, height. A 2009 study estimated that 93,000 single nucleotide polymorphisms are required to explain 80% of the population variation in height[15]. This isn’t to say that there aren’t single genes that can have a strong influence. For example, the hormone EPO is considered a performance-enhancing drug and is produced by a single gene. It’s not entirely crazy then to imagine that the gene could be genetically engineered to produce more EPO, thereby making an individual more athletically gifted[16]. But the World Anti-Doping Agency already tests for performance-enhancing gene therapies in athletes, and recently updated its 2003 ban to include all forms of gene editing[17], as hard as that may be to enforce.

“This isn’t to say that there aren’t single genes that can have a strong influence.”

Recent publication covers spotlight genetic enhancements.
“Not only is the regulatory landscape unfavorable for creating a super baby, the biology makes it difficult. The reality is that most human traits are extremely complex.”

Despite the concerns over designer babies, many scientists and doctors are calling for a regulatory path forward to allow gene editing in human embryos for research\(^{18-20}\). The goal would be to understand basic human biology, and potentially, to prevent extreme cases of genetic disease. The World Health Organization estimates there are about 10,000 diseases known to be caused by a mutation in a single gene\(^{21}\). Many of these are extremely debilitating. As a parent, it’s easy for me to understand why someone would want to edit the DNA of their embryos to prevent their future children from suffering. When we have the capability to prevent suffering, isn’t there a moral obligation to do so? But it’s not that simple.

Some argue that there are already approved medical procedures in place that can prevent transmission of a genetic disease. For women who are already pregnant, prenatal genetic testing is now a relatively routine procedure. Women who haven’t gotten pregnant yet but want to ensure their children don’t get their disease-causing alleles can undergo IVF and preimplantation genetic diagnosis (PGD) to choose embryos without the mutation. For many people, it is hard to imagine spending the resources and social capital to develop a new procedure that could risk creating unforeseen consequences for their child and their children’s descendants, when options like PGD and adoption are already available and safe.

To complicate things even further, what counts as a disease worthy of eradication, and who gets to decide? I’ll give a personal example: I have Obsessive Compulsive Disorder (OCD). While not a monogenetic disorder, it does have a genetic component\(^{22}\). Assuming a genetic treatment could be developed, I don’t know if I’d use it, let alone choose to correct any of my future embryos. Perhaps you’re thinking, well that’s because it’s not a big deal. You’d be wrong. Like most diseases, OCD can manifest on a spectrum, and in severe cases can cause extreme disruption of an individual’s life and require costly treatments. As I write this, my OCD is in remission, but for at least a year my OCD manifested itself as an extreme case. I couldn’t leave my house for
days, sometimes weeks at a time, and barely slept or ate. My hands would bleed from the persistent washing and picking, and I constantly felt trapped in a hell of my own mind. I lost friends, and wasn’t able to work. Luckily there are evidence-based treatments for my disorder, and I was able to get help, partly because my family was able to pay for it. What I’ve since realized is that much of what makes me “me” is linked at least in part to my OCD. When it doesn’t hijack my life, it can help me. A mild manifestation of my OCD is perfectionism. This has helped me become an excellent student and get into one of the best universities in the world to obtain my Ph.D. It keeps me considering the many possible views and outcomes of any given situation, and thereby gives me strong analytical skills. I like to think I have something to offer the world, though that is up to the world to decide.

I think it’s safe to say that designer babies won’t be available any time in the near future. But what about using CRISPR in human embryos to prevent disease? This application is coming. Researchers around the world are conducting experiments in human embryos to fix harmful mutations. I don’t know yet how I feel about this, but I know if it’s going to happen, it will need to be regulated responsibly. To me, the key issue will be deciding which diseases should be prevented by editing. Deciding where the line between prevention and enhancement lies will also be necessary. Making sure we preserve societal infrastructure for those individuals who will continue to be born with genetic diseases will be critical. Perhaps most importantly, engaging those communities directly affected by this application is essential. As a scientific community, we need to seek broad public input and provide accurate information to help inform policy makers. While societal consensus on ethical issues and policy decisions should be the goal, it may not always be obtainable, and in those circumstances, somebody will have to decide. The best we can do is make the most informed decisions with the input of as many stakeholders as possible.
REFERENCES


Lea Witkowsky, Ph.D.

Lea Witkowsky is a Project and Policy Analyst at the Innovative Genomics Institute, a non-profit, academic research organization formed through a partnership between UC Berkeley and UC San Francisco. The institute’s mission is to develop and deploy genome engineering to cure disease, ensure food security, and sustain the environment for current and future generations. After becoming interested in the societal and ethical implications of CRISPR-Cas9 during her Ph.D., Lea joined the IGI to work on public engagement and science policy projects. She received her Bachelor of Arts from Willamette University in 2006, and her Ph.D. in Molecular and Cell Biology from the University of California Berkeley in 2016 where she worked with Dr. Robert Tjian studying mechanisms of human transcription and the influence of chromatin on CRISPR-Cas9 gene editing.
Ever since I was young, I have been fascinated by artificial intelligence (AI) and determined to create human-level AI.

Not long ago, this ambition was seen as a fanciful dream, reserved for the cinema screen or video games. However, with the rapid development of AI, these conversations are making their way into the mainstream, and the issue of ethics is taking center stage.

In 2014, I founded GoodAI, a research and development company based in Prague. Our aim is to develop general artificial intelligence – as fast as possible – to help humanity and understand the universe.
GENERAL VERSUS NARROW AI

When discussing AI, it is important to understand the difference between general and narrow AI.

General AI is a system that can adapt the way it approaches novel tasks, thus becoming more efficient at solving future objectives. The aim of general AI is to solve tasks that not even its creators can anticipate. It is often referred to as human-level AI, or strong AI, and it has not been created yet.

Narrow AI, we see every day. It refers to an AI system that can perform very specific tasks, but does not do much else. For example, Google recently created an AI that mastered the ancient Chinese board game Go. The machine competed in a tournament and beat the best players in the world. However, if you asked it to tell you the difference between a cat and a dog, it couldn’t tell you the answer. It is often referred to as weak AI or specific AI.

Finally, once general AI has been reached, it has been theorized that it will not take long for AI to surpass humans in terms of intelligence, reaching a stage of superintelligence.

I believe the questions of ethics are most important in the development of general AI. Once AI reaches human levels of intelligence, how can we ensure that it will be “good” and share our values?

CREATING MORALS

The outlook of an AI agent is very much determined by its creator, who programs and teaches it.

It is impossible to simply hard code a set of morals, or ethics, into an AI system, that tells it what to do in every different scenario. It is not
good enough just to teach basic concepts such as “right” and “wrong” or “good” and “bad.” Values and morals change with time, and context, and are rarely black and white.

Furthermore, we must aim to teach AI agents to understand things in the way we do. For example, if we give an AI the instruction “help people,” we have to be sure that the AI has the same understanding of “people” as we do.

This is why we aim to instill a deep understanding of human values on our AI. With this understanding it will be able to make complex decisions and judgments in real-life situations.

At GoodAI, our ultimate aim is to create general AI that can be used as a powerful tool by humans. We could use it to augment our own intelligence and help us to solve some of the most pressing global issues.

This stage of development would see AI become part of our everyday activities. We would use it without even thinking, as naturally as we put on a pair of glasses. However, as humans and AI become closer, and possibly even merge, it is the understanding of human values that will be vital to making sure it is safe.

LEARNING LIKE A CHILD

Philosopher Nick Bostrom has outlined a scenario where an AI has been given one objective – to maximize its paperclip collection. In his example, a superintelligent AI decides that eliminating humans will help maximize its paperclip collection efficiently.
I see our AI agents as blank canvases. Our job is to fill them with knowledge so that they can navigate for themselves and make decisions about what is morally and ethically acceptable.

For now, we are teaching the AI. However, with time, it is likely that AI will reach superintelligence and be far smarter than the best human minds in every field.

At this point it may be difficult to draw a line between humans and AI, because humans will be using it to augment their own abilities. At this stage, we will be able to use AI to create new, better values and completely transform society.

RACE FOR GENERAL

Reaching the level of superintelligence seems a long way off, especially since we haven’t reached general AI yet. However, it is essential to make sure that the work we do now ensures the safe development of AI.

As companies, governments, and individuals race to be the first to create a general AI, there is a concern that safety may be neglected. Faster deployment of powerful AI might take priority because of the pressure of economic and military competition, and it could have devastating results if speed comes at the price of safety.

At GoodAI, we run the worldwide General AI Challenge. The second round of the Challenge launches in early 2018, and asks participants to come up with a proposal of practical steps that can be taken to avoid the AI race scenario.

We hope that this will have a positive impact on the development of AI, encourage interdisciplinary discussion among AI researchers, social scientists, game theorists, economists, and so on, and open up the topic of safety in AI development to a wider audience.
Marek Rosa

Marek Rosa is the CEO and CTO of GoodAI, a general artificial intelligence R&D company, and the CEO and founder of Keen Software House, an independent game development studio best known for their best-seller Space Engineers (2mil+ copies sold). Both companies are based in Prague, Czech Republic. Marek has been interested in artificial intelligence since childhood. Marek started his career as a programmer but later transitioned to a leadership role. After the success of the Keen Software House titles, Marek was able to personally fund GoodAI, his new general AI research company building human–level artificial intelligence, with $10mil. GoodAI started in January 2014 and has grown to an international team of 20 researchers.
**CULTURES:** Can you tell us more about your work with the Ethics and Governance of Artificial Intelligence?

**VTP:** The project came after a year of exploration and contemplation around what has been going on in various sectors pertaining to artificial intelligence (AI). We found that there were all kinds of plans being made regarding AI development, but nobody was systematically thinking about the challenges it might pose or the solutions it could be applied to, especially more in terms of the social good aspect. The bigger challenge was whether a government framework is something that the private sectors are willing to talk about and willing to look into. Things are happening at such an exponential rate that it turns out that most of the governmental agencies are not up to date on how to assess AI use. And so, the program was launched with those issues in mind. It involves looking into these kinds of frameworks and the discussions around them, as well as ethical morality and government structure. We also might look into AI and social good, actually promoting research in such projects to see how AI can be applied to solving large issues.
CULTURES: Can you talk a little about how institutions can prepare for ethical issues they may not currently be able to fathom due to the exponential growth of this technology? And do you think that government should be more involved in AI regulation?

VTP: Of course government should be involved. When it comes to any sort of policy design, we need an agency that can implement it and enforce those policies. I think governments are better suited for implementation and enforcement purposes than most of the private world. In regard to the ethical issues, look at the criminal justice system. We know that machine learning and AI are used for different levels of profiling in the criminal justice system. Judges are actively using it in terms of understanding who goes on trial, what the charges are, and things of that nature. The problem is that no one has questioned the historical set of data that drives these algorithms. By and large, we find, and so do my colleagues at other agencies, that these data sets already have a great number of biases around race, gender, and so on. What happens then? We are not only perpetuating the existing biases in the system, but we also are giving it credibility. That is just one example. Then of course you run into the long-term issues of AI – such as the impact it might have on civic society. Civic societies must think about this before it is too late.

CULTURES: Suggestions for individual scientists – what can they do to communicate their work, and what are the ethical implications of using AI?

VTP: Historically, scientists have agreed that their approach to science should be amoral or apolitical so that it can maintain a sense of neutrality. We have seen historically, especially after the Manhattan project, that there was a group of scientists who took certain political stances to say what their research would mean in the long-term. So, I believe that, taking AI into consideration, it is not sufficient for individual scientists and groups of scientists to simply say that their role is to promote research, but that they are not responsible for what happens to the product that they develop, that they are not responsible for what happens to the research they develop when there is an immediate correlation between what scientists are working on and what it might do. I believe that, when it comes to individual responsibility, again, they should maintain some sort of sanctity around data sets and data value so that they know they are not letting algorithms perpetuate the ill habits of a historical system. AI is also an opportunity for self-correction and recognizing when biases exist. It often falls to the scientific team of a company, not to the marketing team, to be cautious about what traits are being made. From a civic society perspective, there has been a shift. It is fine that we are adding AI to medical systems, but are we going to be providing training to the current generation of doctors and medical professionals? Especially for doctors – how will it shift their training in medical school in terms of automation and integrating AI into an operating theater or interdisciplinary medicine? There are things – psychological or otherwise – that people need to be trained in.
AI is a growing billion dollar industry. This has an impact on the poorest nations. How do we ensure everyone rises, not just the top one percent?

VTP: If we look at the current norm, it would be so idealistic to say that there will be a level playing field for AI between developed and undeveloped countries. After all these years of Internet and data-driven devices, and we see this great divide in technology and access to it. I think when it comes to AI for social good, there are three areas that would be useful to mend this gap. One is around education. How do we design and leverage the capabilities of AI to create more tailored, more individualized learning systems in different societies? The second is health care and medicine. How do we create more accessibility to the treatment of complex diseases? Third is the financial system, especially for countries that historically receive aid from developed countries. It is not new that we live in a world where there are systems that are more corrupt than others. If we are able to utilize and leverage the AI system to create more transparency around how aid is being utilized, I think this will help us feed back into the policy-making system to be able to say “okay, you know, it's working or it's not working” and so on. But I think the issue is not just about emerging countries, I think the issue is also with the first world countries. There are already indications of fear of automation and labor displacement and job displacement. The past 50 to 60 years, our attitude has been that there will be more employment because there are people acquiring new skills sets. Companies and politicians – that is what they are selling. We can't bring certain jobs back, but if you learn a new skill set, there will be more opportunity for you. And you know that statement has truth to some degree in regard to automation. But when it comes to AI, people forget that this is a technology that is fundamentally built to replace all other technologies and it is not useful to deny what might arrive in the long term. A bunch of companies like IBM and Microsoft are investing in AI, saying it will result in more technology. It might create certain specialized jobs for a very short period of time, but, if it is doing what it was designed to do, the idea is that it will not require humans to do all these things.

“I believe that ... it is not sufficient for individual scientists and groups of scientists to simply say that their role is to promote research, but that they are not responsible for what happens to the product that they develop, that they are not responsible for what happens to the research they develop when there is an immediate correlation between what scientists are working on and what it might do.”
CULTURES: What about AI excites you the most despite these big uncertainties?

VTP: I think there are a lot of wonderful things that could arise from it. We have a global population struggling to create a more egalitarian society when it comes to access to education and health care. I am hopeful that AI will be able to facilitate that. I am hopeful that AI will create more reach, more education, to help us design new learning platforms that are designed for more individual learning. Next, human beings will rethink humanity all together. After 10,000 years of living, all we have become is working to live in an environment. Our sense of purpose, our sense of identity is driven by day-to-day labor. For the past 50 years, it has stifled human creativity. People do not have free time to do things they wish to do, they do not have time to explore the depths of human relationships or the depths of Mother Nature, so I think that we are able to have these transitions. These are evolutionary transitions, and I think we will be able to rediscover humanity in a new way.

Tenzin Priyadarshi

The Venerable Tenzin Priyadarshi is an innovative thinker, philosopher, educator and a polymath monk. He is Director of the Ethics Initiative at the MIT Media Lab and President & CEO of The Dalai Lama Center for Ethics and Transformative Values at the Massachusetts Institute of Technology, a center dedicated to inquiry, dialogue, and education on the ethical and humane dimensions of life. The Center is a collaborative and nonpartisan think tank, and its programs emphasize responsibility and examine meaningfulness and moral purpose between individuals, organizations, and societies. Six Nobel Peace Laureates serve as The Center’s founding members and its programs run in several countries and are expanding.

Venerable Tenzin’s unusual background encompasses entering a Buddhist monastery at the age of ten and receiving graduate education at Harvard University with degrees ranging from Philosophy to Physics to International Relations. He is a Tribeca Disruptive Fellow and a Fellow at the Center for Advanced Study in Behavioral Sciences at Stanford University.

Venerable Tenzin serves on the boards of number of academic, humanitarian, and religious organizations. He is the recipient of several recognitions and awards, and received Harvard’s Distinguished Alumni Honors in 2013 for his visionary contributions to humanity.
Voices

ASM AMBASSADORS FROM THREE COUNTRIES SHARE THEIR THOUGHTS ON THE CHANGING LANDSCAPE OF TRANSFORMATIVE TECHNOLOGIES.

What type of ethical issues do you think could arise with CRISPR use? With AI use?

FEATURING RESPONSES FROM:

TOMISLAV

Croatia

DIANA

Argentina

SOLIMA

Sudan

TOMISLAV

A pivotal ethical issue that concerns biological technologies (and particularly CRISPR as a revolutionary tool) is that any changes in the germ cells may potentially be passed down to future generations, subsequently introducing them into the population. Furthermore, there is an issue of potentially creating genetic alterations outside of the current human variability range. Where AI is concerned, although the advances and breakthroughs are fast and immense, there are inevitable concerns around data protection, privacy and governance.

SOLIMA

There are several potential ethical issues with CRISPR. For me, the main ones are:

1. Ecological imbalance.
2. Risk assessment (may produce off target mutations, which can be deleterious).
3. Human trait selection guidelines.
4. Predisposing factor to develop new disease.

DIANA

About CRISPR-Cas9 use, my ethical concern is about two main aspects: the manipulation of human embryos for experimentation and the gene editing for a selection of an “improved population” of human beings.

About AI, my ethical concern is if there is a consensus about an “ethically and judiciously” use of such technologies. AI applications represent great advantages for many human activities and necessities, but the problem always relies on who is behind.
Do you think your country’s government should regulate CRISPR? AI? Should the UN set regulations?

**TOMISLAV**

A certain amount of country-wide regulation for using CRISPR and AI in research is not automatically a negative thing, since a cautious approach to powerful and rapidly spreading technologies should always be warranted. However, excessive regulation may cripple further innovation in this field and also give rise to a certain type of political stigma; therefore, a balance has to be found. Anecdotal experience with GMOs showed that regulatory systems tend to differ between the US and Europe (the US tends to endorse product-based regulation, whereas Europe leans towards regulating the process), thus introducing the UN as an arbiter may be a step in the right direction.

**SOLIMA**

I believe that the government of my country, Sudan, should regulate CRISPR-Cas9 with AI under religious, legal, economic and social considerations. The UN should set regulations for the evaluation and control of CRISPR-Cas9 and AI technology.

**DIANNA**

I do not have any certainty about my country emitting potential regulations on both CRISPR and AI. I consider that it will be very difficult to articulate a normative without generating legal voids leaving no coverage in some aspects. Dr. Arroyo mentioned: “...how can regulations on CRISPR-Cas9 or AI usage be set if all potential applications and extent are not fully known?...”

The UN would be an alternative for a global regulation in these issues.
The feared will eventually become the familiar, which is a reason why researchers and all relevant parties should discuss the ethics of CRISPR and AI openly, continuously involving the concerned public. In the end, vast benefits of such technologies are always recognized, while the worst fears never substantiate. However, in order to reap all of the promised benefits, we have to endorse careful thinking about proper implementation and regulation straightaway from the dawn of these technologies. Ultimately, the application of AI and machine learning to CRISPR will create predictive models to make the use of CRISPR painstakingly accurate. Of course, I know we are still far from such utopian application and unification of those two technologies, but I hope I will witness at least a fraction of their potential.

Tomislav Meštrović is a medical doctor and clinical microbiologist with a Ph.D. in biomedical sciences from Zagreb, Croatia. He currently serves as the Antibiotic Action Champion of the British Society for Antimicrobial Chemotherapy (BSAC), Young Ambassador of Science of the American Society of Microbiology (ASM), as well as the acting chair of ASM’s Young Leaders’ Circle. He is also actively involved in ASM Member Engagement Committee. He received numerous travel grants and scholarships from the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the International Union against Sexually Transmitted Infections (IUSTI).

His research interests include antimicrobial resistance, sexually-transmitted diseases and human microbiome.

We considered that a scientific community without conflicts of interest and patents should be responsible for the exhaustive experimentation required before the implementation of new therapies to ensure the benefit of all. New therapies focused on solving genetic disorders would be optimal for improving the daily life quality of a person. But thinking on the improvement or selection of the human individuals by editing genes is an issue that reminds me of historically scary practices performed in the past.

Dr. Vullo received her degree in Chemistry and her Ph.D. in Industrial Microbiology from the Faculty of Sciences, University of Buenos Aires, Argentina. She is Associate Professor at the Universidad Nacional de General Sarmiento and permanent researcher of the National Scientific and Technical Research Council - Argentina. Her research projects are focused on subjects related to Environmental Biotechnology such as microbe-metal interactions for the design of innovative biotreatments of metal loaded wastewaters and the study of Plant Growth Promoting Bacteria for the development of biofertilizers applicable in the restoration of horticultural soils with continuous agrochemical exposure.

The potential for these technologies is vast. CRISPR-Cas9 and AI technology could be used as medical therapies to overcome infectious and inherited disease, to induce genomic alterations in plants improving crop quality or introducing disease resistance.

Solima Sabeel received her BSc. and MSc. in Medical Microbiology from faculty of Medical Laboratory Sciences, University of Khartoum. Now she works as Medical Microbiology lecturer at Ibn Sina University. She attends and speaks at conferences and seminars, assists undergraduate and post graduate researchers, organizes symposiums and forums, leads microbiology discussion groups, and supports the global networking of Sudanese young microbiologists. She worked as Clinical Laboratory Medical Technologist, Khartoum Teaching Hospital. She is the American Society for Microbiology’s Young Ambassador in Sudan. She has published papers on Tuberculosis and analysis genes associated with multidrug resistance mycobacterium tuberculosis.
ON THE GROUND

Read about four companies using artificial intelligence and gene editing to enhance transformative technologies, juggling ethics and innovation as they go.
Calyxt, Inc is a consumer-centric, food- and agriculture-focused company. By combining its leading gene-editing technology and technical expertise with its innovative commercial strategy, Calyxt is pioneering a paradigm shift to deliver both healthier specialty food ingredients, such as healthier oils and high fiber wheat for consumers as well as agriculture advantageous traits, such as herbicide tolerance to farmers.

Calyxt uses TALEN® as its gene-editing technologies rather than CRISPR-Cas9 which they believe works better with highly complex plant genomes.

Q: How do the ethical debates around gene-editing technologies uses in agriculture vary from the debates surrounding the gene-editing technologies used for human gene editing?

A: “At Calyxt, we believe that we can apply safe gene editing technologies to help make the foods that consumers love healthier. Food ingredients that are being developed through gene editing may occur naturally and randomly through evolution, or under a controlled environment through traditional ag technologies. Those processes are imprecise and take many years, if not decades. Calyx’s proprietary technology merely speeds up the natural processes that already take place in nature. As consumers’ tastes evolve and nutrition needs emerge, at Calyxt, we are able to take advantage of the precision, cost-effectiveness and development speed that our proprietary TALEN gene editing technology presents. We will be able to create a next generation of healthier, more nutritionally rich foods for consumers in the near future.”

FEDERICO TRIPODI
CEO, Calyxt
Q: How does the Innovative Genomics Institute’s public engagement work relate to CRISPR-Cas9 and why is it so important to engage in public discussion?

A: “Genome editing can be applied in any organism, raising important ethical questions in diverse arenas. To cultivate understanding and invite non-scientists to make their voices heard, the IGI sponsors a variety of public engagement initiatives. For example, this past August, we co-organized “CRISPRCon.” This event convened stakeholders and invited the public to discuss hot-button issues in gene editing, from equitable access to agriculture. Amongst the IGI’s developing web-based resources is the “Ask a Scientist” program, a service that connects curious members of the public with volunteer experts. Critically, the institute also sponsors social science research to assess public understanding of emerging technologies, inform future engagement strategies, and help ensure that the full potential of genome editing is realized efficiently and responsibly.”

MEGAN HOCHSTRASSER, PH.D.
Science Communications Manager, IGI

The Innovative Genomics Institute

The Innovative Genomics Institute (IGI) is composed of diverse researchers with a powerful combined expertise. After the development of the CRISPR-Cas9 system for rewriting DNA, they saw the potential of applying this technology to solve some of humanity’s greatest problems. Their scientists conduct world-class research, driven by the real possibility to cure human disease, end hunger, and protect the environment.

In addition to their scientific efforts, the IGI is committed to advancing public understanding of genome engineering and providing resources for the broader community.
Q: How can technology help us understand biology and make medicine rational, preventative and effective?

A: Biology -by nature- is infinitely complex. Understanding disease has historically been possible through direct observation and statistical methods. From cell based lab experiments to clinical trials, thousands of observations over decades are required to pin down cause and effect. The proliferation of computing power and digitized data, combined with decades of biological research, has opened the way for a new, more rational approach. We’ve found that the approach most used - building learning systems to analyze large datasets - can be challenging. Without understanding the underlying biological model, even machine systems learning from very large datasets can barely predict biology better than random guessing.

One of the holy grails of computational biology has long been creating an accurate virtual model of human cells. For a decade, this has been our goal at Turbine. Integrating thousands of known biological facts about molecular interactions in human cells, data about mutations and protein levels, and building an artificial intelligence to simulate its behavior and understand it, we focused on one of the most urgent medical challenges: cancer. Two years ago, we delivered several dozen predictions of various cancers’ response to certain drugs accurately. Today, Simulated Cells of over a hundred cancer types have been built by a team of biologists, medical doctors, AI experts, mathematicians and biophysicists. Millions of simulated experiments are now being run by some of the largest pharma companies to find effective cures against the disease, faster.

Drug discovery methods in cancer still lead to 99% failure rate from the lab to drug approval. While this new, rational drug discovery process is in its infancy, the next decade may bring a revolution in drug efficacy like biotechnology did decades ago - but this time, costs could plummet as well, resulting in better, more affordable cures for the millions suffering from cancer around the world.

SZABI NAGY
CEO and Co-Founder of Turbine
Q: As one of the leading genome editing companies, how do you view your role in making transformative therapies for people living with serious diseases?

A: There are few times in our lives when science astonishes us - when we suddenly may be able to do something that once seemed out of reach. We believe that this is one of those moments.

What if we could repair broken genes? What if we could address the root cause of diseases caused by mutations in our DNA? That is what the team at Editas Medicine is striving to achieve.

Editas Medicine is a leading genome editing company dedicated to treating patients with genetically-defined and genetically-treatable diseases. At Editas Medicine, we believe we have entered a new era in genomic medicine as the growth of genomic information in recent years has significantly expanded our understanding of genetically defined diseases. We believe CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology has the potential to achieve accurate, directed changes in DNA and fulfill the promise that started with the sequencing of the human genome - the potential to treat diseases at their source: At the DNA level.

We’re committed to harnessing the power and potential of genome editing to develop transformative medicines for patients suffering from serious diseases.

TIM HUNT
Senior Vice President, Corporate Affairs, Editas Medicine

Editas Medicine is building the leading genome editing company dedicated to treating patients with genetically defined diseases. Editas Medicine focuses their research on eye diseases, muscle diseases, blood diseases, lung diseases, cancer, and liver diseases.

Editas Medicine has developed a proprietary genome editing platform to allow them to design and optimize each element of their products necessary to achieve the desired edit.
When the John J. Reilly Center was founded in 1986, our late benefactor Jack Reilly (who named the Center after his father) sought a way to promote the critical role of the study of the humanities to students going into science and engineering fields. In each of our educational programs and initiatives, we train students to think about not just the ethical dimensions, but the social, cultural, historical, philosophical, religious, political, and economic contexts in which science evolves.
In 2013, the Center entered into international conversations on the ethical, legal, and social challenges posed by emerging technologies in fields such as healthcare, the military, and the environment by producing its first List of Ethical Dilemmas and Policy Issues in Science and Technology. The list has morphed into a student-run initiative that provides a unique opportunity to get undergraduates from around the university to encounter and grapple with work at the bleeding edge of science and medicine they are about to encounter.

Many of the items on our list have in some way touched upon precision medicine and gene editing, including: the self-healing body; CRISPR-Cas9 (which will need to be updated soon in light of CRISPR 2.0!); rapid whole genome sequencing; personal genetic tests/personalized medicine; and human enhancements.

With news of “CRISPR 2.0”, it’s time to look deeper into what this evolving precision medicine might mean for us. Its general definition implies a truly individual experience for each patient, solving medical mysteries such as: Why do different patients respond in different ways to the same medication? Why do some people develop more aggressive or intractable types of disease? Precision medicine will uncover each patient’s unique set of code (their genome), with the hope that medicine could soon be tailored to work with that code and individual outcomes can be predicted. It promises us a new era of bespoke medicine that many are already investigating on their own thanks to the internet.

Besides individualized pharmaceutical cocktails, precision medicine is set to take advantage of gene editing technology, chief among which is CRISPR, so molecularly simple and effective that at this point we’re trying to find ways to just stick it in our ear. If we can send new DNA into the body to replace faulty DNA, haven’t we found a way to get at the root of every concern? Maybe. Maybe not.

There are a series of ethical concerns associated with this potential intervention. A few that are commonly trotted out include: the “playing God” argument (that we have no right to interfere in creation); the “slippery slope” argument (how far can we go before gene editing is just a frivolous pursuit to create the perfect “designer baby,” and by whose standards do we judge this?); the access argument (should people who have extraordinary means still be able to access the technology even if it’s not widely available?); and the (in)equality of access argument (how do we ensure that life-saving treatments are available to everyone, regardless....

Harvard University scientists have modified CRISPR to address DNA point mutations. Essentially, the updated CRISPR allows scientists to target just one base at a time. The technique rewrites errors in the genetic code instead of cutting and replacing whole chunks of DNA.
of cost?). In light of these alone, it seems reasonable that we find a way to discuss the implications of emerging technologies before they go into use. CRISPR was controversial enough to warrant a moratorium on its use from 2015-2017 so scientists, policy makers, and other professionals could take stock of the ethical issues. CRISPRCon, the two-day conference hosted at UC-Berkeley in August 2017, is a great example of how we might go about that. The social sciences illuminate a couple more arguments worth discussing: the demographic argument (just how many people can our fragile planet afford to house and do death and disease help regulate the human population in some necessary way?), and the over-medicalization argument (what counts as a disease that needs to be eliminated instead of simply accepted or accommodated by society?).

But running alongside these obvious ethical concerns is a relatively neglected risk we need to wrap our minds around: precision medicine reduces us to mere code. It doesn't see organs or limbs or bones, or faces, or people, or circumstances, just code. In theory, your genetic code is the key to everything – the way you behave, the way you react to medicine, the reason your cancer continues to grow despite treatment, the reason your depression is intractable. CRISPR is designed to identify malicious (or just unwanted) code, and treat that code with better code. This is a veritable paradigm shift in the way we see not only diseases, but humans themselves.

Viewed from this angle, so many important questions have gone unanswered:

- To what extent does the “disease as code” model take us away from the social, cultural, economic, and political indicators of disease?
- What happens to the future of medical trials, already imperiled by sloppy design, bad math, and a lack of transparency? What good is a medical trial if the cure is only meant for one person? Does this mean we all become our own beta testers?

- What is the role of the doctor in a system where sickness can be analyzed by a computer? The data technician analyzing our blood or saliva sample doesn't need traditional medical training. Our problems are mere algorithms.
- Do diseases risk being seen as “fake” if no biomarkers are identified?
- And what, exactly, will the medical marketplace look like in an era of precision medicine? Will some cures be more expensive than others? Will insurance be necessary? Who creates and dispenses cures?

The possibility of turning medicine into a data science takes medicine out of the hands of doctors and erases the single most important aspect of medical care, compassion. That’s not to say data scientists aren't compassionate people, only that there is no use for that skill when problem-solving
“We’re good at having these debates in the humanities, even if there’s is no consensus on the “right answer.” Now it’s time to bring our STEM and pre-med students into the debate.”

We’re good at having these debates in the humanities, even if there’s is no consensus on the “right answer.” Now it’s time to bring our STEM and pre-med students into the debate. This is not an argument to try to turn our science and engineering instructors into amateur philosophers in order to teach ethics, but rather to recognize yet again that this sort of humanistic approach (which can come through history, theology, literature, art, and the social sciences as well) must go hand-in-hand with STEM and medical training.

In the meantime, institutions like the Reilly Center will continue these conversations among the next generation of medical professionals, scientists, engineers, and other academics. Our relatively simple mission to humanize science is more important every day, and with each new breakthrough.

Jessica Baron

Jessica Baron is part of the University of Notre Dame’s John J. Reilly Center for Science, Technology, and Values and Director of Media and Engagement for the History of Science Society. She earned her Ph.D. in History and Philosophy of Science and currently studies and teaches both the history of public health and future tech in medicine. She built and has managed the Reilly Center’s Top 10 List of Ethical Dilemmas and Policy Issues in Science and Technology since 2013.
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– The CULTURES Team

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