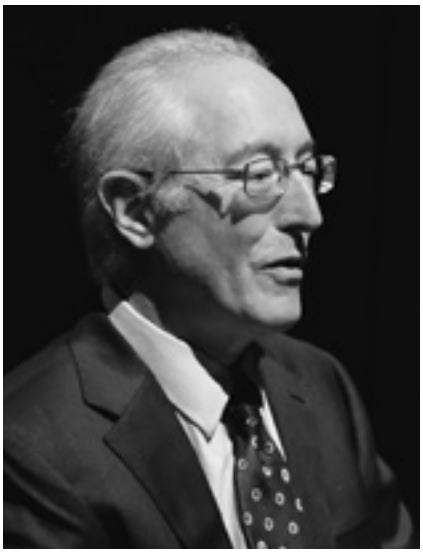
Scientific Advances and Their Impact on Society

On October 21, 2015, at the Sanford Consortium for Regenerative Medicine in La Jolla, California, **Lawrence Goldstein** (Distinguished Professor in the Department of Cellular and Molecular Medicine and the Department of Neurosciences at the University of California, San Diego School of Medicine; Director of the UC San Diego Stem Cell Program; Scientific Director of the Sanford Consortium for Regenerative Medicine; and Director of the Sanford Stem Cell Clinical Center) moderated a panel discussion about scientific advances and their impact on society with **J. Craig Venter** (Co-founder, Executive Chairman, and Chief Executive Officer of Human Longevity, Inc.), **Lisa Madlensky** (Associate Professor in the Department of Family Medicine and Public Health at the University of California, San Diego Medical Center and Program Director and Genetic Counselor at the Family Cancer Genetics Program at the Moores Cancer Center at the University of California, San Diego), and **John H. Evans** (Professor of Sociology and Associate Dean of the Division of Social Science at the University of California, San Diego). The program, which served as the Academy's 2026th Stated Meeting, included a welcome from **Jonathan F. Fanton** (President of the American Academy) and **Gordon N. Gill** (Professor of Medicine and of Cellular and Molecular Medicine Emeritus at the University of California, San Diego School of Medicine). The following is an edited transcript of the discussion.



Lawrence Goldstein

Lawrence Goldstein is Distinguished Professor in the Department of Cellular and Molecular Medicine and the Department of Neurosciences at the University of California, San Diego School of Medicine. He also serves as Director of the UC San Diego Stem Cell Program, as Scientific Director of the Sanford Consortium for Regenerative Medicine, and as Director of the Sanford Stem Cell Clinical Center. He was elected a Fellow of the American Academy in 2008.

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Our topic is scientific advances and their impact on society. How does the public understand new biomedical technologies, and how do laypeople form opinions about these new technologies, particularly when they are controversial?

One area that has received a great deal of press recently is stem cells. This is obviously a new and very exciting area of biomedical technology. Stem cells have enormous plasticity when you grow them in the lab, and we are learning to convert them to cells that have been lost to or damaged by disease; for example, pancreatic cells in the case of diabetes, or certain kinds of brain cells in the case of Parkinson's disease. The hope is that in the coming years, if we can learn to do this efficiently, we can begin to treat these diseases and bring relief to the people who suffer from them.

The other major promise of stem cell technology – probably not so controversial – is to begin to build bits and pieces of organs to provide support at the early stages of organ failure. Eventually we will, I think, learn to make entire organs from stem cells if we learn how to build the appropriate plumbing.

What is sometimes not realized by the public is just how much hard work and time it takes to solve each of these technical problems. An idea that might take thirty seconds to draw on the blackboard can end up being a twenty-year project by the time it is done. The public does not always understand this "time problem," and that sometimes plagues us as a field.

The other problem we tangle with in the stem cell area – one that has gotten recent play – is the source of the cells we use. Sometimes the cells we use come from frozen embryos left over after in vitro fertil-

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ization. More recently you may have heard that fetal tissue is used by researchers such as myself in experiments and in potential therapies where no other option is available.

For example, we use fetal brain cells in my lab's work on Alzheimer's disease, and in the center I direct we are using fetal stem cells derived from the spinal cord in a phase I clinical trial to treat spinal cord injury. These are the types of stem cells that have recently become extremely controversial, often without a lot of understanding driving the controversy.

A third problem that we have been tangling with in recent years is what I refer to as "the snake oil problem." Any new technology frequently has imitators on a street corner near you. And stem cells have this problem too. So-called stem cell snake oil clinics will isolate so-called stem cells from a variety of your organs – fat and bone marrow are the popular ones – and will claim to treat you with these cells for any disease that ails you: ALS, Alzheimer's, you name it. If a clinical trial even vaguely resembles it, these clinics will try to sell you an unproven therapy, taking advantage of gray areas in FDA law and regulation.

Finally, we experience the sorts of "normal" problems that go along with any cutting-edge area of biomedical technology. The issue of cost, for example, and questions of who gets access. And what are the individual versus the group benefits of a given treatment?

One problem that is coming at us relatively quickly is the use of stem cells to make gametes: sperm cells and egg cells. Making them is relatively straightforward, or at least it will be in the coming years. Those cells could then be genetically engineered to be resistant to disease or to give the organism enhancements. We are already seeing the tip of this iceberg as genetic technology is used to produce embryos that are resistant to, for example, mitochondrial diseases.

J. Craig Venter

J. Craig Venter is a Cofounder, Executive Chairman, and CEO of Human Longevity, Inc., a privately held genomics and cell therapy–based diagnostic and therapeutic company focused on extending the healthy, high-performance human life span. He is also Founder, Executive Chairman, and CEO of the J. Craig Venter Institute and a Cofounder, Executive Chairman, and Co-Chief Scientist of Synthetic Genomics, Inc. He was elected a Fellow of the American Academy in 2001.

My team sequenced the first human genome fifteen years ago and had the pleasure of announcing the achievement live on worldwide television with President Bill Clinton and Tony Blair. That genome cost $100 million to sequence and took about nine months to do. Because it was the first, it was a huge challenge. Today, using new technology, we are sequencing 3,000 genomes a month, scaling up to over 10,000 a month.

So we are at a slightly different scale than fifteen years ago, when the first genome was considered such a gargantuan product that every university and every country had to

contribute to it. Sydney Brenner wanted to have prisoners sequence DNA because it was such an arduous task. Things got a whole lot simpler thanks to computers and a few good algorithms.

Just in the last few months here in La Jolla we have sequenced about 20,000 human genomes. We have the largest database of genome data, coupled with phenotype and clinical measurements. And it is already yielding fantastic breakthroughs. We have major programs in oncology, which is probably the area that is changing the fastest in medicine, based on genomic data, because we can find out precisely what has changed. Fortunately, we also have a number of novel approaches to deal with those changes.

So this is now getting to be a data-driven and science-driven aspect of medicine. The biggest challenge is changing the physicians. David Brenner and I are trying to start a program where every medical student at the University of California, San Diego will have their genome sequenced and will then have to analyze it. But at least a third of incoming medical students do not want to know. How can they be ambassadors for the rest of the community and explain to you and interpret your genome if they are afraid to look at their own?

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We are also working with third-party payers, with insurance companies that want to use this data as preventative medicine. We announced a program with Discovery Health in South Africa and England, and they are now offering genome analysis to their 4.4 million members who use their Vitality health program of preventative medicine. Those who follow the program and pay the lowest premiums live eight years longer on average than the ones who pay the highest premiums and do not follow preventative health measures.

The future of genomics will be about detecting things early, preventing disease, or allowing – because of early detection – early treatment. Compare that to the way medicine is practiced now, where we wait until symptoms occur and then try to do something about them.

We just opened the Health Nucleus at Human Longevity. There you can get the most comprehensive physical analysis and examination with MRI imaging, 4-D echocardiogram, and CT imaging, allowing us to generate beautiful, comprehensive photographs of every part of your body, measure any changes, and link it all back to your genome, your microbiome, and thousands of chemicals. It is a great starting point.

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One of the first to go through it was a physician in his forties. From just the 4-D echocardiogram we discovered a greatly distended aorta. His first symptom would have been sudden death. He is also a weightlifter and has hypertension. So the question was when, not if, he was going to have a blowout. The problem proved to be genetic. His father had the same disorder – it was corrected with surgery early on – but his doctors thought it was just an anomaly. They had no idea he had this condition.

When I told the head of one major clinic in the United States about this, he said it was a heart surgeon's wet dream. You do not get a second chance to learn about aneurysms. Even if you are in the operating room at the time, the chances of recovery are low. But thanks to early detection, we found something that a simple procedure could correct, giving the patient a different experience going forward.

Lisa Madlensky

Lisa Madlensky is Associate Professor in the Department of Family Medicine and Public Health at the University of California, San Diego Medical Center, and Program Director and Genetic Counselor at the Family Cancer Genetics Program at the Moores Cancer Center at the University of California, San Diego.

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What do these rapid advances in technology and genomics mean to the average person?

Every day I have the honor and privilege of meeting with people who are going through a diagnosis of cancer or who may have had a lot of cancer in their family, and their main question, the number one thing they want to know, is, "What does this mean for my kids?"

Historically, genetic counselors were primarily involved in prenatal genetic testing and pediatric genetic testing. Initially they helped families who had a newborn baby with a serious medical condition that either had not been diagnosed or needed a series of tests to come to a diagnosis. Once we got to the point where a lot of these primarily metabolic diseases were understood, then prenatal testing became an option for many families.

As genetic counselors, we are trained in two domains. One is molecular biology, genetics, and genomics. We have to know the subject matter in order to be able to explain it to people. The other area is counseling, in helping families navigate the information they receive. If you are not at an emotional place where you can actually hear what we are telling you, it is not going to sink in.

Every family is unique in their experience, so we want to take all of this very complex medical information, complex genetic information, and make it work for each individual family. That can mean things like respecting cultural preferences, since different cultures interpret genomic and genetic information differently. We also want to be respectful of people's reproductive choices. So we present ourselves as neutral players. We are there to help families get what they want to get out of the information.

To be successful, we need to improve scientific literacy. We need to help people understand, from a very young age, what our genetic makeup is all about.

We cannot help people who do not come in, though, and about one-third of patients who are referred for genetic counseling never make an appointment. Why? Maybe their insurance does not cover it. Or maybe they cannot get time off from work or coordinate childcare. Or maybe they are afraid of what they might learn.

They could have any number of reasons, and because I never meet these people I cannot tell you anything definite about them. But I can tell you about the experiences of the people who actually do choose to engage. And even among them, some eventually say, "You know what? I am not fully convinced that I want this information."

So our job is to ensure that people are making informed choices. Our job is not to present an agenda, to say, "You should have this testing" or "You need this testing." Instead our job is to say, "Look. Here is what this testing can tell you right now. If we find something in these genes or we find this particular diagnosis, here is how it would affect your medical care, and here is what it could mean for your family."

The majority of people who make an appointment and choose to come in do ultimately choose the genetic testing. But in many cases we have to acknowledge that although we might have the technology to sequence a particular gene, to identify a mutation or a variant at such-and-such location, we do not yet know what that means.

I am very excited that in the future we will have that information, but we have to work in the present with the families that are coming in now. That means they are often very disappointed. For some, the promise of genetics and genomics has been overhyped, oversold, and we are not able to meet their expectations. Instead, all we can say is, "This sounds exciting. Come back in five or

ten years, and maybe we will have answers for you. But right now, I cannot tell you what to do about your medical care or what this means for your family."

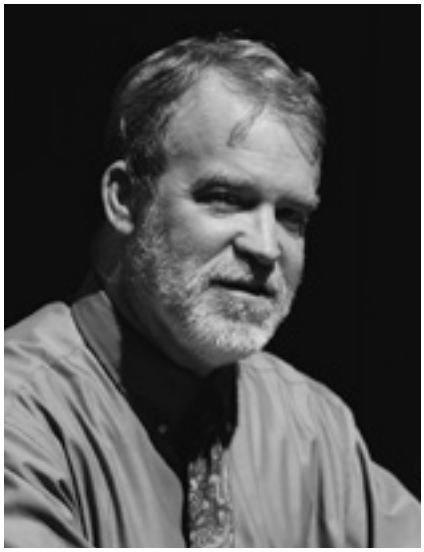
Other times people are delighted, enthusiastic about the opportunity to get a diagnosis that has escaped their family for years. We call this "ending the diagnostic odyssey."

Ultimately, people choose to engage or not to engage for a wide range of reasons. I see patients from very poor and underserved communities, people with graduate degrees in genetics and genomics, and a lot of biotech executives. Everybody can learn something.

I would like to share an anecdote with you about one of my patients. She tested positive for breast cancer. Her mother's side of the family had a lot of early onset breast cancer and ovarian cancer. So we knew where the cancer, genetically speaking, had come from. To us it was quite obvious. But my patient said, "There is no way I have this gene, because I look just like my dad. I know I have all of his genes."

So we had to take a big step back, all the way to first principles, breaking down concepts and helping her integrate from scratch the fact that this really was real. But if you take another step back, you can see that her reaction – "This couldn't possibly be me. I'm not going to believe that this is true." – is also a coping mechanism. Our job is to put all of these pieces together in a way that helps people make health decisions that will work for them and will be appropriate for them.

But to be successful there, we really need to start with improving scientific literacy. We need to help people understand, from a very young age, what our genetic makeup is all about. What can it tell us? What can't it tell us? Moving forward, that is going to be an important priority.



John H. Evans

John H. Evans is Professor of Sociology and Associate Dean of the Division of Social Science at the University of California, San Diego.

When developing surveys to identify how members of the public form opinions about controversial issues in the life sciences – such as embryonic stem cell research, germ line or somatic human genetic engineering, cloning, and gene editing – you use statistical procedures to ask, "What type of person is likely to be more or less opposed to these technologies?" Belonging to some groups turns out to have no particular effect on one's disposition toward these technologies. Men and women, for example, have roughly the same attitudes toward all these technologies. People of different classes and races have basically the same views of these technologies.

What does matter is how much education a person has and what their exact religion is. By talking briefly about these two, I want to dispel some myths that exist in this area. I believe that if the scientific community were to focus on these myths, it could better understand the public on these issues.

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Surveys show that the more educated a person is, the more likely he or she is to support the sorts of new technologies scientists are interested in. Why would this be? Three decades ago the answer would have been, "Well, people with more education are more intelligent, and following the scientist's agenda is the more intelligent thing to do." That is not taken as a serious argument anymore.

The more serious version of the argument is that the public would not be opposed if they had the technical understanding that scientists have. In 1970, Sir Peter Medawar commented on public fears of genetic manipulation of microorganisms, saying, "I find it difficult to excuse the lack of confidence which otherwise quite sensible people have in the scientific profession, for their fearfulness, laymen have only themselves to blame, and their nightmares are a judgment on them for their deep-seated scientific illiteracy."

Contemporary elite scientists tend to also think that opposition from the public comes from the public's lack of knowledge about science. In other words, scientists believe in what science communication scholars call the "knowledge deficit model," the belief that "Ignorance is at the root of all social conflict over science. Once citizens are brought up to speed on the science, they will more likely judge scientific issues as scientists do, and the controversy will go away."

This model is "the great myth in science communication." People who have studied the matter have concluded that an individual's knowledge of science and technology has little to nothing to do with whether he or she supports science or technology. It turns out that the conflict is not over knowledge or facts but over values. According to one meta-analysis of the literature, "Scientists often believe public debates should turn on logic and cross-benefit analyses, whereas the public wants consideration of factors such as fairness, ethics, and accountability."

Thus, the reason people with higher levels of education are more supportive of the innovations being made by scientists is not that they understand the science better but that higher education tends to teach the same set of values that are shared by the scientific and medical community. So while educating the public about stem cells might be inherently good, such education is not going to make people more supportive of controversial science and technology.

The second characteristic that shows up in these surveys is religion, which is actually a much bigger predictor of attitudes than education is. The myth is that religious people, particularly Protestants, are "opposed to scientific knowledge." People reach back to the story – another myth, actually – of Galileo being put in jail by the Pope. The assumption is that religions have one method for making claims about the natural world – transcendent revelation through mechanisms such as the supernaturally inspired Bible – while scientists have a different method: the use of observation and reason. Therefore, this assumption continues, religious people will be less supportive of all science because they believe in revelation and not observation. But this also is a myth.

Studies show that the religious public, by and large, is equally supportive of science as a way of describing the natural world. So, Catholics (those in the United States at least), Protestants, Jews, and other religious groups have no modern history of conflict with science over facts about the world.

Conservative Protestants do have a history of conflict with science over human origins, Darwin, and the like. But studies show that if you gather the most conservative Protestants you can measure in a survey (i.e., the approximately 10 percent of the public who are members of conservative Protestant denominations, are biblical literalists, and attend church every week) and compare them to nonreligious people, you find no difference in the likelihood that they are scientists, in the number of scientific facts they know, in whether they know how the scientific method works, in the number of science classes taken, and so on.

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They disagree with some facts – like human origins and the age of the earth – but they also know what scientists have to say about these things. They just disagree. They want to believe a few fact claims from the religious tradition instead of the scientific one.

But in general, when you interview the public, which is what I do for a living, what you find is that religious people, including conservative Protestants, love science. They love discovering the world. But they disagree about the values that are implicit in certain scientific claims or innovations.

I suspect many of you have seen the 1960 movie *Inherit the Wind*; it is a fictionalized account of the Scopes Monkey Trial. The defender of the fundamentalist position at the trial was the two-time Democratic Party nominee William Jennings Bryan. In the movie, he is portrayed as opposed to teaching Darwin because the Bible has a different account of human origins. But in reality, he was also opposed to Darwin because he believed that the values and morals Darwin had implicitly taught had damaged the morals of the youth of Germany and caused World War I.

Now, whether Bryan's view makes any sense or is true is beside the point. Bryan was representative of the community at the time in thinking that concerns with Darwinism had to do with morals, not just facts. That belief is shared by anti-evolution people to this day. If you look at the intelligent design people, they are primarily motivated by moral concerns.

I recently published a paper looking at conservative Protestants and global warming research. Once you control for the fact that conservative Protestants tend to be disproportionally embedded in political conservatism – essentially, they watch a lot of Fox News – you find that conservative Protestants are as likely as anybody else to believe scientific claims about climate change. Opposition to scientific claims does not come from their religion, but from their political conservatism.

What they do not want is for scientists to be involved in the political debates about what to do about climate change. Why would that be? They think scientists do not share their values. What leads religious people to oppose the scientific community on some issues is not knowledge – or a lack of knowledge – about facts, but differences in values.

Something you will soon be hearing a lot about is gene editing using a technology called CRISPR. Let's say you could success-

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fully use somatic cell human gene therapy to cure an individual of sickle cell anemia. A defective gene would be replaced or a functional gene inserted into parts of the human body that cause the disease. That individual person would be healed.

All Americans would say that was a good thing. The studies I have conducted suggest that even the most ardent fundamentalist Protestants would agree, although they would describe their agreement in a way most people would not; that is, they would say, "It's great that God gave us the brains to invent medicine to solve these problems."

Now, many scientists would say, "That change in that person is going to die with them. What we really need to do is change the reproductive cells so they can't pass that trait onto others. Ideally, we could remove the trait from the entire human genome." Supposedly this sort of thing could be done with CRISPR, which is what everyone is talking about.

But educating the public about how CRISPR works is not going to change people's views about what it can do. And here is where you get the values divide. Many religious people would say something like, "Human beings lack the wisdom to design themselves." And the people who advocate changing the genes in an embryo would say, "We design ourselves all the time." The religious people would then say, "I would have gotten off this train long ago," and the advocates of the new technology would respond by arguing, "You are already on this train whether you like it or not." The point is that the public derives its opinion about science and technology from values and that these values are largely derived from their education and their religious beliefs.

I love scientific innovation. I look forward to the latest medical advances. In my opinion, though, the disconnect between those doing cutting-edge science and the public arises from the scientific community's discomfort talking about the values their work advances. Instead, scientists are more comfortable – and, given their training, this makes sense – talking about facts. But I think science and the public would have greater understanding if the debate shifted to values. ■

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