

Contact Press Relations: email: press@gladstone.ucsf.edu | phone: 415 734 5000

The Future of Medicine

Advances in genomics and stem cell biology highlight the importance of basic research

BY DEEPAK SRIVASTAVA, MD

In the last few years, exciting developments in science and medicine have taken place; developments that stand to entirely transform the way physicians treat patients.

In 2020, when a patient comes to me suffering from heart disease, I will be able to prescribe a drug that I know will work for them based on their unique genetic code. Perhaps I'll even be able to give them a simple injection that could spur their own heart cells to repair damage to cardiac muscle.

Truly revolutionary advances in two specific areas are powering the future of medicine. The first is **genomics**, which allows us to read the whole genetic code of individual patients. The second is a revolutionary form of **stem cell technology** developed by one of my Gladstone colleagues, [Shinya Yamanaka](#), MD, PhD. These advances will allow us to leverage what we know about molecular genetics to transform the way we approach medicine.

But we are not there yet. To achieve those goals, we need to complete three milestones. First, we will have to find a way to easily and inexpensively know, in depth, the entire genetic code of every person. Second, we will have to correlate each person's genetic code with his or her risk for various diseases. And third, we will have to understand why and how genetic variants lead to disease.

Genomic Medicine Comes of Age

We are well on our way to reaching that first goal. In the last few years, advances in DNA sequencing have occurred rapidly, and many companies have developed machines that can sequence genomes at a much lower cost and in a shorter time. Today, we can discover the *entire* DNA sequence of one person's genome in a few days for just over \$1,000. At this cost, it will be possible for whole populations to know their entire genetic code in the coming years, and scientists and physicians can then correlate that genetic code with disease risk.

But we will need to know more than just the DNA sequence. We have to know what it actually means in terms of health and disease. The answer lies in the relatively new science of bioinformatics. At Gladstone, [Katherine Pollard](#), PhD, one of the leaders in the field, has written novel algorithms to analyze and interpret whole genome sequence data. This is an enormous problem, as each genome is composed of 3 billion individual components of DNA. She and her colleagues around the country are trying to

understand the variations of the human genome on a broad scale, ultimately correlating those variations with disease.

Dr. Pollard and her colleagues are quickly realizing that our DNA reveals only a fraction of who we are. In fact, a vast array of microorganisms, including bacteria and viruses, dwell in or on our bodies and together form a microbial ecosystem, or ‘[microbiome](#).’ As a member of the National Institutes of Health’s [Human Microbiome Project](#), Dr. Pollard and her team are using supercomputing to collect and analyze the genetic information within the microbiome and understand the role it plays in human health and disease.

The Power of Regenerative Medicine

The second group of advances has occurred in the area of stem cell biology.

Some years ago, the scientific community was excited by the prospect of generating stem cells by taking a skin cell from a patient with a genetic mutation, removing the nucleus, and putting it into an egg without a nucleus. This procedure was used to clone [Dolly](#) the sheep, but this process proved nearly impossible to replicate in humans.

The technical problems have been overshadowed by ethical ones, namely the idea of making human embryos that would be destroyed to harvest embryonic stem cells. In August of 2001, various federal policies and guidelines put a significant restriction on human embryonic stem cell research. In California we overcame many of those issues through Proposition 71, a taxpayer-based initiative that created the [California Institute for Regenerative Medicine](#) (CIRM).

Nevertheless, the technical and ethical issues surrounding human embryonic stem cell research remained a major roadblock worldwide. Fortunately, cutting-edge technology in this area has fundamentally and permanently transformed the landscape of stem cell biology and how we view the use of genes and proteins in cells. Dr. Yamanaka, who trained at Gladstone as a postdoctoral fellow in the mid-1990s and then returned to Japan to begin his independent career, did that work. Six years ago, he returned to Gladstone and is a senior investigator with us now, maintaining a lab here in San Francisco and at [Kyoto University](#) in Japan.

In brief, Dr. Yamanaka discovered how to directly transform a skin cell from an adult into a group of cells that behave just like embryonic stem cells in almost every way. And he did it by introducing just four genes that were so powerful that they “reprogrammed” the whole genome of the cell—without going through the stages of making a human embryo. Nobody thought this could ever occur. This technology is simple, easy and has spread across the world like wildfire. Because of this work, he won the [2012 Nobel Prize](#) in Medicine.

Practically, what this technology allows us to do is to take a cell from a patient, introduce these four factors, and reprogram the cell into what Dr. Yamanaka called *induced pluripotent stem cells*, or iPS cells. At Gladstone, we have made iPS cells from many patients to treat and understand their specific disease, particularly those involving the brain and heart. iPS technology allows us to understand the cellular consequences of genetic changes that are being identified through sequencing of patient genomes. We are using the iPS cells as human models of disease, to screen for new drug therapies and to test them for efficacy and toxic side effects. In the future, we hope to use these cells to repair organs.

Gladstone researchers are also building on Dr. Yamanaka's iPS cell technology. In my lab, as well as the labs of Gladstone Investigators [Yadong Huang](#), MD, PhD, and [Sheng Ding](#), PhD, we are finding ways to directly reprogram skin cells into [heart cells](#) or [neurons](#)—without first having to revert back to the stem cell-like state. Recently, our lab demonstrated that scar-forming cells in the heart could be reprogrammed into new beating cardiac muscle that regenerated damaged hearts while also improving the heart's ability to pump blood throughout the body. This was the first use of so-called “in vivo” reprogramming to regenerate a damaged organ and improve function, and represents a new paradigm in regenerative medicine that could be applied to many diseases. And in another true testament to the ingenuity of Gladstone scientists, my colleague Dr. Ding is exploring ways of using [small molecules](#), rather than genetic material, to kick start the reprogramming process.

In 2011, Gladstone established, along with the Roddenberry Foundation, the [Roddenberry Center for Stem Cell Biology and Medicine](#) at Gladstone. This center honors the “Live Long and Prosper” motto of Star Trek Creator Eugene Roddenberry, who imagined a world where futuristic progress in science helped humanity. With support by organizations such as CIRM and the Roddenberry Foundation—in concert with continued high-caliber research from Gladstone scientists—I firmly believe we will continue to break barriers in the field of regenerative medicine.

Genomics and stem cell biology: two areas of research and discovery that are rooted in basic science, but are currently revolutionizing how we understand and treat disease. I am proud of how research at Gladstone is advancing these two fields. I am optimistic that as we continue to refine our work and collaborate with our industry partners to spur drug development, the way that physicians like myself treat some of humanity's worst diseases will forever be altered. And a new era of medicine can begin in earnest.