The Medical Revolution:

How Technology Is Changing Health Care

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Genetic Technology: A New Medical Era Dawns

In the final months of 2019 and early months of 2020, the deadly coronavirus COVID-19 emerged somewhere in China and spread across large sectors of that nation. From there, it passed into neighboring countries and, via air and sea travelers, to nations around the globe. By mid-April 2020, more than 2 million people worldwide had contracted the virus, and more than 135,000 of them had died.

As those grim numbers continued to climb in the weeks that followed, eighty-seven-year-old retired medical researcher Stanley Plotkin quietly watched with an overpowering feeling of déjà vu. The onslaught of the COVID-19 pandemic did indeed strongly remind him of what he had gone through back in 1964. In that year, a large-scale outbreak of rubella, or German measles, also caused by a virus, rapidly swept across the United States. Roughly 12.5 million people—about one in fifteen US citizens—contracted the disease. Particularly at risk were pregnant women and the fetuses in their wombs; in the years that immediately followed, more than twenty thousand US babies were born blind, deaf, or with heart defects and/or other serious birth defects.

At the time, Plotkin was hard at work in his lab at the Wistar Institute in Philadelphia, Pennsylvania. Desperately, he and his assistants tried to devise a vaccine to fight the rubella pandemic and save as many lives as possible. A vaccine is essentially a small sample of a disease that, when introduced into the body of a healthy person, can provide him or her with immunity to that illness. In 1965 Plotkin's team made a major breakthrough with its historic development of the RA 27/3 antirubella vaccine, which virtually all young children receive today.

Plotkin's past scientific triumph was not forgotten among medical researchers who early in 2020 were frantically searching for a vaccine to halt COVID-19. The directors of several vaccine companies approached him, explaining their progress to date and seeking his input. "There are at least 40 vaccine candidates being developed"[6] to fight the virus, he remarked in late March of that year.

Among those possible vaccines, some were derived from genetic materials, the main substances in human cells that determine one's physical

A nurse in China monitors the condition of a COVID-19 patient. Medical researchers worldwide are trying different techniques, including the use of genetic materials, in their efforts to develop a vaccine.

characteristics. Those materials contain individual particles called genes, the term from which the word *genetic* derives. If a genetic vaccine turns out to be COVID-19's nemesis, Plotkin said, the world would need "large numbers of doses" as fast as possible. "We need to have companies ready to go into super-action and that needs to be done now."[7]

A Priceless Technological Tool

One of the biggest and most important contributions that genetic technology has made to medicine has been the worldwide search for a cancer vaccine. To aid in that effort, between 2006 and 2020 the National Cancer Institute and the National Human Genome Research Institute teamed up to provide the researchers with a priceless tool called the Cancer Genome Atlas (TCGA). A broad database, it contains detailed information about more than twenty thousand primary cancer samples representing thirty-three separate kinds of cancer. This storehouse of data, which continues to grow each month, has already spawned improvements in the ability to diagnose, treat, and prevent cancer. Moreover, the data is available for anyone in the research community to use for free. According to Carolyn Hutter and Jean Claude Zenklusen, both of the National Cancer Institute,

> It is difficult to overstate the value of the TCGA dataset. Its richness has enabled researchers to catalog specific genomic and molecular changes that occur in cancer, to define a more meaningful taxonomy of cancer types and subtypes, and to even investigate questions that were not imagined at the outset of the project, such as the mining of the data to discover new viruses and other microbial agents. The TCGA marker papers have served as additional resources for understanding the molecular features of these cancers, and a launching pad for individual researchers to deepen the exploration of the data generated.

Quoted in Carolyn Hutter and Jean Claude Zenklusen, "The Cancer Genome Atlas: Creating Lasting Value Beyond Its Data," *Cell* 173, no. 2 (April 5, 2018). www.sciencedirect.com.

Genetic vaccines are not the only form of genetic technology that is presently transforming modern medicine. Another is gene therapy, in which doctors try to prevent disease by injecting copies of selected human genes into a person's cells. Still another, more recent genetic technology has been dubbed precision, or personal, medicine; it uses a person's own genetic material to diagnose and treat an illness.

Fixing "Bad" Genes

These genetic applications of modern technology are introducing exciting new advances into medical science, says biotechnology expert and author Jamie Metzl. "Our growing understanding of how genes and biology function," he states,

> is opening the door to incredible medical applications like using . . . gene therapies to fight cancer and other diseases. But the healthcare applications of genetic technologies are only a station along the way to where these technologies are taking us. . . . [Seeing] all of life, including our own, as increasingly able to be manipulated will force us to think more deeply about what values will guide us as we begin altering biology more aggressively.[8]

This forward-thinking outlook is well illustrated by one of the examples of genetic technology Metzl uses—gene therapy. Still in its infancy as a technology, it is based on the idea that faulty or damaged genes in a person's body that are making him or her sick can be altered in some way. There are presently three principal approaches to the technology. In the first, a "bad" gene, one that is poorly functioning or even nonfunctioning, is replaced by a copy of a "good," or healthy, gene. According to the world-famous Mayo Clinic in Rochester, Minnesota,

> Some cells become diseased because certain genes work incorrectly or no longer work at all. Replacing the defective

genes may help treat certain diseases. For instance, a gene called p53 normally prevents tumor growth. Several types of cancer have been linked to problems with the p53 gene. If doctors could replace the defective p53 gene, that might trigger the cancer cells to die.[9]

The key to making this approach work is finding a proper vector, or carrier, for the healthy gene. This is because if one inserts the new gene directly into a cell or cells, it will remain inert and not function. Instead, doctors place the gene in a vector, usually a virus, that will deliver it by infecting the cells. Of course, researchers first modify the vector virus so that it cannot cause disease. Then the virus containing the replacement gene can be either injected with a needle or given intravenously via the fluids in an IV tube.

"Some cells become diseased because certain genes work incorrectly or no longer work at all."[9]

—The Mayo Clinic

The second major approach to gene therapy involves fixing faulty genes, often ones that have mutated, or changed in form, and now cause disease. The goal is to turn off, or shut down, the unhealthy gene so that it will no longer cause illness.

In the third approach to gene therapy, doctors make injections designed to retrain the sick person's immune system. Sometimes that system does not attack diseased cells as it normally would because it no longer sees them as intruders. In this case, gene therapy helps the immune system to recognize the threat.

Accessing an Individual's Genome

Another promising aspect of genetic technology that is helping to create a new medical era is precision medicine, which in recent years has also come to be called "personalized medicine." It is an approach to patient care that employs an individual's own genetic profile, or DNA information, to diagnose and treat disease. DNA is the genetic molecule that carries an individual's hereditary infor-

After undergoing genetic testing, actress Angelina Jolie learned that she carried a gene mutation that increased her risk of developing breast cancer. She chose to have a preventive double mastectomy.

mation. Thus, in personalized medical treatment, the therapy targets the medical condition of one person rather than a general community of people. Often, closely examining that person's genetic makeup can determine the best approach to treatment.

One famous example of this approach was the case of well-known actress Angelina Jolie. In 2013 she announced publicly that she had had a double mastectomy (surgical removal of both breasts) to keep from getting breast cancer in the future. The award-winning actress said she had decided to take that serious step after having her genome (entire collection of genes) examined by medical researchers. The analysis had found that she

Why RNA Instead of DNA?

Most vaccines that use genetic technology zero in on DNA, the complex molecule that carries hereditary, or genetic, information. However, researchers looking for a vaccine to combat the coronavirus COVID-19 focused most of their attention on a similar but somewhat less complex genetic chemical known as RNA. In human beings and other animals, RNA conveys genetic information from DNA to help in manufacturing the proteins that make up the structure of the body's cells and tissues.

The main reason that RNA turned out to be so vital to the search for a COVID-19 vaccine is that the virus that causes that disease has no DNA. Instead, its basic genetic material is RNA. When the disease invades a human cell, the virus's RNA cannot replicate itself on its own. So it hijacks the person's own protein-making machinery within the cells to help make copies of itself and thereby reproduce and spread. The goal of vaccine researchers, therefore, is to find a way to target those RNA-making proteins. Without them, the virus cannot reproduce and spread.

carried an inherited gene mutation that greatly raised her risk of eventually developing breast cancer. By removing her breasts, therefore, in a single stroke she vastly decreased her chances of getting that dreaded disease. In an interview, Jolie explained,

> I wanted to write this to tell other women that the decision to have a mastectomy was not easy. But it is one I am very happy that I made. My chances of developing breast cancer have dropped from 87 percent to under 5 percent. I can tell my children that they don't need to fear they will lose me to breast cancer. For any woman reading this, I hope it helps you to know you have options [and can] make your own informed choices.[10]

Source Notes

Introduction
From Human to High-Tech

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Chapter One
Genetic Technology: A New Medical Era Dawns

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