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Patents; An obsession with DNA and the human genome leads to development of a technology.

By Teresa Riordan (NYT) 958 words

AS a 23-year-old Harvard medical student, Eugene Chan came up with a bold, even arrogant thought: would it be possible to map any given individual genome swiftly and inexpensively by mimicking the way that DNA naturally acts when it duplicates itself?

This idea came to him several years before the announced completion in June 2000 of the Human Genome Project, which ultimately took about 10 years and $3 billion to map a single, generic human genome.

Mr. Chan spent his free time obsessing on the idea. His tiny dorm room in Vanderbilt Hall became a warren of scientific papers. And when other students dropped by to invite him out for a beer he would demur, instead hunkering down on the weekends to work out his theory.

Mr. Chan wrote a 200-page plan for carrying out his vision. Then, 18 months after entering medical school he dropped out -- with the blessing of his mother and his father, an organic chemist who spent his career dreaming up pharmaceutical innovations at Hoffman-LaRoche.

This month Mr. Chan, now 28, received United States patent 6,355,420 for what he says is a "totally new way of sequencing that mimics the way that nature reads genetic information."

When he was starting out, Mr. Chan persuaded his older brother, Ian, to leave his job as a buyout specialist at Morgan Stanley to help him start U.S. Genomics. The company is based in Woburn, Mass., a longtime center of chemical production that has become home to many technology start-ups drawn to its affordable industrial space.

The Chan brothers have raised $25 million in venture capital. U.S. Genomics also has a scientific advisory board that includes Louis Kunkel, a professor of pediatrics and genetics at the Harvard Medical School, and Alexander Rich, a pioneer in molecular biology.

Mr. Chan's strategy is first to put the DNA, which is normally coiled up like a ball of spaghetti, on a chip that causes the DNA to straighten out as it naturally does when it prepares to copy itself.

The chip then passes through an optical detector -- made with technology like that used to see distant stars -- which records the stretched-out DNA as it flies by, working much as an optical

sensor in a DVD player does.

Mr. Chan argues that his company's technology has the potential to decipher an entire genome in the same amount of time it takes DNA to replicate itself, about 30 minutes.

Why is this important? At the molecular level, the DNA of any two people on earth is more than 99.9 percent identical. Yet their genomes vary in myriad, subtle ways. It is the understanding of these minute variations, which account for everything from eye color to predisposition to breast cancer, that is likely to lay the groundwork for the next genetics revolution.

"To truly understand genomics, you are going to need access to millions of genomes," Mr. Chan said.

In the medical realm, this information could be used to help determine what antibiotic might work best for a patient or whether he should radically change dietary habits to help lower a high risk of a heart attack. But the data have many other potential applications.

Mr. Chan is not the only scientist-entrepreneur attempting to read genomes rapidly. For example, Perlegen Sciences, an affiliate of Affymetrix, puts DNA on silicon wafers to compare differences in the DNA of individuals.

But Mr. Chan says that his company's approach is potentially cheaper, faster and more accurate than other techniques. Those rely on some form of PCR -- polymerase chain reaction -- which essentially involves sequencing DNA by making lots of copies of it, cutting them into small pieces and then reassembling them.

Of course, patenting an idea is one thing. Making it commercially viable is another. So far the company has built several instruments, each of which can read 200,000 base pairs of DNA in a run that lasts several minutes. By the end of the year, Mr. Chan hopes to be able to read a million bases a run and, ultimately, an entire genome -- about 3 billion base pairs -- in a half-hour.

As such technology develops, society will have to grapple with fundamental questions about its use. Some medical ethicists raise the issue of discrimination by health insurers, if they can demand access to each policyholder's genome. And Troy Duster, a sociologist at the University of California at Berkeley, has warned that genetic profiling of criminals, for example, may ultimately lead to a "spurious link" of race and deviant social behavior.

Mr. Chan, an American of Chinese descent, said that he was sensitive to these concerns and that the company was sponsoring seminars by speakers who would discuss these issues with employees.

"Who owns the genetic information and where is the data going to be stored?" Mr. Chan said. "Those are huge questions. We need to pay a lot of attention to them because at the end of the day this technology is going to affect individuals."
