in the 1970s, calls the new center "a hybrid between a Max Planck Institute and a pharmaceutical company … that promotes the interests of both parties."

GSK is eager to tap into the huge repository of patient tissue samples and clinical data available through the institute's scientists and doctors, whereas Max Planck scientists hunger for advanced sequencing and computing power. The Bavarian government will contribute $3.5 million over the next 3 to 5 years. Max Planck scientists will retain the right to patent any discoveries from projects they initiate, but GSK will have first refusal on whether to license them from the Max Planck Society.

The center will focus on finding patterns of genetic variations in patients with a variety of common diseases. These variations, called single-nucleotide polymorphisms (SNPs), represent a change in a single base pair in the human genome that can help scientists home in on disease-related genes.

The first target will be unipolar depression. It's a tall task, says Kenneth Kidd of Yale University School of Medicine, who is not involved in the project. Although having a family member with depression is a risk factor for the disorder, no one has been able to pin down genes that might play a role. Most doctors believe depression has multiple causes that vary among patients. "Diagnosing depression is as precise as diagnosing a headache," agrees Florian Holsboer, director of the psychiatry institute. But he hopes that comparing patterns of tens of thousands of SNPs in 1000 depressed patients with those in healthy controls will provide clues about what triggers the disease and why patients respond differently to treatment.

Whereas psychiatry institute scientists will focus on central nervous system disorders, GSK will join other scientists—each of whom will negotiate intellectual property rights—to investigate a range of diseases. Ullrich, for one, will lead a group developing a large-scale screen for genes related to cancer development.

–GRETCHEN VOGEL

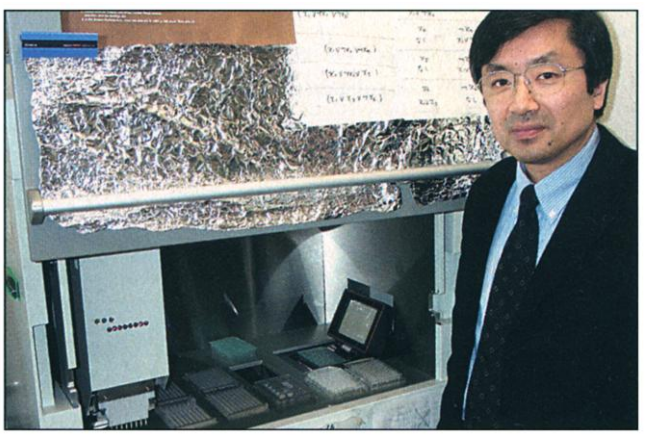
MOLECULAR COMPUTING

DNA-Based Computer Takes Aim at Genes

TOKYO—Olympus Optical Co. surprised computer scientists last week by announcing the development of the "world's first DNA computer for gene analysis." But experts disagree about whether Olympus's machine is really a computer.

"I think they've got a device for genetic analysis," says University of Tokyo biochemist Kensaku Sakamoto, who works on DNA computing. "But to function as a general-purpose computer, it still has a ways to go." Takashi Yokomori, a computer scientist at Waseda University in Tokyo, is more generous. "If you take a broad view of information processing, then what Olympus has developed is a splendid DNA computer," he says.

Researchers around the world have been working on DNA computing since the mid-1990s in hopes of harnessing the molecule's ability to store huge volumes of information and to react in many ways simultaneously for use in massively parallel computations. Efforts have focused on problems in Boolean logic, in which statements are linked by "and" and "or" into formulas, such as ((a = 1) OR (b = 1)) AND ((a = 0) OR (b = 1)). The goal is to find a set of variables that satisfies the formula. Researchers have devised ways of representing such expressions as strings of DNA. They create molecules representing each possible solution to the formula and then, using restriction enzymes and other tricks of DNA manipulation, eliminate the molecules representing unworkable solutions.



Real thing? Akira Suyama says his machine for analyzing gene expression is the first practical DNA computer.

CREDIT: D. NORMILE

DNA computing has solved simple problems in math, logic, and even chess (*Science*, 18 February 2000, p. 1182; 19 May 2000, p. 1152). The technology has remained a laboratory curiosity, however, because creating a molecule for each possible solution can demand literally tons of biochemical material to solve complex problems, and all of the chemical shaking and baking must be done by hand.

University of Tokyo biophysicist Akira Suyama, whose work led to the Olympus machine, says he has found a simpler way. First, he uses an algorithm that solves the problem in steps, building more and more complex DNA "formulas" as it goes and chemically weeding out failed solutions at the end of each round. That approach cuts the number of dead-end molecules by orders of magnitude, but at the cost of more chemistry. So Suyama automated the process, adding an electronic computer to control sample handling and processing. As a "killer application" for his machine, Suyama chose gene-expression profiling, a procedure increasingly used in research and drug development to study which genes are expressed in the course of diseases, among other problems. The work led to a partnership with Olympus, which hopes to both sell DNA computers and offer analytic and diagnostic services.

Sakamoto praises his colleague's work on automating DNA computing as having "big long-term potential." But he thinks gene-expression profiling is so specific a task that the device doesn't qualify as a general-purpose computer. Suyama acknowledges that his pride-and-joy algorithm doesn't come into play in the Olympus machine. But he says that whether it is addressing Boolean logic problems or analyzing gene expression, "it is the same hardware, with just a change in the source program."

Semantics aside, potential users are eager to see what Suyama's machine can do. Sumio Sugano, a molecular biologist at the University of Tokyo's Human Genome Center, says one "extremely important" advantage is that the Olympus machine promises to measure absolute levels of gene expression in a sample. Current technology can only compare whether a particular gene is expressed more or less than other genes. Also, for limited numbers of genes, the Olympus machine returns results in just hours, instead of the day or more required by DNA arrays. And researchers can select a different set of genes for profiling with a bit of reprogramming instead of developing a new array.

Olympus researcher Nobuhiko Morimoto says the machine will be put through its paces at NovusGene Inc., a new Olympus subsidiary gearing up to offer genetic analysis services to research labs and clinics. "Our target is to offer gene-expression profiling for about half of current prices," which run about $5000 to check expression levels of 500 or so genes in a sample. If all goes well, Morimoto says, Olympus may use the machine to offer profiling services or even sell DNA computers in 2003.

–DENNIS NORMILE