HUMAN GENOME

Généthon to Sequence Promoters

In its short 4-year life, the Généthon genome center, in Evry, near Paris, has carved out a position as a world leader in human genome mapping. Now, it is hoping to move into the front ranks of another area of human genomics: large-scale DNA sequencing. To do this, it is embarking on its first major collaboration with a for-profit company—a potentially controversial move for a lab funded through public donations. Last week, Généthon's paymaster, the French Muscular Dystrophy Association (AFM), announced an $11-million, 2-year joint initiative with Genset, a Paris-based genomics company, to establish an independent lab within Généthon. Dubbed the Très Grand Séquençage (TGS) laboratory, it will employ some 25 staff members at Evry and operate a battery of more than 20 automated DNA sequencers, working around the clock.

Several labs worldwide are planning similar-sized sequencing efforts, but the TGS project is unique because it is targeted at the promoter sequences that regulate gene expression. When proteins called transcription factors bind to these promoter sequences, the sequences trigger the production of messenger RNA (mRNA)—genetic messages copied from stretches of DNA that code for proteins. Several major sequencing labs are working on complementary DNA—DNA copies derived in the lab from this mRNA—to identify the coding regions of the roughly 100,000 genes contained in the human genome. Marc Vasseur, Genset's chief scientist, argues that by targeting the sequences that regulate mRNA production, TGS will complement these efforts.

Collaborating with Genset was a necessity for AFM: It could not have afforded to launch the project alone, given that it is also planning a major effort, dubbed Généthon II, to clone the genes underlying neuromuscular disease (*Science*, 18 March, p. 1554). Nevertheless, AFM general secretary Pierre Birambeau is confident that the terms of the agreement with Genset will deflect any criticism of Généthon's new link with the world of commerce: Sequence data derived from the project will be made public 6 months after collection, and any revenues that subsequently accrue to AFM will be plowed back into research on neuromuscular diseases.

The project could help in "discovering connections between genes."

—Moshe Yaniv

TGS's main strategy, says Vasseur, will be to make multiple copies of the beginning of each mRNA protein-coding message. These amplified sequences will then be used to probe the genome, binding to the DNA from which they were transcribed. By sequencing about 1000 bases of DNA upstream from that point, Vasseur claims, it should be possible to hit the majority of the corresponding promoter sequences. "I think it's a worthwhile thing to try," agrees gene control expert Robert Tjian of the University of California, Berkeley. But for a given gene, he warns, the sequences that bind to transcription factors may be spread over many thousands of bases of DNA and are not always easy to identify merely by examining the raw sequence data. Nevertheless, other researchers are more optimistic that the TGS project will yield useful information. "It certainly will be interesting in discovering connections between genes," says gene expression researcher Moshe Yaniv of the Pasteur Institute in Paris. Comparison of promoter sequences from different genes, he says, should indicate which genes are controlled by the same transcription factors.

Both Genset and AFM also hope the TGS project will lead to clinical advances. For Genset, the targets are conditions such as cancer and inflammatory disease, including arthritis. The company is developing "transcription factor decoys"—short pieces of DNA that mimic the promoter sequences of, say, cancer-causing oncogenes. These should bind to the relevant transcription factor and so "mop them up" and prevent the genes from being activated. AFM, meanwhile, has its long-term sights set on gene therapy for neuromuscular disorders and hopes to find promoter sequences that could be used to control the expression of therapeutic genes.

–Peter Aldhous

U.S. R&D POLICY

Clinton Inaugurates Science Council

Last week, U.S. science and technology policy stood at the top of the President's agenda —for about 30 minutes. That's how long Bill Clinton presided over the first meeting of the National Science and Technology Council (NSTC). The council was created by executive order last November, but it wasn't until 30 June, at 11:30 a.m., that its 24 members—Cabinet secretaries, agency heads, and senior White House officials—finally got together to discuss efforts to coordinate the government's $75-billion R&D portfolio.

The 75-minute session in the Roosevelt Room of the White House (Vice President Al Gore took over after Clinton departed in midmeeting) didn't alter the course of U.S. policy toward research. Rather, its major purpose was to tell the President about the activities of the nine committees that serve as the operating units of the NSTC. These committees, which together form what Gore described at the meeting as "a virtual agency," are supposed to set spending priorities within nine areas that stand at the intersection of science and society—from health, transportation, education, and the environment to national security and civilian technologies. The first tangible results of their labor, which began over the winter and included two large conferences (*Science*, 4 February, p. 604, and 25 March, p. 1675), will appear in the President's 1996 budget request to Congress next February.

The President opened the meeting by stressing the importance of the federal investment in both fundamental and applied research. Then he went around the room, asking each participant to describe his or her activities on behalf of science and technology. "The discussions were strategic, not tactical," said a White House aide.

The NSTC is, in theory, on a par with the National Security Council in the White House hierarchy. But there's little chance the two councils will be equal in influence. The security council meets frequently, and its members place a high priority on attending. Last week's NSTC meeting took 7 months to arrange, in part because of the difficulty of finding time on the President's schedule. Even so, the meeting was called with less than 2 days' notice, and some of the members were forced to send stand-ins: Nine of the 24 principals dispatched their deputies or lower ranking officials. Among the no-shows was National Institutes of Health (NIH) Director Harold Varmus, who had lobbied hard for NIH membership on the council. Varmus and his family were bicycling through France as part of a long-planned vacation, and NIH's seat was occupied by deputy director Ruth Kirschstein.

There was no mention at the meeting of the President's Committee of Advisors on Science and Technology, created last fall but yet to be formed. Its 15 members are supposed to provide the president with input from the academic and private sectors on science and technology matters; the committee's charter expires in November 1995.

–Jeffrey Mervis