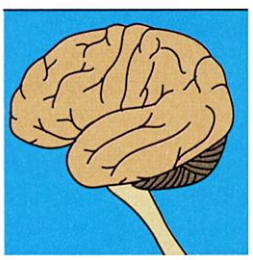
NEW SCIENCE:

Brain Calls Dibs on Many Genes

The human brain is an expensive tool: A huge proportion of human genes are thought to be involved in constructing, wiring up, and maintaining the nervous system. Neuroscientists hope the completed genome will help them to nail down the brain's share. Current estimates range from "a fair chunk" of the genome to "40%" to "most."

No one knows what all these genes do, but placing them on gene chips to see which ones are expressed by developing neurons is like "having a new type of microscope, a new way of looking at cells," says neurobiologist Ben Barres of Stanford University. His team is using such chips, as well as protein analysis, to spot molecular signals passed between neurons and support cells called glia early in development, when neurons start transmitting messages.

The completed genome will also accelerate the search for genes at fault in neurodegenerative diseases. Neurogeneticist



Huda Zoghbi of Baylor College of Medicine in Houston looks for candidate genes in the *Drosophila* genome, then tries to find homologs in the human sequence. Making the jump from fruit fly to human used to take a year of lab time, she says; now she'll be able to search computerized databases to find candidate genes in minutes.

Other neuroscientists hope the genome will help solve otherwise intractable questions about human behavior. For example, psychiatrist Eric Nestler of the University of Texas Southwestern Medical Center in Dallas and computational biologist David Landsman of the National Library of Medicine in Bethesda, Maryland, point out in this week's issue of *Nature* that newly identified genes might help make sense of addiction. Cocaine acts on certain dopamine transporters, which differ between people; correlating people's transporter subtypes with their propensity for cocaine addiction might reveal why some people are more vulnerable to the drug than others, they suggest.

–LAURA HELMUTH

the project would produce a "rough draft," covering 90% of the genome, by the spring of 2001. Scientists were clamoring for the data even in rough form, Collins said by way of explanation. Yet he also admitted that producing a rough draft and making it public was a strategic move to undercut any patent position Celera or other businesses might claim.

In a crucial test of the shotgun strategy, Celera first tackled the 180-megabase genome of the fruit fly *Drosophila melanogaster*. Venter teamed up with a publicly funded team headed by Gerald Rubin of UC Berkeley, and by March 2000, they had pulled it off. This proved that the shotgun methods could work on a big, complex genome, said Venter (*Science*, 25 February 2000, p. 1374).

The race was on, punctuated by dueling press releases. First Venter announced in October 1999 that his crew had sequenced 1 billion bases of the human genome—a feat pooh-poohed by NIH, which noted that Celera hadn't released the data for other researchers to check. Then NIH jumped into the game, announcing in November that it had completed 1 billion bases, holding a "birthday" party at the National Academy of Sciences, complete with balloons and T-shirts emblazoned with the double helix. Venter countered in January 2000 that his crew had compiled DNA sequence covering 90% of the human genome, the public consortium asserted in March that it had completed 2 billion bases, and so on. Issues of data access heated up too, with the public consortium denouncing Venter for his plan to release his data on the Celera Web site rather than in GenBank, the public database. The feud became increasingly ugly, with each side disparaging the other's work and credibility in the press. Leaders in the scientific community urged them to stop squabbling and work together.

The two had, in fact, begun talking about a possible collaboration in December 1999. Eric Lander, who runs the Whitehead/MIT Genome Center, was the main go-between. The two approaches are complementary, he said, and collaborating would speed the process.

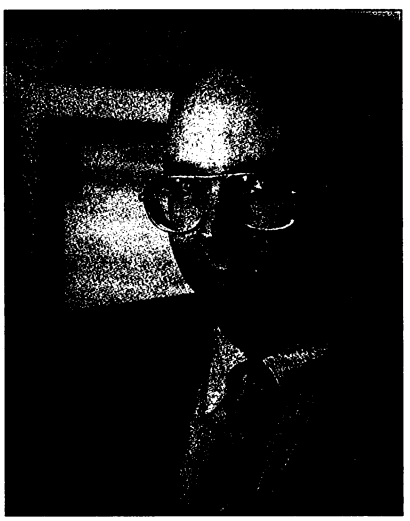
But in March, the discussions foundered amid considerable acrimony when the Wellcome Trust leaked to the press a letter from Collins to Venter, citing irreconcilable differences (*Science*, 10 March 2000, p. 1723). The sniping, seemingly at its peak, escalated further, until many considered it an embarrassment. "If they were my children, I would give them both a time out," said one leading scientist at the time.

Behind the scenes, Ari Patrinos of DOE played intermediary, finally brokering a truce under which both groups would announce their drafts at the same time, thereby sharing the glory. Venter still would not deposit his data in GenBank, as the consortium wanted, but he did concede that the public data has been useful in his own work. Defusing the issue of priority and credit, the two agreed to publish simultaneously, perhaps even in the same journal. Collins and Venter granted an exclusive interview to *Time*, which heralded, "The race is over," and pictured the beaming duo side by side in their lab coats. They were all smiles, too, at a White House ceremony in June where President Clinton lauded both scientists for their phenomenal achievement, and Collins and Venter lavished praise on one another (*Science*, 30 June 2000, p. 2294).

The façade held for 5 months—longer than many would have predicted—before all hell broke loose over plans to publish their papers (see p. 1189). At issue, again, was Venter's refusal to deposit his data in GenBank and the terms he might impose on commercial or academic users (*Science*, 15 December 2000, p. 2042). The two did manage to achieve simultaneous publications—but in separate journals.

In their magnanimous moments, both concede that their race has speeded the project, to everyone's benefit. "Ten, 15 years from now, nobody is going to care about all this fuss and bother," says Collins. "They're going to care that we got the fly sequence done, and shortly after that we got the human sequence done, and shortly after that we got the mouse sequence done. And all this back and forthing over who did what and what strategy was used and which money was public and which was private is probably going to sink below the radar screen. And hallelujah."

–LESLIE ROBERTS



J. Craig Venter. Threw down the gauntlet with his commercial plan to shotgun sequence the human genome.

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