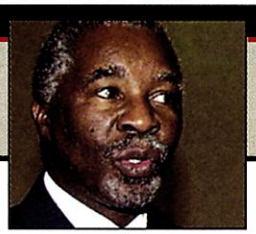
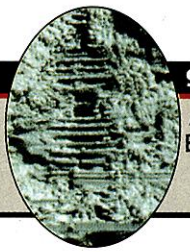


PAGE 941
Mbeki's talkfest



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SPACE BIOLOGY

Goldin Shakes Up NASA's Life Sciences Program

These are boom times for the life sciences, as the National Institutes of Health (NIH) and other federal agencies rack up record budgets to study everything from the workings of the brain to life in deep-sea vents. But one community has yet to cash in on the biological bonanza: Faced with repeated delays to the international space station and surrounded by a sometimes hostile engineering culture, NASA life scientists are struggling to garner resources from inside the agency and respect from their often skeptical peers outside.

Last week, NASA Administrator Dan Goldin moved decisively to shake up the agency's troubled $300 million life and microgravity sciences effort. On 1 May he announced the transfer of the office's chief, Arnauld Nicogossian, to a new position and the start of an expedited search for his successor. Meanwhile, NASA chief scientist Kathie Olsen is reviewing the agency's biological program, which has come under repeated criticism from the National Research Council for its inbred culture, insufficient peer review, and tendency to overstate its findings (*Science*, 10 March, p. 1728). Life scientists hope the moves are the first steps toward creating a world-class research program at an agency that has traditionally given short shrift to the field.

High hopes. NASA wants to improve the quality of life sciences and microgravity research on the ground and in space.

"There is an opportunity here to bring new blood into the leadership of life and microgravity sciences, and to spearhead a new approach with the outside research community," says Ken Baldwin, a physiologist at the University of California, Irvine. "It would be really exciting if Dan [Goldin] is willing to make a fresh start so we could have a program worthy of the $60 billion [space station] lab we are building," adds Andrew Gaffney, a Vanderbilt University cardiologist and former NASA scientist and astronaut.

Any major reform effort faces formidable obstacles, however. The entire life and microgravity sciences and applications program accounts for only 2% of the agency's $14 billion annual budget, which is devoted mainly to large engineering projects, and only 10% of that slice goes for fundamental biological research. About half is spent on a host of microgravity research projects in biotechnology, fluid physics, and combustion and materials science, with another quarter for biomedical research on measures to counter the health hazards of space living. The rest involves technology associated with human space flight and astronaut health. "The priority has always been, and rightly so, the health and safety of astronauts," notes Frank Sulzman, who retired last year as a manager in NASA's life and microgravity sciences office.

The agency's culture also is vastly different from that found in universities. "NASA has a quasi-military mindset, not accustomed to the open debate of academe," says Sulzman. "It's follow the leader, and dissent is disloyalty." In addition, he says, NASA's scientific acumen is shaped by astronomy and astrophysics, which are based on observational research. "The culture at NASA just doesn't get experimental research, in which you need more controls and to set parameters in objective and rational ways," says Sulzman. Unfortunately, those controls and parameters often conflict with other needs on a crowded and complex spacecraft.

Many scientists say that NASA's course in the life sciences has been set over many years by Nicogossian, a physician by training, and his allies George Abbey and Carolyn Huntoon, the current and former heads, respectively, of NASA's Johnson Space Center in Houston. "The Abbey-Huntoon-Nicogossian Mafia," says Gaffney, "ran the program not on the basis of what was the best science. ... Maybe those days are over." Other researchers privately concur with that analysis. Adds one: "Arnauld used a physician's approach—and that approach is not one that has helped the life sciences flourish."

Neither Abbey nor Huntoon could be reached for comment, but Nicogossian bristles at such criticism. He says his office is improving interdisciplinary research, strengthening ties with NIH, and reaching out to the broader life sciences community. "We are set to change things," says Nicogossian, who will assume the new job of chief health and medical officer for the agency. Nicogossian will run programs concerned with astronaut health and safety, leaving the life and microgravity sciences office with a stronger research focus.

Other sources say that a new cadre of prominent biologists hired by Goldin is behind the changes. Olsen, a neurobiologist, says now is "an opportune time" to reconsider the office's focus as part of her review. And Nobel Prize–winning biologist Baruch Blumberg—who now heads the Astrobiology Institute at NASA's Ames Research Center in Mountain View, California—says that as a result of the review of biology, "there is going to be more of it," although the details have not been worked out.

NASA plans to pick a new life sciences chief within the next few months, and outside scientists are hoping for a researcher with management and program experience. "We need leadership by someone who is actively immersed in biological research," says Gary Stein, a cell biologist at the University of Massachusetts Medical School in Amherst.

Outside researchers say the new chief needs to strengthen peer review, encourage more ground-based experiments as precursors to space flight, and build stronger relationships outside the traditional community. "You need to elevate peer-reviewed, ground-based science to build a stable of stellar scientists, so you have the crème de la crème

CREDIT: NASA

once the station is ready," says Baldwin.

One pressing problem is how to maintain interest in a program with few research opportunities until the space station is ready to do science in 2005. "We're at a very critical stage in building the space station," says Gaffney, "and not to do good science once it is ready would be an absolute tragedy."

–ANDREW LAWLER

HUMAN GENOME PROJECT

Chromosome 21 Done, Phase Two Begun

Chalk up two achievements—one public relations, the other scientific—for the international consortium in the race to sequence the human genome. This week, on the eve of an annual genome meeting at Cold Spring Harbor Laboratory in New York—and, perhaps, to preempt an expected statement from rival Celera Genomics of Rockville, Maryland—the international consortium announced on 8 May that it has completed (almost) "phase one" of the project, the rough draft of the human genome. (85% of the promised 90% of the draft sequence is now available in GenBank, says the consortium.) On 9 May, the consortium entered "phase two" and turned its collective sequencing firepower to "finishing" the human genome—that is, producing a 99.99% accurate sequence. Celera

Gold standard. The highly accurate sequence of chromosome 21 should help illuminate Down syndrome.

CREDIT: (RIGHT) RCSB

head J. Craig Venter dismissed the announcement as an "artificial" milestone and "science by press release"—a tactic he has used himself.

But Venter lauded the consortium's other announcement: the complete sequence of chromosome 21, only the second chromosome to be finished. Already, this chromosome, published electronically this week and in print in the 18 May issue of *Nature*, has reached the gold standard for which the consortium is striving for the entire genome, says Yoshiyuki Sakaki, who directs the human genome sequencing effort at the Institute of Physical and Chemical Research (RIKEN) outside Tokyo and whose team did half the sequencing.

Together, the 62 scientists from 13 labs have determined the identities of 33.5 million bases of the long arm and another 280,000 bases of the short arm of chromosome 21. Just three clone gaps remain—stretches, each about 30,000 bases long, that could not be determined with current technology. By contrast, chromosome 22, which is roughly the same size and was completed last December, has 10 such gaps (*Nature*, 2 December 1999). In another technical tour de force, the chromosome 21 team can also claim the longest contiguous stretch of DNA ever sequenced, at 25.5 million bases, says Sakaki.

Sequencing proceeded so quickly in part because several groups interested in Down syndrome had begun mapping chromosome 21 in the 1980s, before the Human Genome Project even existed. In Down syndrome, an extra copy of chromosome 21 results in mental retardation, heart problems, and other abnormalities. Now the task of figuring out just what goes wrong in this devastating disease will be far easier. Instead of finding the expected 800 to 1000 genes, gene prediction programs came up with just 225. "We now have a real definition of who the [genetic] players are," says Roger Reeves, a geneticist at Johns Hopkins University School of Medicine.

The paucity of genes on chromosome 21—one 7-million-base stretch contains just one gene—may have broader implications as well: If the gene prediction programs prove correct, then the entire human genome could have less than the 100,000 genes previously estimated.

As sequencers enter the home stretch, competing claims of genome accomplishments should be coming fast and furious. But, says Reeves, it will be quite a while before any sequence beats the accuracy and completeness of chromosome 21.

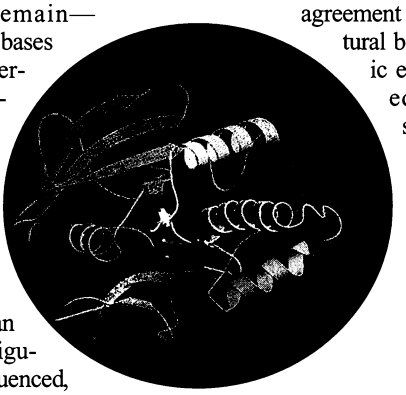
–ELIZABETH PENNISI

With reporting by Leslie Roberts.

STRUCTURAL GENOMICS

Protein Data Justice for All

Scientists who crack protein structures and colleagues who want to decipher what these proteins do are on the verge of a watershed agreement that would usher structural biology into the genomic era. The carefully crafted guidelines are designed to help coordinate international financing of publicly funded protein structure efforts and ensure prompt release of structure data so that no team has an unfair advantage in working out the functions of unknown proteins.



Fast and fair. New guidelines urge teams to quickly submit structures to repositories such as the Protein Data Bank, which last week released this image of human protein tyrosine phosphatase–1B.

The guidelines, being finalized as *Science* went to press, come at a time when robotics and computer automation promise to transform structural biology into a high-speed effort, dubbed "structural genomics," in which researchers will churn out thousands of protein structures in the next 5 years. Nurturing this souped-up approach, the National Institutes of Health (NIH) this fall plans to fund up to six structural genomics pilot centers to establish and test techniques for high-throughput x-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, the workhorse technologies of structural biology. Similar approaches are being adopted or considered in Japan, the United Kingdom, France, Brazil, and Germany (*Science*, 17 March, p. 1954).

To help coordinate these efforts, officials at NIH and Britain's Wellcome Trust last month brought some 50 leading protein specialists to the Wellcome Trust Genome Campus in Cambridge, U.K., for a brainstorming session on how to release data quickly and fairly. They had a gulf to bridge.