Editor in the field
Princeton's Lewis-Sigler Institute

It's not about the building, insists David Botstein, director of the two-year-old Lewis-Sigler Institute for Integrative Genomics, a home for people working at the interface of quantitative and other kinds of biology. "I came here specifically because I thought what the field needs more than beautiful buildings is a new generation of people who speak the same language," he says.

Still, the Carl Icahn Laboratory, which houses the Institute, makes such an impression that any discussion about the future of genomics at Princeton properly begins with the architecture. "This building is a work of art," Botstein acknowledges, adding quickly, "I had nothing to do with it." Designed by architect Rafael Viñoly in consultation with Princeton's president, Shirley Tilghman, the Icahn building takes up 90,000 ft^2 next to the Lewis Thomas Laboratory, home to molecular biology. Viewed from a distance, the lab has the scale and gently curving sweep of a glass-encased airport terminal, without the attendant crowds and chaos of modern air travel. The outer walkway features two-story louvres that move and filter the sunlight, projecting double-helical shadows onto the spacious inner atrium. Inside, a 13-ft by 7-ft display wall, consisting of 12 Hitachi display cubes, will soon be installed to allow the visualization of microarray results and other genomic data sets. This twenty-first-century whiteboard will compete for attention with the centerpiece of the atrium—a remarkable sculpture designed by Frank Gehry. The structure, which the locals suggest is aardvark-shaped, has a wavelike outer metal casing and is *sui generis*. Housing a conference table and chairs, it's big enough to host a seminar or, with its dark wooden interior and mood lighting, a séance.

Like the building, Botstein also inherited the term 'integrative genomics,' which he seems uninterested in putting too fine a point on. His vision, which jibed well enough with that of the Princeton administration to lure him from Stanford, is to educate a new kind of biologist—a truly quantitative biologist—and, at the same time, to lead a research institute that engages the efforts of biologists, chemists, physicists, computer scientists and engineers in making sense of the data that high-throughput approaches are generating. "What we see is an opportunity to think about biology in ways that weren't possible before," he notes.

The educational mission of the Institute is not an afterthought, and Botstein talks at length about the need to reintroduce biologists to advanced mathematics. "Within C.P. Snow's two cultures of science and non-science, where biologists and physicists are on the same side, there is almost as deep a valley between biologists and quantitative folks." Physicist Leon Lederman has argued for some time that biologists are too poorly grounded in physics and chemistry, a sentiment with which Botstein agrees. "The chemist will say, well, this reaction is diffusion-limited. Most biologists have no idea what he's talking about." And so Botstein and his colleagues have put together "an integrated, quantitative introduction to the natural sciences," advertised to freshmen under the heading "Hungry for something new?"

The rationale is early intervention. Botstein explains, "If you take a child and move it from one culture and language to another when the child is about 10, at the end of the day you won't be able to tell that they had been moved. But if it's much above 10, then they sound like Henry Kissinger." So far, 33 freshmen have signed on and are learning the introductory material for biology, chemistry, physics and computer science in one course. Funding for forward-looking student laboratories in functional genomics is in the pipeline from the US National Institute of General Medical Sciences.

On the research side, the Institute will eventually house approximately 15 research groups. Current members form an eclectic mix of investigators, including geneticists (Jim Broach and Leonid Kruglyak), computational biologists (Stas Shvartsman, Mona Singh and Olga Troyanskaya), chemical biologists (Joshua Rabinowitz), neurobiologists (John Hopfield and David Tank) and many who have a common interest in what Botstein calls "running into the ground the annotation of the biological functions of genes" (Botstein, Krugylak, Saeed Tavazoie and others). New additions include Manuel Llinas, who takes genomic approaches to study *Plasmodium falciparum*, and Coleen Murphy, a *Caenorhabditis elegans* geneticist working on the mechanisms of aging. Lewis-Sigler also has a program for fellows, which enables recent PhD graduates to conduct independent research for five years without having to seek external grant support. Current fellows include Maitreya Dunham, who studies experimental evolution in yeast; William Ryu, a behavioral biologist; and new recruit Amy Caudy, formerly a member of Greg Hannon's lab at Cold Spring Harbor.

All this takes money, and the institute has a healthy initial endowment. Botstein views the endowment as "a way of providing the research infrastructure for people who work at the interface of the more quantitative sciences—computational infrastructure, microarrays, imaging. We want to be at the hub of that activity." If the hub is as successful as Botstein hopes, it will be interesting to observe the kind of integrative results that it generates in the coming years, as well as the kind of individual that it sends out into the world, armed with the broadest possible view of life science. ■

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