Singapore's Model System

The Genome Institute of Singapore started with something many institutes don't: a clean slate. With that came the freedom to rethink exactly how a systems biology center should work.

By Jennifer Crebs

In a city-state famous for its top-down governance structure, the Genome Institute of Singapore is approaching systems biology from the bottom up. Minimal bureaucracy, nimble infrastructures, and brand new facilities present a sort of *tabula rasa* for a center — and an entire nation, even — with big ambitions on the bioscience front.

That's precisely what attracted Edison Liu to take on the post of executive director at the GIS five years ago. When Singapore's government invited Liu, he saw it as an opportunity to establish an institute fundamentally focused on genomics, but structured such that interactive research teams could address a complex set of biological problems. His vision for the institute flows naturally from his definition of systems biology itself, "where we attend to the component details, but we are more interested in how the parts fit together in the large scale."

Liu, former division head at the US National Cancer Institute, says that assembling a genomics center in the context of Singapore's newly emergent economy allows him to sidestep a lot of difficulties that beset institutions in countries with longer histories of bioscientific research. "It's a little bit like working in a yeast system," he says. "In a funny way, because of its compactness, Singapore allows us to be able to do things we would never be able to do in another jurisdiction."

Singapore's strengths include a flourishing economy, one of the highest rates of scientific and mathematical literacy in the world, and a national leadership extremely interested and engaged in scientific progress. Most recently, the government committed to spending close to $8 billion over the next five years to strengthen the nation's research and development capabilities.

So it's clear that government agencies are vested in the success of bioscientific research, and their interest doesn't just begin and end with budget line items. For instance, Liu tells of a meeting held between members of the Cabinet-appointed Bioethics Advisory Committee, on which he stands, and Singapore's senior judiciary. The committee has a mandate to ensure that decisions regarding the biomedical sciences and research are based on good science and high ethical and legal standards. The chief justices were interested in learning about such issues in order to be prepared for the inevitable day when bioethical issues become legal ones. This is almost an unthinkable scenario in the US, Liu says. "Certainly when I was at the NIH, we never met with Supreme Court justices."

Liu welcomes the outside interest in

the activities of the institute. "If we were doing research here in isolation of some of the ethical concerns of the nation, sooner or later there will be a clash. So it's best to have both intersect early and dialogues happening simultaneously. And that's exactly what is happening here."

NEITHER CUBES NOR CORES

The GIS is housed in a research building called the Genome, a 7,200-square-meter facility set in the Biopolis, itself a biomedical research complex of seven buildings spread across 185,000 square meters. Government agencies, other publicly funded research institutes, and more than 25 pharma and biotech outposts are also located there. The high concentration of specialized research organizations makes it easy for scientists to strike up extramural collaborations. Access to resources at nearby organizations, such as the Institute for Molecular Cell Biology or the Bioinformatics Institute, ensures that the Biopolis has very little redundancy.

A key infrastructural motif of the GIS is interactivity: biologists work side-by-side with bioinformatics and genomic technology groups. "Clearly, the execution of the systems approach is currently such that no single human being can cover all of those disciplines," Liu says. "Unlike the old paradigm of PI-to-PI, binary interactions, you sometimes need three, four, five experts working in tandem to accomplish the final goal." With that in mind, Liu and the institute's leaders have strived to create and broker interactions among research staff across the center's disciplines.

Very early on in the planning of the GIS, it was decided that there would be no core facilities in the traditional sense. Instead, Liu says that "every technology is a platform that has its own scientific goals and purity, but whose responsibility it is to support and to help others within the institute." So while groups

working in areas such as sequencing, genotyping, and high content arrays have a core function, they in fact are more akin to collaborators to biology and bioinformatics teams. Biological teams include groups working on stem cell development, cancer and cancer pharmacology, comparative genomics, and infectious disease. Bioinformatics at the institute covers a spectrum of specialties, from database interrogation to applied mathematics.

At the institute, biology and bioinformatics groups work alongside specialized technology platform teams. Guillaume Bourque, a group leader in Information and Mathematical Sciences, says that this is one of the primary reasons that he decided to join the institute two years ago. Prior to coming to Singapore, his experiences collaborating with biological labs were not very interactive at all — they were pretty much limited to passing on data via e-mail.

But these days, Bourque's work to generate evolutionary interpretations of whole-genome transcription factor binding site maps is closely informed by the hands-on feedback of co-investigators in biology and tech development. When needed, such as when colleague Yijun Ruan generates huge amounts of sequence data in his metagenomic projects, Bourque can access high-performance computing tools at the nearby Bioinformatics Institute. "It's really quite an incredible place," Bourque says of the GIS, adding

that "everything seems possible when the infrastructure is this good."

The institute's emphasis on interactivity is echoed in the very architecture of the Genome building. There are no cubicles for individual PIs; instead, research groups sit together in an open plan where laboratory space is arranged on dais. To encourage interaction between floors, the institute offers weekly seminar series to researchers and trainees alike.

Individual research programs at the GIS are administered exclusively with funds from the national Agency for Science Technology and Research. Liu credits this central block funding as crucial to the institute's success, especially when it comes to inculcate a collaborative spirit across teams and disciplines. "If I had to rely on an R01 mechanism to feed the institute based on individual PI grants, then the natural force will be for the PIs to attend to their own grants and not to the collective framework," he says.

In the central funding framework, the institute holds regular meetings every two to three months where scientific ideas for new funding are vetted by the entire community. The absolute transparency when it comes to dispersal of funds means that everybody knows what everybody else is doing, Liu says. He adds that the setup also "engages each individual to become less self-serving than if they were just writing a grant for themselves." **GT**