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## Inside Biotech

# Bioinformatics takes lead role in building biotech startups

By Lucy Caldwell-Stair, Special to Mass High Tech

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When researchers at Sirtris Pharmaceuticals in Cambridge needed to know, two years ago, whether their potential drug traveled the same pathway as a similar protein found in nature, they employed a new computer method that quickly confirmed that the proteins were indeed similar. The results gave them the green light to proceed with development.

The causal modeling platform that Sirtris, now a GSK company, used belongs to Genstruct Inc., a systems biology firm located in Cambridge. Such bioinformatics platforms promise to speed drug delivery, better predict toxic effects, make drugs for patient subpopulations, find biomarkers for diagnostics and speed patent research.

Small biotechs and startups such as Sirtris have just as much incentive to use these high-powered tools as do large pharmaceutical firms.

"In many ways, it's more appropriate for startups because they tend to explore novel and unique spaces, and more foundation work is needed," said Keith Elliston, CEO of Genstruct.

Elliston said that to develop a drug for Alzheimer's disease, for example, researchers must understand how genes associated with a disease influence other genes and proteins in a network of thousands of interactions that take place over time. "The traditional way is to do

hundreds of different experiments, compared to one experiment with our modeling," he said.

A researcher first gathers small-scale experimental data and forms a rough hypothesis of the chain of events that leads to a healthy — or disease-causing — cellular pathway. Genstruct's models evaluate the data using built-in, known cause-effect relationships culled from primary scientific articles. The result is a reconstruction of the pathway, which becomes a more exact hypothesis for the researcher's follow-up lab experiments.

Privately held Genstruct has done more than 50 engagements and was profitable last year, said Elliston. A new collaboration with genomics company Gene Logic Inc., based in Maryland, applies the model to predicting toxicity.

GenomeQuest Inc. in Westborough specializes in making sense of the mountains of genetic sequencing data that researchers produce these days.

"There's been a 10,000-fold increase in the last three years in the volume of data generated per instrument," said GenomeQuest CEO Ron Ranauro. "Now we can interrogate every DNA molecule against all known knowledge bases, when before only a fraction could be sequenced," he said.

First, partner company 454 Life Sciences in Branford, Conn., sequences the raw samples sent in from research labs. Then GenomeQuest annotates them quickly and accurately, which "increases the quality of science and gives new ideas for new biology," Ranauro said.

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Entrepreneur and MIT blackjack guy Semyon Dukach talks to the AFP about Global Cycle Solutions, the MIT\$100K finalist and development-track winner that developed a bicycle-powered corn-sheller for use in developing countries. Dukach told MHT in January that he was looking for a nonprofit to join to help others as he worked on StartupHive.org. You'll have to click here to watch the AFP's ...

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"Academic research labs are among the first to adopt such data-driven biology, using their considerable money from grants and seed capital. Pharma and biotech are not far behind," Ranauro said.

Researchers don't need to be computer programmers. "End-user biologists can interact with large volumes of biological data in ways that don't require programming skills," he said.

GenomeQuest's 160 customers can license software or have GenomeQuest analyze the data for them. According to Ranauro, this next-generation sequencing is challenging older techniques. Compared to microarray analysis, "we can find things that a researcher is not even looking for and things that are expressed at low levels," he said.

The Broad Institute in Cambridge has its share of data bottlenecks. Last month, it upgraded to a computational solution from GeneData, a Swiss company with offices in Lexington.

"We went with GeneData because our new robotics increased its scale tenfold and our old product couldn't do the analysis with enough accuracy," said David DeCaprio, assistant director for chemical biology platform. Although customers come from both large and small research facilities, Broad's services are increasingly important to biotech startups, he said.

"We enable an investigator to do research that otherwise could only be done in big pharma," he said. "This is critical because there's a trend for big pharma to depend more on small biotech and academics to do the basic biological research, such as screening."

Typically, a researcher wants to know what compounds would inhibit or encourage a certain gene. Such a request requires high throughput screening, starting with a search through public libraries of drug candidate compounds. Over 700,000 possibilities might be identified initially.

Then robots conduct experiments to measure how these compounds interact with the gene of interest. GeneData's software is able to account for problems in the robotic experiments such as cells dying, compounds drying and equipment breaking, all in record time.

"The trickiest part is ensuring high quality data of screens that can involve hundreds of thousands of data points," said DeCaprio.

Last month, Genedata won a 2009 Bio-IT World best practices award for a joint bioinformatics project with Amgen. Many of its users are pharmaceutical companies that are looking at proprietary compounds acquired through mergers, said Kurt Zingler, general manager of GeneData in the U.S.

**Sirtris Pharmaceuticals**

A GSK company  
Cambridge  
Business: Drugs to treat diseases related to aging  
Web: [www.sirtrispharma.com/](http://www.sirtrispharma.com/)

**Genstruct Inc.**

Cambridge  
Business: Computational systems for biology  
Web: [www.genstruct.com](http://www.genstruct.com)

**GenomeQuest Inc.**

Westborough  
Business: Web-based sequence data management  
Web: [www.genomequest.com/](http://www.genomequest.com/)

**454 Life Sciences**

A Roche unit  
Branford, Conn.  
Business: Genome and DNA sequencing services  
Web: [www.454.com/](http://www.454.com/)

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