Cell biology gets plugged in

The choice of potential drug targets thrown up by genomics data is overwhelming, which is why several firms are now offering drug companies a model solution. Diane Gershon reports.

A handful of companies have surfaced in recent years that are pinning their hopes on computational cell biology. Their rationale is simple. Many drug companies have invested heavily in bioinformatics to deal with the deluge of data flowing from the Human Genome Project, as well as from proteomics and DNA-chip technologies. Although this has produced many more potential drug targets, it has not necessarily led to a better understanding of the clinical relevance of the targets or of drugs directed against them. Given the high cost of clinical trials, tools that help drug firms to decide where to focus their research and resources could potentially be of considerable value to them.

With this in mind, start-ups such as Entelos in Menlo Park, California; Gene Network Sciences (GNS) in Ithaca, New York; Physiome Sciences in Princeton, New Jersey; Cellnomica in Fort Myers, Florida; and Genomatica in San Diego, California, are combining mathematical theory and computer simulation with experimental data to develop computational modelling technologies which, they hope, will turn data into real predictions about drug targets and candidates.

"The motivation comes from the clinical-trial end of drug development, but the real source of the issue is down to target selection," says Thomas Paterson, chief scientific officer at Entelos. The company's roots go back to the early 1990s, when several of the company's founders began to apply simulation and decision-support technologies, similar to those used in the aerospace and defence industries, to problems in drug research. This became the company's core PhysioLab technology, which it now uses to develop dynamic, large-scale computer models of human disease. It specifically focuses on chronic, complex diseases such as obesity and diabetes.

Rather than modelling cells, "we actually model multiple organ, tissue and cell systems that participate in a disease process", says Paterson. "What models allow you to do is to be very explicit with your hypothesis, and then to test the implications of that hypothesis in a very rigorous, systematic way." But it is results that count, and Paterson points to several case studies where, he says, Entelos successfully predicted the outcome of two different asthma clinical trials.

BACKGROUND COUNTS

But modellers are hard to come by, says Colin Hill, chief executive and co-founder of GNS, which is focusing its efforts on oncology and infectious diseases. These are individuals with a background in engineering or physics, which provides familiarity with mathematical equations and numerical analysis, but also with some proficiency in computer programming and some knowledge of biology. "Very few people have these three backgrounds," he says. It takes someone who goes well beyond bioinformatics and the creation of data-mining algorithms and sequence-search algorithms, he adds.

Earlier this month, at the Beyond Genome conference in San Diego, GNS announced that it had created the largest known data-driven computer model of a human cancer cell. But Hill acknowledges this is only a first step and that the model will be refined. "It still only represents a couple of per cent of the circuitry within the cell," he says.

At the moment, a lack of quantitative time-series data is limiting the field, says Hill. Although GNS has its own wet lab to collect some of this data, it has hooked up with some proteomics firms and is seeking other partners on the experimental side. And, even with its 200 processors from IBM, Hill says GNS will very quickly need more computing power. **Diane Gershon**

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Colin Hill sees huge potential for model cells (below).

GNS