

BioCentury

Emerging Company Profile

BioSeek: Human cell systems

By **Walter Yang**
Staff Writer

Ideally, model systems would accurately reflect the complexity of the human body in its entirety. Companies are approaching this objective from a variety of angles: some are purely computational and others use model organisms. BioSeek Inc. is taking a direct approach by developing systems using primary cells obtained from the human body.

"The best model for the human cell is the human cell" said BioSeek President Rolf Ehrhardt. "It's not a worm. It's not a fly. It's not a rat."

But the problem with currently available human cell lines, according to Ehrhardt, is they are engineered tumor cells that don't reflect the natural and complex regulatory activity inherent in humans. Thus BioSeek works with primary cells directly isolated from human bodies. In these cells, multiple regulatory pathways remain intact, reflecting human pathophysiology.

For BioSeek, the main technological hurdle to using these cells was reproducibility, which the company said it has achieved using a variety of proprietary technologies that include culture and monitoring techniques and cell selection. Ehrhardt said the methods have "allowed us to achieve very good CVs in our assays — typically less than 10%." CVs — coefficients of variation — are used to measure the reproducibility of an assay. The lower the coefficient, the better.

BioSeek Inc.

Burlingame, Calif.

Technology: Primary human cell-based drug discovery technology

Disease focus: Autoimmune/inflammation, cardiovascular

Clinical status: N/A

Founded: 2000 by Rolf Ehrhardt, Ellen Berg and Eugene Butcher

Corporate partners: Not disclosed

University collaborators: Not disclosed

Number employees: 27

Funds raised: \$9 million

Investors: Bay City Capital, Fremont Ventures, Vanguard Ventures, Smlile Investors and private investors

CEO: Peter Staple

Patents: None issued

Additionally, BioSeek doesn't work with only one type of primary cell at a time. It combines different kinds of primary cells. The company has used endothelial cells, fibroblasts, lymphocytes, and dendritic cells.

"Our systems incorporate combinations of different types of cells in proprietary formats — thus one advantage is that we can detect effects on cell-cell communication," said Ehrhardt.

The cells can be manipulated to reflect certain diseases by turning on and off

specific pathways using genetic engineering techniques as well as adding soluble macromolecules like cytokines and growth factors. The company already has primary cell models focused on inflammatory disorders and is creating angiogenesis and cardiovascular models, Ehrhardt said.

Once a system or combination of primary cells is chosen, researchers can collect a variety of data, including protein expression, protein-protein interactions and folding activity of proteins. Applications run the gamut of the drug discovery value chain from determining gene function to testing safety and efficacy of a drug candidate.

For instance, researchers interested in validating the function of a gene in an inflammation model could take a combination of primary cells that model a specific inflammatory disease, and knock out the gene using antisense. Alternatively, researchers can use retroviral vectors to overexpress a given gene within the cells. The technology also is useful in mapping pathways. According to Ehrhardt, BioSeek was able to map more than 11 genes in the NF-kappa B (NF-kB) pathway within three weeks. He noted that several of these genes would not be detected using current technologies, such as two-hybrid systems and expression profiling, because the expressed proteins either do not directly interact with each other or are not differentially expressed.

"We functionally mapped 1,500 genes

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BioSeek,

from previous page

in 2002 and are looking to map 2,000 genes this year," he said.

Further down the value chain, the primary cell systems can be used to find and optimize leads, conduct preclinical toxicology and efficacy work, and reprofile already marketed drugs. Because a variety of expression and interaction data from a number of proteins are accessible using these assays, Ehrhardt said, researchers can determine off-target effects of a therapeutic compound that could result in side-effects in the clinic.

Ultimately, the company sees its primary cell systems replacing animal models, not only for target identification and validation, but also for preclinical toxicology. While transgenic animal models take 6-18 months to set up, Ehrhardt said BioSeek can do such work in a week with its primary cells.

According to CEO Peter Staple, BioSeek is following a two-pronged business strategy that includes internal drug discovery and helping partners improve on their compounds. The company has started some pilot programs around compounds with partners, he said.

For internal discovery, BioSeek will need to add chemistry and compound libraries. The company is still expanding its model systems based on primary cells, but Staple said BioSeek has in-licensed from NIH an anti-inflammatory monoclonal antibody target for inflammatory bowel disease.