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Building a Better Understanding of the Brain

Spotlight on *Neurome*

By DAVID R. HENDRICKS, Editor

The human brain is an amazingly complex organ, containing approximately one hundred billion neurons, with half of the genes in the human genome expressed primarily or exclusively within the brain. While advances in medical technology, such as magnetic resonance imaging (MRI) and the Human Genome Project have increased our understanding, basic research into the brain has been hampered by the lack of a standardized approach to collect, analyze, and organize the data generated by researchers.

Founded in October 2000, Neurome, Inc. seeks to provide quantitative and standardized methodology for research into the structure, organization, and gene expression patterns of the brain. "Neurome is really the culmination of fifteen years of ongoing collaboration among the founders of the company, each bringing our own area of expertise together to create new and better ways of conducting basic research on brain function," explained Warren G. Young, Ph.D., President and Chief Technology Officer and Co-Founder of Neurome. "Our goal is to develop world-class methods and workflows to apply towards research on brain function, from the whole brain down to the level of gene expression and function."

Warren G. Young, Ph.D.
President and Chief Technology Officer

FAST Facts Today

NEUROME

Year formed: ***October, 2000***

Year Founded: ***2000***

Technology: ***Standardized, quantitative databases of mouse models of the human brain***

Ownership: ***Private***

Collaborative partners: ***Elan Pharmaceuticals***

Venture Capital raised: ***$9 million from Digital Gene Technologies, Elan Corporation, plc and private investors.***

Number of employees: ***21***

Web site: ***http://www.neurome.com***

Address: *11149 North Torrey Pines Road, La Jolla, CA 92037-1031*

The Technology for Analyzing Brain Function

Currently, many neuroscience labs and commercial enterprises are dedicating enormous resources to the development and analysis of mouse models of brain disorders. Why mouse models? Because the mouse is the

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mammal for which we have the most detailed genetic information, and thus is most appropriate for genetic manipulation aimed at modeling disease. However, the characterization of such a mouse requires that researchers spend a large amount of time examining images of the brain to analyze the disease pathology, a process that is arduous and subject to imprecision.

Neurome has developed a set of technologies (the Neurome Technologies) which standardize the imaging of brain sections, increase the speed of data generation from these brain sections, and enable the display of the data in scientifically powerful quantitative formats.

Neurome's MiceSlice™ technology controls the acquisition and preparation of mouse brain sections, where brain sections are collected and imaged via a high throughput process. Neurome's NeuroZoom™ software then drives the collection of images and collects the data from the images in a quantitative, statistically meaningful manner. All of these data are then stored in Neurome's BrainArchive™, an evolving database of quantitative gene expression data gathered over the course of numerous brain research experiments. Neurome's BrainPrint™ technology generates quantitative, volumetric data comparisons for the researcher in a visual context.

"We start with the brain, either image it in vivo or section it after dissection, and then apply all of the Neurome Technologies to extract quantitative data on specific regions of gene expression, down to the cellular or subcellular space," Young explained.

This ability to analyze and compare the data is useful in many different settings. For example, Prozac is a well-known anti-depressant. It is also well known that Prozac acts as a selective serotonin re-uptake inhibitor, suppressing the brain's serotonin uptake, which increases the amount of free serotonin, thus elevating one's mood. Importantly, while Prozac is considered effective, it also has several undesirable side effects.

The Neurome Technologies permit a precise, quantitative study of not only how a given class of central nervous system drugs impacts a mouse model of brain disease, but also how potential pharmaceutical alternatives to those drugs will impact that same mouse model. Pharmaceutical and biotechnology companies developing new selective serotonin re-uptake inhibitors could utilize the NeuromeTechnologies to assess both the effectiveness of these alternatives in comparison to currently prescribed drugs such as Prozac, as well as any potential side effects. This application of the Neurome Technologies would

advance a company's drug research efforts, providing valuable information to assist in selecting those drug leads that possess the best chances of success in the clinic.

Understanding Alzheimer's Disease

The Neurome Technologies are also being applied in basic brain research. Shortly after Neurome's formation, the Company entered into a collaborative agreement with Elan Corporation to perform research into a mouse model of Alzheimer's disease. Alzheimer's disease currently affects around 4 million Americans and is the leading cause of dementia, the umbrella term for several symptoms which include the gradual loss of memory, problems with reasoning, judgment and orientation, and a decline in the ability to perform routine, basic tasks.

While the exact causes of Alzheimer's disease are not yet known, it is known that some forms of the disease are hereditary (genetic) in nature. Studies in transgenic mouse models of this type of Alzheimer's have suggested that certain antibodies reduce the amount of beta amyloid protein within brain tissue, potentially indicating a method of treating the hereditary form of Alzheimer's disease.

In collaboration with Elan Corporation, Neurome has conducted an analysis of their mouse model of Alzheimer's disease. Utilizing magnetic resonance microscopy (MRM) and stereologic and morphometric imaging, Neurome identified and quantified volumes of various brain regions in both a control mouse and the mouse model of Alzheimer's disease at forty, one hundred, three hundred sixty-five and six hundred thirty days of age. MRM had not previously been utilized to quantify mouse models of Alzheimer's disease.

The results of this study were recently published in the Proceedings of the National Academy of Sciences . Compared to the control mouse, the Alzheimer's disease mouse model showed significant differences in hippocampal volumes at one hundred days, before the accumulation of beta amyloid proteins or plaques, which are the hallmarks of the disease. "This suggests that the initial progression of this type of Alzheimer's disease occurs much earlier than generally believed, maybe as early as the equivalent age of the twenties or thirties in humans," Young explained. "Additionally, the study served to validate our technology, since it permitted the comparison of MRM quantitative analysis to more traditional stereologic and morphometric analysis and supported the idea of a dependable relationship between the two methods."

NEUROME

"We are a post-genomic company, not seeking to discover new genes or proteins, but to understand how genes and proteins impact function in our area of specialty, the brain. This is a high value market for big pharmaceutical companies and we feel we have much to offer for companies in this space."

–Warren G. Young, Ph.D.

Company Background and Financing

In the late 1990s, the founders of Neurome competed for and won a series of Small Business Administration grants, which were used to demonstrate the feasibility of the founders' concept for the advancement of brain research. In October of 2000, Neurome was officially formed and raised 9 million dollars of initial funding. Initial investors included Elan Corporation, Digital Gene Technologies, and several private investors. In addition to an equity investment of funds, Digital Gene Technologies also provided generous incubation support to Neurome. The incubation support agreement concluded in November of 2002.

Separately from its equity investment, also in October 2000, Elan and Neurome entered into a collaborative research effort as described above. The agreement called for the payment to Neurome of up to 4 million dollars over a 3-year term. While Elan Corporation has been limiting its partnerships and joint ventures, it has continued its relationship with Neurome. Neurome does not anticipate that this will change, instead noting that Elan has been very interested in continuing to work with Neurome.

Despite the current difficult climate for funding, Neurome is well along in the process for raising a second round of financing. This second round of financing will seek between five and fifteen million dollars and be used to grow the company. Young hopes to conclude this round of financing in the first quarter of 2003.

Neurome is also in the process of seeking additional office space, looking for around twenty five thousand square feet of total space. This would permit expansion of its work force to between sixty to seventy people from its current twenty-one.

Corporate Strategy

Neurome's strategy is two-fold. Neurome will provide the tools for companies investigating potential therapeutic avenues for various disorders of the brain while also enabling and conducting further discovery into the nature of brain disorders.

Neurome is excited about its potential to provide both services to other companies. "We are a post-genomic company, not seeking to discover new genes or proteins, but to understand how genes and proteins impact function in our area of specialty, the brain," Young stated. "This is a high value market for big pharmaceutical companies and we feel we have much to offer for companies in this space." Neurome is also participating in the thrill of discovery in biomedical research. Neurome's ability to quantitatively analyze mouse models of the human brain has the potential to speed the development of even better, more accurate models, paving the way for future research and development of new ways to treat diseases of the nervous system.

There is an old saying that a house is only as good as the foundation upon which it is built. Neurome is building a strong and technologically advanced foundation for the advancement of research into the complexities of the human brain, one that promises to support new advances in the battle against diseases like depression and Alzheimer's disease.

David R. Hendricks is editor of the Business News. Mr. Hendricks holds a Bachelor of Arts in History from the Point Loma College and a Juris Doctorate from the University of Southern California.