Reprint from September 22, 2003

BioCentury

ARTICLE REPRINT THE BERNSTEIN REPORT ON BIOBUSINESS

Emerging Company Profile

Neurome: Mice, slice & zoom

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Senior Writer

The sheer complexity of the brain, with its multiple cell types and highly specific system of intercellular communication, has kept the study of central nervous system disorders from entering the high throughput realm of research that is applied to many other disease areas. Nonetheless, Neurome Inc. believes quantitative approaches still can provide new insights into the causes of CNS diseases and ultimately predict what brain areas should be targeted with drug therapies.

CEO Floyd Bloom noted that brain cells are "highly heterogeneous, and the way they speak to each other is very specific," involving multiple neurotransmitters and receptor subtypes. Although existing CNS drugs are targeted at this communication network, he said their success has been hit or miss because the nature and causes of the diseases remain unknown.

Furthermore, while genetic elements are believed to contribute to vulnerability or resistance to most CNS diseases, the early phases of the disorders are uncharacterized. Thus, it is not known how genetic mutations produce the cellular pathologies that lead to these diseases.

Increased use of animal models could provide answers to such questions. Neurome intends to work on the interface between gene expression studies of brain tissue and animal models, providing a cellular, circuit and brain region context for genetic information that can be related to observations in animal models.

To do so, the company must gather data in a standardized, quantitative manner, which the company said is in contrast with the way brain research has been conducted to date.

"Conventionally, samples are gathered from a limited area and examined microscopically in a subjective way," Bloom said. "We do quantitative morphometry, which is the use of computer controlled processes to analyze the size, shape and length of neuronal processes" as well their place in neural circuits. For example, he said, the method allows Neurome to discern modest differences in neurons in normal versus diseased tissue.

Under a deal with Elan Corp. plc (ELN, Dublin, Ireland), Neurome receives up to $4 million in service revenue to use ELN's mouse model of Alzheimer's disease to identify molecules and pathways to treat and diagnose AD. ELN receives detailed, quantitative descriptions of the physical changes to cells in the mouse model over time, which will be used to evaluate medications that interfere with the neurotoxic effects of mutated amyloid precursor protein (APP). The companies will share ownership of any resulting applications *(see BioCentury, Oct. 23, 2000)*.

In contrast to other animal models of AD — which focus on reproducing the neuronal plaques and tangles that occur in the late stages of the disease — ELN's model reproduces a mutation in the gene encoding APP known to be related to human AD from association studies conducted in Sweden.

Using the model, Bloom said, "we have found that changes in mouse brains occur long before plaques form." At these early stages, amyloid sheets form in circuits in the

Neurome Inc.

La Jolla, Calif.

Technology: Quantitative, standardized, 3-D volumetric data on gene expression within the brain to depict molecular, cellular and circuitry patterns

Disease focus: CNS diseases

Clinical status: NA

Founded: 2000 by Floyd Bloom, Warren Young and John Morrison

Corporate partners: Elan Corp. plc and La Jolla Pharmaceutical Co.

University collaborators: NA

Number of employees: 24

Funds raised: $9 million

Investors: Digital Gene Technologies; Elan Corp. plc; and private investors

CEO: Floyd Bloom

Patents: None issued

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hippocampus and entorhinal cortex, which are known to be vulnerable to degeneration in human AD.

Bloom said the finding suggests that agents designed to prevent the breakdown of the mutated APP could be used at this early stage "to prevent the pathology that sets the stage for later plaque deposition."

Neurome published the work this year in the *Proceedings of the National Academy of Sciences.*

To build the three-dimensional reconstruction of mouse brains that led to the findings, Neurome used magnetic resonance imaging to identify regions of the brain where it should concentrate its efforts. Following eight months of MRI work, Neurome used its high throughput MiceSlice technology for standardized preparation of brain sections, and NeuroZoom technology for computer-assisted extraction and analysis of data from microscope images of the tissue.

These methods also provide data for a three-dimensional database of the mouse brain. The database will show where genes are expressed within cells, circuits and brain systems, simultaneously revealing information about the functions certain brain cells perform. "The database will be useful for companies with unique mRNA discoveries — we can give them guidance on what target is best for what disease," Bloom said.

In July, Neurome signed a deal with La Jolla Pharmaceutical Co. (LJPC, La Jolla, Calif.) related to the CNS symptoms experienced by some patients with systemic lupus erythematosus, an autoimmune disease characterized by antibodies to double-stranded DNA. CNS symptoms include lack of focused thinking and emotional outbursts. Neurome will look at whether "antibodies in the sera of patients with these symptoms show reactivity with proteins in the brain," Bloom said.

Bloom said Neurome initially will use a fee-for-service model, but it hopes ultimately to share in the fruits of product development once the company has demonstrated how its methods can save time and improve work-flow in CNS drug discovery.