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## NEWCO NEWS

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### **Afraxis Stabilizes Synapses in Fragile X, Autism, Alzheimer's**

By Trista Morrison  
Staff Writer

Start-up Afraxis Inc. is using kinase inhibitors to repair neurons, stabilize synaptic connections and modify the course of neurological diseases like Fragile X syndrome, autism, Alzheimer's disease and schizophrenia.

Autism has made headlines of late thanks to *The Lancet's* retraction of its 1998 study linking vaccines to autism. The study incited a backlash against life-saving vaccines, although study author Andrew Wakefield was financially tied to a lawyer hoping to sue vaccine makers, and *The Lancet* now admits Wakefield hand-selected and paid study participants.

Amid all that racket, it's not surprising that most folks have overlooked little Afraxis. Besides, the San Diego-based company has been operating in stealth mode since its founding in 2007 by venture capitalist Jay Lichter and Nobel Prize-winning scientist Susumu Tonegawa, of the Massachusetts Institute of Technology.

Lichter approached Tonegawa after reading a scientific paper in which the researcher described a possible cure for Fragile X syndrome, a genetic mental disorder that is the most common known cause of autism. The technology involved targeting p21-activated kinase (PAK), an enzyme that regulates the cytoskeleton within the dendritic spine of neurons. Overexpression of PAK causes the dendritic spines to become misshapen and unable to form a strong synaptic connection with the axon of another neuron. However, inhibiting PAK allows the dendritic spines to mature.

In July 2007, Tonegawa and others published a paper in the *Proceedings of the National Academy of Sciences* showing that PAK inhibition corrected dendritic spine abnormalities and behavioral abnormalities in a mouse model of Fragile X. Lichter was hooked. "It was the first disease modification of a neurological disorder," he told *BioWorld Today*.

He contacted Tonegawa, and the two started Afraxis to develop PAK inhibitors.

Lichter said the Afraxis team has about six such compounds that have shown “very good” activity in mice. The biotech is now optimizing them for pharmacokinetics and blood-brain barrier penetration, with the hope of selecting a lead candidate by midyear. After that, Lichter anticipates starting a safety trial in healthy volunteers in 2011 and moving into Fragile X patients in 2012. Lichter said Afraxis also plans to test what happens after treatment with the drug has been stopped. If the synapses stay intact, it may provide a rationale for drug holidays.

And Lichter expects the lead PAK inhibitor to have utility beyond Fragile X, a concept Afraxis’ academic collaborators are already exploring. Akira Sawa and Akiko Hayashi-Takagi at Johns Hopkins University School of Medicine published a paper last month in *Nature Neuroscience* implicating increased PAK levels and dendritic spine deformities in schizophrenia. Additionally, Dennis Selkoe of Harvard Medical School is researching a link to Alzheimer’s disease – a particularly tough target as evidenced by last week’s failure of Medivation Inc. and Pfizer Inc.’s Dimebon (latrepirdine), not to mention previous failures by Neurochem Inc. and Myriad Genetics Inc.

Autism, too, has proven insurmountable for drug developers. Neuropharm Group plc’s Prozac (fluoxetine) reformulation failed a Phase III trial. Currently Curemark LLC is in Phase III with CM-AT, which targets protein digestion disorders associated with autism, and Seaside Therapeutics LLC is in Phase I with STX107, a selective mGluR5 antagonist for Fragile X.

Lichter’s venture firm, Avalon Ventures, has been the sole supporter of Afraxis thus far and is prepared to carry the company through its first trial in Fragile X patients. Yet Lichter said other venture funds have already begun to show an interest, despite the start-up’s early stage.

As to partnering plans, “we hired a VP of corporate development so that sort of tips our hand,” Lichter said.

Although mainly virtual, Afraxis recently hired Carmine Stengone as its vice president of corporate development. Stengone previously held positions at Phenomix Corp. and Anadys Pharmaceuticals Inc.

Afraxis also hired David Campbell, another Phenomix alum, as its chief scientific officer.