



Tuesday, June 01, 2010

Neural Stimulation for Autoimmune Diseases

A startup is developing an implanted stimulator to treat such illnesses as arthritis and inflammatory bowel diseases.

By Emily Singer

[Setpoint Medical](http://www.setpointmedical.com/) (<http://www.setpointmedical.com/>), a startup based in Boston, is developing a nerve stimulator designed to dampen the out-of-control immune system that triggers autoimmune diseases, such as inflammatory bowel disease and rheumatoid arthritis. The technology is based on a decade of research elucidating how the brain controls the immune system, particularly inflammation. The treatment has not yet been tested in patients, but based on animal research, scientists hope it will provide an alternative treatment that is more effective and have fewer side effects than existing drugs.

Over the last decade, [Kevin Tracey](http://www.feinsteininstitute.org/cs/Satellite?c=eHA_Content_C&cid=1228244132183&pagename=NSLIJ%2FCentral_Template) (http://www.feinsteininstitute.org/cs/Satellite?c=eHA_Content_C&cid=1228244132183&pagename=NSLIJ%2FCentral_Template), an immunologist and neurosurgeon at the Feinstein Institute for Medical Research in Manhasset, NY, has shown that inflammation is controlled in part by the vagus nerve, which carries signals between the brain and a number of visceral organs. Most notably for immune function, it makes direct connections to the spleen, which houses different types of immune cells poised for release at times of infection.

Numerous animal studies have shown that stimulating the vagus nerve can put a brake on the immune system, stopping the rapid recruitment of immune cells to the site of injury or infection. "Think of it as a thermostat for the immune system," says [James Broderick](http://www.morgenthaler.com/ventures/team/team-member/jim-broderick-m-d/) (<http://www.morgenthaler.com/ventures/team/team-member/jim-broderick-m-d/>), interim president of the company and a partner at Morgenthaler Ventures, Setpoint's key investor. "This reflex puts a damper on the immune system."

The effect is similar to that of a popular class of drugs, called TNF alpha blockers, used to treat arthritis and other autoimmune diseases. These drugs block the release of an immune signaling molecule that is central to inducing inflammation. While they work effectively in 50 to 70 percent of patients, the drugs can lose their effectiveness over time and have been linked to some serious side effects, such as infection and

cancer. Vagus nerve stimulation blocks both the signal molecule and other cytokines involved in inflammation.

To translate these findings into clinical treatments, Tracey founded Setpoint in 2007. Researchers are currently running animal and human tests to determine the most effective parameters for stimulating the nerve to block the immune response. Broderick says that preliminary tests using the company's first generation device in 12 healthy volunteers show that the effect is potent in humans and comparable to that seen in animal research.

Devices that stimulate the vagus nerve are already approved for the treatment of epilepsy and chronic pain and are being explored for a number of other [disorders](http://www.technologyreview.com/biomedicine/25370/) (<http://www.technologyreview.com/biomedicine/25370/>). However, Broderick says the device under development at Setpoint will be different. "You need to know how to trigger the nerve to have the effect you'd like," he says, declining to give further details for proprietary reasons.

In comparison to drugs used to treat autoimmune disease, "the promise is twofold," says [Lawrence Steinman](http://med.stanford.edu/profiles/Lawrence_Steinman/) (http://med.stanford.edu/profiles/Lawrence_Steinman/), a neurologist at Stanford University who is not involved with the company. "It may work better than drugs or adjunctively with drugs. And it may be easier to control." For example, if someone gets sick, the device could be turned off immediately, while drugs can take days to clear from the system. "However, it will be difficult to answer those possibilities until we see the clinical data," he says. "If everything holds up in the clinic, Tracey's insights will be transformative."

Animal studies do suggest a benefit over drugs: "Electric stimulation of the vagus nerve seems to be more efficient than [chemicals that target cellular receptors directly]," says [Jon Lampa](http://ki.se/ki/jsp/polopoly.jsp?d=22011&a=53537&l=en) (<http://ki.se/ki/jsp/polopoly.jsp?d=22011&a=53537&l=en>), a rheumatologist at the Karolinska Institute in Sweden who has worked with Tracey and is likely to oversee some of Setpoint's future clinical trials.

The company plans to have a device ready to begin clinical testing next year. The first application will be for inflammatory bowel disease.

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Upcoming Events

Tech Connect World (<http://www.techconnectworld.com>)

Anaheim, CA

Monday, June 21, 2010 - Friday, June 25, 2010

<http://www.techconnectworld.com> (<http://www.techconnectworld.com>)

2010 IEEE Conference on Innovative Technologies for an Efficient and Reliable Electricity Supply (<http://www.ieee-energy.org/>)

Waltham, Massachusetts

Sunday, September 27, 2009 - Tuesday, September 28, 2010

<http://www.ieee-energy.org/> (<http://www.ieee-energy.org/>)