

A Breakthrough Treatment For Sufferers Of Psoriasis

Biogen

Dana-Farber Cancer Institute



Researchers at Harvard University's Dana-Farber Cancer Institute join forces with a Boston-area biotechnology company to develop a new treatment for psoriasis. Their joint studies of immune molecules and functions yield an effective therapeutic that provides relief for this painful illness.

I have had chronic plaque psoriasis since I was 4 years old and it usually covered my entire body. Oftentimes, it was difficult to deal with since friends and strangers weren't very sympathetic," says one individual.

Another reports, "I was diagnosed with chronic plaque psoriasis ... It started out as a small patch ... but then it was out of control covering my face, arms and legs. Since I frequently missed work — not wanting to show my face looking the way I did — my job was in jeopardy."

Yet another patient describes:

“In my early 20s, my friends were dating, building careers, and enjoying life. Meanwhile, I could barely stand to look at myself in the mirror.”

The patient testimonials speak volumes. Living with a medical condition like chronic plaque psoriasis is one of those things that you have to personally experience to understand. It is not a life threatening illness, nor is it a disorder that can rely on public health campaigns to raise awareness, understanding and sympathy. Instead, it is a painful and oftentimes disfiguring illness that can seriously compromise the patient's quality of life. When a therapeutic called Amevive became available, those lives got better.

Biogen Idec, a global biotechnology company headquartered in Cambridge, Massachusetts, is the present manufacturer of Amevive. The discovery that led to the development of this biologic therapy goes back almost 20 years when the company joined forces with Harvard scientist Timothy Springer, Ph.D. Springer, at that time an associate professor at Dana-Farber Cancer Institute, a teaching affiliate of Harvard Medical School, and now a professor of Pathology at Harvard's CBR Institute for Biomedical Research, was studying molecules of the immune system with a particular focus on the immune pathways involved in fighting cancer.

Collaboration Between Academia and Industry Advances Research

Springer's research strategy entailed making monoclonal antibodies to proteins that are present on the surface of human white blood cells, called T lymphocytes or T-cells. By screening for antibodies that could block the ability of lymphocytes to kill their target cells, Springer reasoned he might discover new proteins with important biologic activity.

With the help of graduate student Michael Dustin, Ph.D., now an investigator at the Skirball Institute of Biomolecular Medicine at New York University, Springer identified three novel proteins called lymphocyte function associated antigens, or LFA's, and named them LFA1, LFA2 and LFA3. Then, they conducted rigorous cell biology experiments to figure out how and why these proteins normally functioned. "We knew that since these were important in normal lymphocyte function, when the immune system got out of control, they should be able to block or dampen this over activity," Springer says. "We thought that blockers of these molecules would be good therapeutics for a whole range of autoimmune diseases."

Springer turned to the technology transfer office at Dana-Farber for some assistance. He researched his options for collaborations with industry to determine the most efficient way to develop LFA3 as a therapeutic agent. What resulted was the implementation of a funded research agreement with Biogen, a local biotechnology company. Biogen sponsored several subsequent and key steps in the development of LFA3 that were carried out by Springer and colleagues at Dana-Farber. This research led to the generation of intellectual property owned in part by Dana-Farber and Biogen. The intellectual property was eventually licensed exclusively to Biogen which then initiated an internal research program to develop clinical products.

"This was a fine example of collaboration and partnership between academia and industry," says Anthony del Campo, vice president for research and technology ventures at Dana-Farber. "Amevive represents an excellent technology transfer story and shows how discovery and innovation at the academic level can eventually make it to the marketplace."

With the help of scientists at Biogen, the protein sequence of LFA3 was used to identify a LFA3 cDNA clone. Researchers then used this clone to develop a fusion protein that interacts with a particular receptor (CD2) on T-cells, serving to inhibit the binding of endogenous LFA3. By inhibiting T-cell activation, the LFA3 fusion protein effectively interferes with the T-cell mediated inflammatory response. This type of inflammatory

reaction is precisely the underlying etiology of psoriasis.

Therapy Targets Overactive Immune Cells

Though a detailed picture of all the molecules and pathways that converge to trigger psoriasis is not yet known, scientists understand that malfunctioning T-cells travel to the surface of the skin and cause an inflammatory reaction. Skin cells respond by multiplying seven to 12 times faster than normal, forming itchy and painful psoriatic plaques on the skin surface. Often cracked or blistering, these plaques can develop anywhere on the skin, though they usually appear on the scalp, knees, elbows and torso. Typically chronic and with no real cure, this autoimmune disease affects about 2 percent of the population worldwide; in the U.S. alone, 4.5 to 6 million people have a moderate to severe form of chronic plaque psoriasis.

The LFA3-fusion protein received approval from the U.S. Food and Drug Administration for the treatment of patients with moderate to severe psoriasis in January 2003 and is marketed by Biogen, now Biogen Idec, as Amevive. Its generic name is 'alefacept,' a mnemonic for L-F-A-cept. Since its approval this biologic therapy has provided treatment for more than 12,000 patients. Designed to target overactive immune cells, Amevive is administered by injection, either intramuscularly or intravenously, once a week for a total of 12 injections per treatment course.

The deeply personal testimonials Amevive users share on a Web site devoted to this therapy explain how their quality of life has improved. There is hope that many of the other immunologic proteins found to mediate T-cell responses will provide the key to treating a host of autoimmune diseases for which there are now no effective therapeutics.

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