

Profile of Lawrence Steinman

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Amyloid is often considered to be a trigger for neurodegenerative disease. Lawrence Steinman, the Zimmermann Professor of Pediatrics, Neurology, and Neurological Sciences at Stanford University, has shown that amyloid proteins, which clump together in sticky tendrils, instead protect against neurodegenerative disease (1). Different kinds of proteins can form amyloids, and β -amyloid is a specific type associated with Alzheimer's disease. In his Inaugural Article, Steinman, elected to the National Academy of Sciences in 2015, investigates why injecting different types of amyloid proteins, including β -amyloid, dampens the immune response and reverses paralysis in a mouse model of multiple sclerosis (MS) (2).

Immunology by Way of Physics

The son of a pharmacist and teacher, Steinman was born in Culver City, California in 1947. "I grew up in a very protected time, after World War II and after the Depression," Steinman says. With the advent of Sputnik and the Space Race, "The time was wonderful to be a kid interested in science," he explains. Steinman enjoyed math and physics and published his first paper, on a mathematical theory, while still in high school (3).

In 1964, Steinman began his freshman year at Dartmouth College. "Having grown up in Southern California, I wanted to try something really different," he says. Initially, Steinman wanted to be a physicist or mathematician and majored in physics. During the summer after his junior year, Steinman arranged to work at the Salk Institute in the laboratory of physicist Edwin Lennox. Surprisingly, this experience provided Steinman's initial exposure to immunology. "My first job in science was doing an experiment on

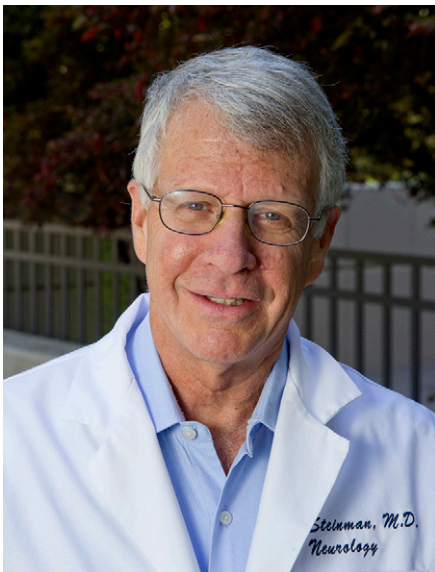
genetic control of the immune response to influenza," he says.

With a growing interest in clinical science, Steinman began to think about medical school, seeking out schools with a strong research component. Upon entering Harvard Medical School in 1968, Steinman aspired to a career devoted to treating patients, doing research, and teaching. Steinman adds that he didn't anticipate what has become a fourth pillar, namely, that he would go on to found businesses and start biotech companies. Steinman's opportunity to pursue research came early. Interested in neurobiology, Steinman took the opportunity to work with neuroscientist Torsten Wiesel and attempted the task of injecting dye into delicate neuronal cells in the visual cortex. The work proved difficult. "I thought, maybe I should do something easier technically, maybe immunology."

Experience with the Pipeline

Steinman received his medical degree in 1973, and, after a brief fellowship in neurosurgery at Stanford, traveled to the Weizmann Institute of Science in Rehovot, Israel for a postdoctoral fellowship in chemical immunology with Michael Sela. The laboratory was developing glatiramer, an MS drug still in use today. MS is an autoimmune disease in which the body mistakenly treats one of its own proteins as a foreign invader. In this case, inflammation targeted at nerve cell sheaths results in demyelination and progressive disability as scar tissue accumulates. Steinman investigated how the immune system gets sensitized to myelin basic protein, part of the protective myelin sheath, using a mouse model of MS. The work showed that mice develop experimental autoimmune encephalomyelitis (EAE) only when macrophages, the immune system's sentinel cells, take up myelin basic protein and present it to the immune system, triggering an inflammatory cascade; the protein did not trigger the cascade on its own (4).

When he finished his residency in 1980, Steinman decided to continue working on MS in the neurobiology department at Stanford. "Since I was going to focus on the brain and disease, it was natural," Steinman says. MS, he adds, was the "most prevalent



Lawrence Steinman. Image courtesy of Norbert von der Groeben (Stanford School of Medicine, Stanford, CA).

This is a Profile of a recently elected member of the National Academy of Sciences to accompany the member's Inaugural Article on page 15016 in issue 49 of volume 112.

targeted in MS, you wouldn't get anything close to consensus," notes Steinman.

Steinman finds himself devoting much of his time trying to garner industry interest in his research. "Except for a few fortunate people, we all have to be salesmen for the science if we want to see these

therapies developed," he says. Once a clinical trial begins, however, Steinman is out of the picture. "I am an interested observer, but don't participate," he notes. "The ethical environment, with which I agree, is that if you discover something at the bench, you best keep your hands out of the testing."

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