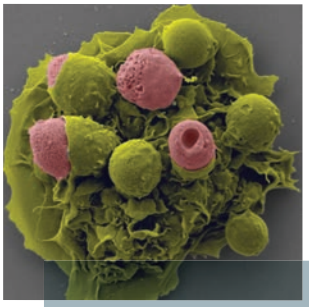

salk
Where cures begin.

Greg Lemke

Professor
Molecular Neurobiology Laboratory
Françoise Gilot-Salk Chair

The Problem

To keep the body healthy, immune cells rely on receptors that sense compounds and signal the cells to take specific actions, for example, attacking a pathogen or clearing away dead cells. Interruptions in a class of these cell receptors, known as receptor tyrosine kinases, can lead to inflammation, cancer growth and autoimmune diseases (such as lupus, rheumatoid arthritis and multiple sclerosis). In order to understand what goes wrong in cell receptor signaling—and how to fix it—researchers must understand how receptors are established and controlled, for example, during brain development or an immune response.

The Approach

Greg Lemke discovered a family of three receptor tyrosine kinases, called TAM receptors, which play a crucial role in telling immune cells how to handle infection from bacteria, viruses and other pathogens, as well as normal cellular debris. His lab showed how problems with the TAM receptors (called Axl, Mer and Tyro3) or their pathways are associated with increased levels of drug-resistant cancer as well as inflammation and autoimmune disease. Understanding how to separate the roles of each receptor could lead to new classes of drugs to fight viruses and bacteria. Aside from immune function, TAM receptors are involved in the healthy development of the nervous system.

Lemke also focuses on another major family of receptor tyrosine kinases, called Eph receptors. These are one of the earliest to show up in the developing brain of a fetus and help to guide neuronal connections. Eph receptors help neurons—like those that link the eyes to the brain—know where to go as they grow.

The Innovations and Discoveries

- Lemke's lab unveiled critical differences between the Axl and Mer receptors, and found that they activate immune cells in an inflamed setting and normal setting, respectively. This distinction points the way to more targeted therapies for autoimmune and cancer treatments.
- Lemke discovered a powerful mechanism by which viruses such as influenza, West Nile and dengue fever evade the body's immune response and infect humans. A substance called phosphatidylserine, located on the surfaces of these notorious "enveloped" viruses, directly activates TAM receptors to prevent the immune system from launching a response. The finding could lead to new antiviral drugs that block the interaction.
- In the area of vision, he revealed how retinal cells missing the TAM receptor Mer results in blindness. He also showed how proteins Vax2, Vax1 and Pax6 interact to create a functioning vision system (optic nerve and eyes).

For more information, please visit:
www.salk.edu/scientist/greg-lemke

Autoimmune Disease, Cancer, Developmental Biology, Infectious Disease, Inflammation, Immunology, Neurobiology, Vision