UCSD Biologists discover new clues to regulation of immune response

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Contact: Yvonne Baskin, (619) 534-3120

UCSD BIOLOGISTS FIND NEW CLUES TO REGULATION OF IMMUNE RESPONSE

University of California, San Diego biologists have confirmed the existence of two distinct categories of white blood cells called helper T cells in the body. The finding may lead to a better understanding of how and why the immune system responds differently to bacteria, viruses, wounds, allergens and other threats.

It may also point the way to new disease therapies that stimulate specific aspects of the immune response. Helper T cells regulate both major kinds of immunity: cellular, which is involved in the destruction of infected or diseased cells; and humoral, which leads to the production of antibodies.

In AIDS patients, it is the destruction of helper T cells by the AIDS virus that results in the failure of the immune system.

A research team led by Susan L. Swain, associate professor-in-residence of biology at UCSD, recently published the work on helper T cells in Immunological Reviews, and Swain has been awarded a five-year, $1.1 million grant from the National Institute of Allergy and Infectious Diseases to pursue its implications.

Other researchers involved in the project are biology professor Richard W. Dutton, biology postdoctoral fellows Andrew Weinberg and Joseph Voland, and UCSD Cancer Center research associate Michele English. Swain and Dutton are also members of both the Cancer Center and the Center for Molecular Genetics at UCSD.

The first suspicion that two types of helper T cells existed came in 1986 from a group led by Tim Mosmann at DNAX Research Institute in Palo Alto. That group used cell lines that had been growing in culture for many generations. Swain's group has discovered that these same two categories can be identified in normal T cells in the body.

The UCSD team also found that these two categories of helper T cells Thland Th2--secrete different sets of hormone-like molecules called lymphokines. These are the molecules that immune cells use to signal other immune cells to specialize, mature and go into action.

Thl cells secrete interleukin 2 and gamma interferon, Swain said. Lymphoid organs of animals contain some of this kind of helper cells, which can respond quickly to foreign antigens.

Th2 cells, on the other hand, secrete interleukins 4 and 5, but only after they have been primed for action for several days by the signals from invading pathogens.

"The thinking is that some Thl cells which respond quickly may be 'memory cells,' that is, the progeny of cells that in the animal's past have been stimulated by a specific antigen and remain ready to respond quickly when they encounter it again," Swain said. "This quick response is the basis for immunity, the thing that makes vaccination effective."

The interleukin 2 secreted by Thl cells spurs the body's inflammatory responses at the site of wounds or organ transplants. And along with gamma interferon, it calls out cytotoxic (cell-killing) T cells needed to attack and destroy virus-infected cells.

In contrast, interleukins 4 and 5 secreted by Th2 cells are primarily involved in influencing the antibody-secreting B cells. Antibodies are key to the body's defenses against bacteria. When this system is inappropriately stimulated by relatively harmless foreign antigens such as dust and pollen, the result can be an allergy.

Interleukin 5 was isolated and identified by Dutton and Swain in 1981, and interleukin 4 was identified in the same year. But researchers had been unable until now to identify significant numbers of normal cells that secrete these two lymphokines.

Many immune cells arise from precursor cells that remain inactive and immature until they are primed.

"Most of the research on lymphokine secretion by T cells has been done with unprimed cells," Swain said. "It wasn't known that there was a subset of helper T cells that required priming.

"When we prime, we think we're revealing the presence of naive T cells that have not encountered antigen before. This gives us a way to study the development of both types of T cells from precursors and perhaps see how we could intervene to push the immune response in different ways."

Immunology researchers have been surprised to find over the past five years that so many different lymphokines exist and that each has multiple roles and target cells.

"These T-cell subsets could give us a way to begin to understand why there is this apparent redundancy in the system," Swain said. "Perhaps each type of T cell is effective for a distinct function at a specific time and place, but some of the tasks overlap."

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