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IL-12 Shows Promise as Adjuvant in Vaccines

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Scientists at the University of Pennsylvania School of Veterinary Medicine and The Wistar Institute have shown that Interleukin-12 (IL-12) dramatically enhances the effectiveness of a vaccine against leishmaniasis in laboratory mice and suggests that IL-12 may be extremely useful as an adjuvant in vaccines against other infectious diseases. An adjuvant is a substance that when added to a vaccine is capable of strengthening its effectiveness in protecting an individual against a disease. The findings were published in the January 14, 1994 issue of *Science*.

"Leishmaniasis is a tropical disease that can cause severe disfigurement and even death, and in the last six years has been targeted by the World Health Organization for the development of a vaccine," says Dr. Phillip Scott, assistant professor at the University of Pennsylvania School of Veterinary Medicine and senior author of the article. "In addition, experimental infections with the protozoan parasite causing this disease, known as *Leishmania major*, have frequently been used to understand basic immunologic responses associated with many different infections."

"IL-12 has a key role in regulating the immune system and may also be involved in several diseases," says Giorgio Trinchieri, M.D., professor at Wistar and a discoverer of IL-12. "It

appears that IL-12 helps to regulate inflammation and the immune response to bacteria and other infectious agents, and possibly to HIV."

The finding is important because, by using IL-12, scientists may be able to boost immune responses to other diseases, such as tuberculosis and leprosy. It has even been suggested by Dr. Jonas Salk (*Science*, May 1993) that IL-12 might be used as an adjuvant in preventive or post-exposure vaccination to AIDS. The work of Dr. Trinchieri has previously shown that in a test tube IL-12 can indeed correct some of the immunological deficiency of blood cells taken from HIV patients (*Journal of Experimental Medicine*, March 1992), and these results have recently been extended by a study at the National Cancer Institute (*Science*, December 10, 1993). Genetics Institute, Inc. in Massachusetts hopes to begin Phase I trials of IL-12 in HIV-positive patients soon (*Science*, October 8, 1993).

Protective immunity induced by vaccination is dependent upon the capacity of the vaccine to elicit the appropriate immune response to either resist, control or eliminate the pathogen (disease-causing organism). Depending upon the pathogen, protection may require very different types of immune responses.

● One type of immune response is associated with the development of cells that

destroy the pathogen, and is referred to as cell-mediated immunity, while the other requires the production of antibodies, and is known as humoral immunity.

It is now known that particular CD4+ T cell subsets determine which of these responses develop following immunization. The CD4+ T cells that direct the development of cell-mediated immunity are known as Th1 cells, while those responsible for the development of humoral immunity are known as Th2 cells.

An essential role of adjuvants in vaccines is to direct the development of these CD4+ T cell subsets, such that the appropriate Th subset expands and a protective immune response is generated. However, in the past it has been poorly understood how adjuvants perform this role. Based on the current study, it has now been established that IL-12 primes animals for the cell-mediated type of immune response. Since elimination of the parasite, *Leishmania*, requires cell-mediated immunity, inclusion of IL-12 with the vaccine leads to the development of protection.

IL-12 was first discovered at Wistar in the late 1980's by a research group led by Dr. Trinchieri, and later was purified and cloned in 1989 in collaboration with Genetics Institute. ■

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A veterinarian and her clients reach out

From time to time we report on unusual activities of one of our alumnae. Following is a report by Eileen Rowan, V'77, who, together with her clients, has reached out to the Lakota Sioux of South Dakota.

It all started 4 years ago when I visited Taos, New Mexico on a ski trip, and began reading up on the local Pueblo Indian culture. We began sending feathers and an occasional fur pelt to the Taos Pueblo Indians, for use on their Native American dress. It has progressed to our



The five Sioux at Disney's Magic Kingdom

sort of adopting the Lakota Sioux of South Dakota, since they are by far the poorest of all our North American Indians. The reservation runs 85% unemployment and 50% welfare. There are no major cities anywhere close by. Their reservation lacks rich mineral deposits, and there is no tourism. Forget gambling casinos...there is no population to pull from.

So now we have an ongoing commitment to send out badly needed warm clothes for the bitter cold winters. Old ski clothes are prized, and given to