Scientists find potential new way to enhance vaccines

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Researchers at The Scripps Research Institute have discovered a potential new way to stimulate the immune system to prevent or clear a viral infection. By blocking the action of a key protein in the mouse immune system, they were able to boost immune "memory" in those mice -- work that may one day help doctors increase the effectiveness of human vaccines designed to prevent viral infections.

Immune memory in humans (or mice) is what allows the body -- after an initial exposure to a virus -- to quickly recognize, respond to, and eliminate that same virus upon some later exposure. Viral vaccines basically work through this mechanism.

Not all vaccines are 100 percent effective, however, and doctors would like to have ways of enhancing the ability of vaccines to induce immune memory. As described in an advance online Early Edition of the journal Proceedings of the National Academy of Sciences *(PNAS)* on January 26, 2010, the Scripps Research scientists were able to do just that. They significantly boosted immune memory in mice by blocking a protein called interleukin-10 (IL-10).

"Theoretically, it is possible to enhance vaccination by using this type of approach," says Scripps Research Professor Michael Oldstone, M.D., who led the research.

The work capitalizes on an earlier observation that Oldstone and his colleagues made a few years ago that some viruses use components of

the immune systems of their hosts to their advantage.

During the initial immune response to a viral infection, the body produces a number of proteins that help speed the creation of immune cells that specifically target the virus. These cells clear the virus from the bloodstream and destroy any host cells that are already infected. At the same time, the body carefully balances the "positive" signals that induce immunity with "negative ones" that dampen the immune response. The purpose of this dampening is to prevent runaway immune responses that could damage a person's own body and lead to autoimmunity.

The protein IL-10, for instance, dampens the immune system by shutting down production of CD4 and CD8 T cells—a function that Oldstone and his colleagues identified a few years ago. Some viruses have evolved ways of taking advantage of this. They have the ability to turn up the production of IL-10, essentially shutting down parts of the immune system, which allows them to establish persistent infections.

A few years ago, Oldstone and his colleagues began to wonder whether the opposite action would have the reverse effect. Would blocking IL-10 increase the effectiveness of a vaccine? Last year, they set out to answer this question by looking at genetic knockout mice that were missing the genes necessary to produce IL-10.

They found that, during a viral infection, mice that cannot generate IL-10 produced more CD4+ T cell immune cells as compared to control mice. Oldstone and his colleagues also showed the same effect can be achieved by blocking the IL-10 receptor in normal mice. They showed that giving antibodies designed to specifically target and block IL-10 to mice had the same effect: they enhanced immune response to the virus.

It may be possible to achieve the same effect in humans, says Oldstone. If a chemical that blocks IL-10 could be formulated and administered

with a vaccine, it may specifically enhance the effectiveness of that vaccine. However, even if such chemicals could be discovered, it would likely take years to develop and test their safety and effectiveness before they were ready for widespread commercial use.

More information: www.pnas.org/content/early/201 … /0914500107.abstract

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