MedicalXpress

Protein serves as a natural boost for immune system fight against tumors

January 30 2014

Substances called adjuvants that enhance the body's immune response are critical to getting the most out of vaccines. These boosters stimulate the regular production of antibodies—caused by foreign substances in the body—toxins, bacteria, foreign blood cells, and the cells of transplanted organs.

But, biologists think that vaccine adjuvants could be much better: The currently available licensed adjuvants are poor inducers of T helper cells and even worse at inciting killer T cells that clear viruses, as well as eradicate cancer cells.

The lab of David Weiner, PhD, professor of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, identifies new adjuvants that can produce the desired T-cell response. "Different molecular adjuvants, such as cytokines, are being studied as a way to increase the efficacy of vaccines," explains Weiner. "The development of DNA-based vaccines with cytokine adjuvants has emerged as particularly promising for inducing antiviral and anti-tumor, cell-mediated immune responses."

Daniel Villarreal, a graduate student in the Weiner lab, and colleagues report in *Cancer Research* this week that the protein IL-33 boosts the immune system of a human papilloma virus animal model of cancer. IL-33 is a cytokine, a small protein that signals immune cells such as T cells to travel to a site of infection or injury.

Although still experimental, DNA vaccines are a conceptual leap forward over standard vaccines, as they are not live and never expose the person being vaccinated to a true pathogen or infectious agent. They are transient and do their job by fooling the host's immune system into believing there is an infectious agent invading their cells so that the host responds by producing protective levels of T cells, in particular CD8 killer T cells. DNA vaccines have been studied in animal models of viral, bacterial, and parasitic disease, as well as animal models of tumors. Due to major advances in their immune potency DNA vaccines are being studied in human clinical trials for treating cancer and infectious diseases.

The team showed that IL-33 can further enhance the response of memory T cells, the long-lived cells that can patrol and protect the body from infections and cancers, when given with a DNA vaccine compared to a vaccine without IL-33. What's more, IL-33 and the DNA vaccine augmented immunological responses in both CD4 helper T cells and CD8 killer T cells, with a large proportion of CD8 killer T cells demonstrating a further improvement in the ability of DNA vaccines to drive the immune system to kill tumor cells in animals.

"Our results support the further study and possible development of IL-33 as adjuvants in vaccinations against pathogens, including in the context of antitumor immunotherapy," says Weiner. Additional cancer and infectious diseases studies in diverse animal models are in progress.

Provided by University of Pennsylvania School of Medicine