Toxoplasma gondii can stop cancer in its tracks as a vaccine

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Toxoplasma gondii (*T. gondii*) is a single-celled parasite that is happiest in a cat's intestines, but it can live in any warm blooded animal. Found worldwide, T. gondii affects about one-third of the world's population, 60 million of which are Americans. Most people have no symptoms, but some experience a flu-like illness. Those with suppressed immune systems, however, can develop a serious infection if they are unable to

fend off T. gondii.

An Anti-Cancer Agent in Nature?

A healthy immune system responds vigorously to T. gondii in a manner that parallels how the immune system attacks a tumor.

"We know biologically this parasite has figured out how to stimulate the exact immune responses you want to fight cancer," said David J. Bzik, PhD, professor of Microbiology and Immunology, Geisel School of Medicine at Dartmouth.

In response to T. gondii, the body produces natural killer cells and cytotoxic T cells. These cell types wage war against cancer cells. Cancer can shut down the body's defensive mechanisms, but introducing T. gondii into a tumor environment can jump start the immune system.

"The biology of this organism is inherently different from other microbe-based immunotherapeutic strategies that typically just tickle immune cells from the outside," said Barbara Fox, senior research associate of Microbiology and Immunology. "By gaining preferential access to the inside of powerful innate immune cell types, our mutated strain of T. gondii reprograms the natural power of the immune system to clear tumor cells and cancer."

Engineering T. gondii as a Cancer Vaccine

Since it isn't safe to inject a cancer patient with live replicating strains of T. gondii, Bzik and Fox created "cps," an immunotherapeutic vaccine. Based on the parasite's biochemical pathways, they delete a Toxoplasma gene needed to make a building block of its genome and create a mutant parasite that can be grown in the laboratory but is unable to reproduce in

animals or people. Cps is both nonreplicating and safe. Even when the host is immune deficient, cps still retains that unique biology that stimulates the ideal vaccine responses.

"Aggressive cancers too often seem like fast moving train wrecks. Cps is the microscopic, but super strong, hero that catches the wayward trains, halts their progression, and shrinks them until they disappear," said Bzik.

Laboratory Success in Melanoma and Ovarian Cancers

Published laboratory studies from the Geisel School of Medicine at Dartmouth labs have tested the cps vaccine in extremely aggressive lethal mouse models of melanoma or ovarian cancer and found unprecedented high rates of cancer survival.

"Cps stimulates amazingly effective immunotherapy against cancers, superior to anything seen before," said Bzik. "The ability of cps to communicate in different and unique ways with the cancer and special cells of the immune system breaks the control that cancer has leveraged over the immune system."

A Promising Future for a Personalized Cancer Vaccine

This new weapon against cancer could even be tailored to the individual patient. "In translating cps therapy to the clinic, we imagine cps will be introduced into cells isolated from the patient. Then Trojan Horse cells harboring cps will be given back to the patient as an immunotherapeutic cancer vaccine to generate the ideal immune responses necessary to eradicate their cancer cells and to also provide life-long immunity against any future recurrence of that cancer," said Bzik.

Fox and Bzik say a lot more study is needed before cps leaves the laboratory. They are trying to understand how and why it works so well by examining its molecular targets and mechanisms.

"Cancer immunotherapy using cps holds incredible promise for creating beneficial new cancer treatments and cancer vaccines," said Bzik.

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