

Immunotherapy for pancreatic cancer boosts survival by more than 75 percent in mice

October 29 2015



Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

A new study in mice by researchers at Fred Hutchinson Cancer Research Center has found that a specialized type of immunotherapy—even when used without chemotherapy or radiation—can boost survival from

pancreatic cancer, a nearly almost-lethal disease, by more than 75 percent. The findings are so promising, human clinical trials are planned within the next year.

The study, led by Drs. Sunil Hingorani and Phil Greenberg, both members of the Clinical Research Division at Fred Hutch, tested the immunotherapy on mice genetically engineered to grow pancreatic tumors very similar to those of human [pancreatic cancer](#). The mouse model, developed by Hingorani, already has led to a first-in-humans clinical trial that is showing [early promise](#) in some patients with advanced pancreatic cancer.

Pancreatic cancer is notoriously difficult to treat, said Hingorani, because it recruits the body's natural systems to construct both a tough physical barrier around tumors as well as an immune-cloaking device that keeps other, disease-fighting immune [cells](#) from recognizing the cancer.

Unlike any other cancer, pancreatic tumors are able to survive with a significantly decreased blood supply. As a consequence, chemotherapy, commonly administered via the bloodstream, has a difficult time getting inside. The tumors not only commonly grow quite large before patients will ever notice something is wrong, but they are very prone to metastasize, or spread to other sites in the body.

The investigators' new study, published Thursday in *Cancer Cell*, breaches pancreatic cancer's physical and immunological walls by using immunotherapy, a type of treatment that harnesses or refines the body's own immune system, to recognize and destroy cancer cells. The researchers devised a therapy using T cells, disease-fighting immune cells, that they engineered in the lab to recognize and attack pancreatic cancer.

T-cell therapy is showing promise as a treatment for several types of blood cancers, based on early results from Fred Hutch and other research centers, but aiming these cells at solid tumors like pancreatic cancer has historically proven more difficult, Hingorani said. Part of the challenge comes from the access to tumor cells—or lack thereof. T-cell therapy is administered through the bloodstream, like chemo. It's easy enough to see why [solid tumors](#) may present more of a challenge to treat with this kind of immunotherapy than blood cancers such as leukemia and lymphoma.

The researchers didn't think the engineered T cells would stand a chance against pancreatic cancer on their own. But they needed somewhere to start, Greenberg said.

But to their surprise, the T cells—engineered to recognize and kill cells bearing a protein called mesothelin, which is overproduced by virtually all [pancreatic tumors](#)—got into the mice's tumors and started attacking them.

In the mouse model of the disease—which is actually slightly more aggressive than the human version, Hingorani said—animals that received T cells engineered to recognize a non-cancerous protein survived on average 54 days after their cancer became detectable. Those that received the mesothelin-directed cells lived an average of 96 days, a 78 percent bump.

Although the researchers weren't expecting to take this first version of the T-cell therapy to clinic, that's now their plan. Their team has already built the human version of the special T-cell protein that recognizes mesothelin. They're planning to launch a phase 1 clinical trial to test the therapy's safety in patients with advanced pancreatic cancer within the next year.

"As best we can tell, this would be a better therapy than anything that exists for pancreatic cancer right now," Greenberg said. "It's hard to be this optimistic without ever having treated a pancreatic cancer patient with this [therapy], but the biology of what we're doing looks so remarkably true and good."

Provided by Fred Hutchinson Cancer Research Center

Citation: Immunotherapy for pancreatic cancer boosts survival by more than 75 percent in mice (2015, October 29) retrieved 8 May 2024 from <https://medicalxpress.com/news/2015-10-immunotherapy-pancreatic-cancer-boosts-survival.html>

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