Experimental KRAS vaccine may help prevent pancreatic cancer

An experimental vaccine shows promise for the prevention of pancreatic cancer in a recent trial. Image credit: Adene Sanchez/ Getty Images

- **Pancreatic cancer is a serious cancer type that can be difficult to catch early.**
- **One potential target area is a protein called KRAS that can mutate in pancreatic cancer.**
- **One study in people at risk for pancreatic cancer found that a vaccine that targeted KRAS was safe and produced a good immune response.**
- **The results point to a way to prevent pancreatic cancer as research moves forward.**

Pancreatic cancer accounts for 8% of cancer deathsTrusted Source in the United States, and it is challenging to catch pancreatic cancer earlyTrusted Source. Finding ways to treat and potentially prevent pancreatic cancer is a critical area of research.

One study evaluated a peptide vaccine in people who were at a high risk for pancreatic cancer. This vaccine targeted the mutated protein, KRAS, which is found in the most common pancreatic cancer, pancreatic ductal adenocarcinomaTrusted Source (PDAC).

The study, which appears in Cancer Discovery, found that using this vaccine to target KRAS mutations produced a long-term immune response. This discovery could lead to a full-fledged strategy to prevent pancreatic cancer.

Why target the KRAS protein

This research explored a possible way to prevent PDAC, noting that one possible target is mutant KRAS.

Study author Elizabeth M. Jaffee, MD, Deputy Director of The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, explained to *Medical News Today*:

“Pancreatic cancer takes 10 years or more to develop. It starts in normal pancreas cells with a mutation in the protein KRAS. KRAS normally regulates cell growth, division, and survival to maintain the health of organs like the pancreas. The mutation in this protein results in uncontrolled growth. But for pancreatic cancer to develop, additional mutations have to occur. Over 90% of pancreatic cancers start with this mutation, and the cancer remains dependent on this mutation.”

Prior to this research the team had developed a vaccineTrusted Source targeting the six most common KRAS mutations present in PDAC, which they had tested in individuals who already had PDAC with favorable results.

The current study focused on participants at risk for PDAC, such as those with a close relative with PDAC. All participants also had “radiographic evidence of a pancreatic abnormality,” the study paper details.

In all, researchers were able to work with 20 participants, and participants’ median age was 66.5 years old.

Researchers gave participants 5 doses of the related vaccine, over several weeks, with the last booster dose happening on week 13. Participants tolerated the injections well, with only mild adverse events such as fatigue.

The research team conducted a number of tests and analyses, including using information from particular blood cells from participants.

Vaccine leads to solid response against pancreatic cancer

The vaccine produced a solid T-cellTrusted Source response, a specific white blood cell type. This mutant KRAS-specific T-cell response occurred for 90% of participants.

They did find that the T-cell response was greater against certain KRAS mutations than others, but 50% of participants still had a significant T-cell response against all six mutations.

Additional testing in particular blood cells found that the response against KRAS mutations was highest for a subtype of T cells called CD4+ T cells.

Researchers followed up with participants for a median of 16.5 months. During this time, no participants experienced PDAC or had pancreatic lesions that required surgical intervention.

Three participants even saw a pancreatic cyst resolve and three others saw a decrease in cyst size. Compared to an unvaccinated cohort similar to the intervention group, the vaccinated group had greater cyst reduction and resolution.

Long-term follow-up also suggested that the response of T-cells could be maintained and be useful in the long term. Additional testing at various timepoints further confirmed that the vaccine “can generate a durable repertoire of functional, [mutant]KRAS-specific T cells,” the researchers write.

Jaffee highlighted:

“This study tested a vaccine that induces immunity against the KRAS mutation to eradicate the earliest changes in the pancreas cell that starts its journey to become a cancer. The goal is to stop this progression from happening. We tested it in healthy individuals who have either a family history or a genetic predisposition and had small cysts on their pancreas observed on MRI. We found that the vaccine induced immune responses against the mutations in KRAS and remained detectable for at least 2 years.”

What were the study limitations?

This study provides more information and hopes of preventing pancreatic cancer, but it still has limitations. For one, it only included 20 participants, so more data with a larger number of individuals will likely be helpful.

Certain follow-ups also included an even smaller number of participants, further indicating the need for more research. The trial type also carried limitations, such as how it was non-randomized.

Researchers acknowledge that they also had a limited ability to see how the immune response correlated to cyst stability and cases of PDAC in the long term. They also note that the cyst resolutions that they did observe could actually be from technical limitations of the imaging they used.

They note that the most common lesions that are precursors to PDAC aren't easy to find radiographically. Most of the cysts they observed were not these most common lesions. Further research and analysis of pancreatic cancer precursors will likely be helpful.

Not all participants received vaccines that targeted one particular KRAS mutation, although the T-cell response was still about the same for those who did and those who did not. There is also the possibility of skewed data on T-cell phenotypesTrusted Source, or what researchers were able to observe about the T-cells' characteristics.

The maximum amount of follow-up was 2 years, so additional long-term data may be helpful, as well as looking into the need for booster shots, since the immune response did experience declines.

Vaccine could expand prevention options

Overall, the findings indicate a possible pathway towards preventing pancreatic cancer, which would add to options when it comes to addressing this challenging cancer type.

Nilesh Vora, MD, a board-certified hematologist and medical oncologist and medical director of the MemorialCare Todd Cancer Institute at Long Beach Medical Center in Long Beach, CA, who was not involved in this study, noted that "this strategy introduces a potential shift from treatment to prevention."

"Currently, most pancreatic cancer therapies focus on managing disease after diagnosis, often at advanced stages," said Vora. "A vaccine-based approach could expand our toolkit by offering a proactive option aimed at preventing cancer from developing in the first place, particularly in high-risk individuals. Over time, this could complement existing therapies and improve overall outcomes."

Jaffee also emphasized that "this is the first study showing it is possible to induce an immune response against a cancer-causing protein at the earliest stages of cancer development."

"We cannot say for sure that the resolution of cysts is directly related to the immune responses we test in the blood. The cysts are too small to biopsy," she cautioned.

"But these findings suggest we need to do further studies to try and prevent cancer. It is safe and may prevent cancer development and morbidity associated with treatment for advanced precancers which require surgery," the study author concluded.

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https://www.medicalnewstoday.com/articles/experimental-kras-vaccine-may-help-prevent-pancreatic-cancer#Vaccine-could-expand-prevention-options