Medical Xpress

# Radioactive bacteria targets metastatic pancreatic cancer

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Researchers at Albert Einstein College of Medicine of Yeshiva University have developed a therapy for pancreatic cancer that uses *Listeria* bacteria to selectively infect tumor cells and deliver radioisotopes into them. The experimental treatment dramatically decreased the number of metastases (cancers that have spread to other parts of the body) in a mouse model of highly aggressive pancreatic cancer without harming healthy tissue. The study was published today in the online edition of the *Proceedings of the National Academy of Sciences*.

"We're encouraged that we've been able to achieve a 90 percent reduction in metastases in our first round of experiments," said co-senior author Claudia Gravekamp, Ph.D., associate professor of microbiology & immunology at Einstein who studies new approaches to treating metastatic cancer. "With further improvements, our approach has the potential to start a new era in the treatment of metastatic pancreatic cancer."

Pancreatic cancer is among the deadliest of cancers, with a five-year survival rate of only 4 percent. The National Cancer Institute predicts that this year, 45,220 new cases of pancreatic cancer will be diagnosed and 38,460 people will die from the disease. Pancreatic cancer confined to the pancreas can be treated through surgery. But early pancreatic cancer is difficult to detect, since it rarely causes noticeable signs or symptoms. Most pancreatic cancer cases are diagnosed only after the cancer has spread (metastasized), typically resulting in jaundice, pain, weight loss and fatigue. But there is no cure for metastatic pancreatic cancer, and treatment focuses mainly on improving quality of life.

Several years ago, scientists observed that an attenuated (weakened) form of *Listeria monocytogenes* can infect cancer cells, but not normal cells. In a 2009 study, Dr. Gravekamp discovered the reason: The tumor microenvironment suppresses the body's immune response, allowing *Listeria* to survive inside the tumors. By contrast, the weakened bacteria are rapidly eliminated in normal tissues. (*Listeria* in its wild form causes foodborne illnesses, particularly in immunocompromised people.)

Scientists later showed that *Listeria* could be harnessed to carry an anti-cancer drug to tumor cells in laboratory cultures, but this concept was never tested in an animal model. These findings prompted Dr. Gravekamp to investigate *Listeria*-tumor interactions and how *Listeria* could be used to attack cancer cells.

The idea of attaching radioisotopes (commonly used in cancer therapy) to *Listeria* was suggested by Ekaterina Dadachova, Ph.D., professor of radiology and of microbiology & immunology at Einstein and the paper's co-senior author. Dr. Dadachova, who is also the Sylvia and Robert S. Olnick Faculty Scholar in Cancer Research, is a pioneer in developing radioimmunotherapies —patented treatments in which radioisotopes are attached to antibodies to selectively target cells including cancer cells, microbes or cells infected with HIV. When the antibodies bind to antigens that are unique to the cells being targeted, the radioisotopes emit radiation that selectively kills the cells.

Working together, Drs. Gravekamp and Dadachova coupled a radioactive isotope called rhenium to the weakened *Listeria* bacteria. "We chose rhenium because it emits beta particles, which are very effective in treating cancer," said Dr. Dadachova. "Also, rhenium has a half-life of 17 hours, so it is cleared from the body relatively quickly, minimizing damage to healthy tissue."

Mice with metastatic pancreatic cancer were given intra-abdominal injections of the radioactive *Listeria* once a day for seven days, followed by a seven-day "rest" period and four additional daily injections of the radioactive bacteria. After 21 days, the scientists counted the number of metastases in the mice. The treatment had reduced the metastases by 90 percent compared with untreated controls. In addition, the radioactive *Listeria* had concentrated in metastases and to a lesser extent in primary tumors but not in healthy tissues, and the treated mice did not appear to suffer any ill effects.

The treatment may have the potential for clearing an even higher percentage of metastases. "We stopped the experiment at 21 days because that's when the control mice start dying," said Dr. Dadachova. "Our next step is to assess whether the treatment affects the animals' survival."

"At this point, we can say that we have a therapy that is very effective for reducing metastasis in mice," Dr. Gravekamp noted. "Our goal is to clear 100 percent of the metastases, because every cancer cell that stays behind can potentially form new tumors." The researchers expect the treatment could be improved by fine-tuning the treatment schedule, using higher doses of radiation, or by piggybacking additional anti-cancer agents onto the bacteria. Einstein has filed a patent application related to this research that is currently available for licensing to partners interested in further developing and commercializing this technology.

**More information:** The paper is titled "A non-toxic radioactive Listeria at is a highly effective therapy against metastatic pancreatic cancer."