



WOODBURY, N.Y., May 17, 2018 /PRNewswire-USNewswire/ -- Lustgarten Foundation Distinguished Scholar Douglas Fearon, M.D., a professor at Cold Spring Harbor Laboratory (CSHL), has discovered how pancreatic cancer metastasizes to the liver following surgery, as reported in today's online edition of leading biomedical journal *Science*.

"This discovery is significant because for patients who undergo pancreatic cancer surgery, there is typically a period lasting up to two weeks during which T cells are depleted, owing to a surge in post-operative stress hormone (cortisol) levels," Dr. Fearon said. "If we can keep those cortisol levels down, we might be able to stop the cancer from metastasizing."

Working with mice that model pancreatic ductal adenocarcinoma (PDAC), Dr. Fearon's team discovered that the immune system controls the spread of isolated, solitary dormant cancer cells in the liver of animals that have primary pancreas tumors. These quiescent cancer cells in the liver don't divide, but they can be activated under certain conditions and proliferate to become clinically relevant metastases.

The team thinks solitary cancer cells have already spread to the liver in many patients well before they go to surgery to have their primary tumor removed. They are likely carried there by the bloodstream, having been shed by the primary tumor. Dr. Fearon estimates that in a typical patient, 14 million cancer cells pass through the liver every day. The immune system kills most of the cancer cells deposited in the liver. However, there are some latent, non-dividing solitary cancer cells – called disseminated cancer cells (DCCs) – that are left behind after the immune system has killed all the other cancer cells that are capable of growing. The immune system ignores the DCCs because they lack certain cell surface features that mark them for removal.

Dr. Fearon's team showed that DCCs have a particular abnormality that makes them invisible to the immune system, called ER stress. This refers to a flaw that enables unfolded proteins to clog the organelle of the cell called the endoplasmic reticulum. This ER stress is what enables DCCs to escape destruction by the immune system. When ER stress was blocked, the DCCs became more typical pancreatic cancer cells and were then eliminated by the immune system.

In mice that model this condition, metastases soon appeared in the liver. The affected mice were now like patients who, following surgery, lacked metastatic liver lesions but bore a burden of DCCs – cells which, after a period of latency, became seeds of a lethal metastasis. Dr.

Fearon theorizes that it is during such post-operative periods that DCCs, already present in the liver, lose their immunity and begin to divide in patients who go on to develop metastasis.

Based upon these findings, Dr. Fearon and his team theorize that when T cells in the liver are suppressed after surgery, due to stress and impaired nutrition, the DCCs begin to divide and pancreatic cancer metastases become apparent. Dr. Fearon is currently planning to test whether this post-operative stress can be medically managed and lead to less early relapses following surgery, and therefore improved outcomes for patients.

About the Lustgarten Foundation

The Lustgarten Foundation is America's largest private funder of pancreatic cancer research. Based in Woodbury, N.Y., the Foundation supports research to find a cure for pancreatic cancer, facilitates dialogue within the medical and scientific community, and educates the public about the disease through awareness campaigns and fundraising events. Since its inception, the Lustgarten Foundation has directed \$154 million to research and assembled the best scientific minds with the hope that one day, a cure can be found. Thanks to separate funding to support administrative expenses, 100 percent of every dollar donated goes directly to pancreatic cancer research. For more information, please visit www.lustgarten.org.

SOURCE The Lustgarten Foundation for Pancreatic Cancer Research