Stand Up To Cancer Researchers Identify Potential Treatment Target for Metastatic Pancreatic Cancer Using CTC Chip Technology

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PHILADELPHIA — Researchers with the Stand Up To Cancer CTC Chip Dream Team have identified a potential treatment target in metastatic pancreatic cancer through a detailed analysis of genes expressed in circulating tumor cells (CTCs) – cells that break off from solid tumors and travel through the bloodstream.

In a study that will appear today in the print edition of *Nature* and received advanced publication online earlier this month, the Dream Team reported finding increased expression of WNT2, a member of a known family of oncogenes, in CTCs from mouse models of pancreatic cancer and from human patients.

The SU2C Dream Team “Bioengineering and Clinical Applications of Circulating Tumor Cell Chip” is led by Daniel A. Haber, M.D., Ph.D., director of the Massachusetts General Hospital (MGH) Cancer Center, and Mehmet Toner, Ph.D., director of the Massachusetts General Hospital Center for Bioengineering in Medicine in Boston.

“Studying cancer cells as they circulate in the blood is a critical way to figure out how cancer spreads and finding ways to try to block that,” said Haber. “It has taken a real partnership between engineers, biologists and clinicians to develop the technology to fish out these incredibly rare cells in the blood, study them with molecular tools and start applying these findings toward new treatments.”

Haber and colleagues used the second-generation version of the CTC chip – developed with support from the SU2C grant – to isolate CTCs from mice that were genetically engineered to develop pancreatic cancer. They then compared gene expression between the CTCs in the blood and cancer cells within the pancreatic tumor, to look for genes that helped tumor cells invade into the bloodstream. The team was able to identify several genes that were expressed at higher levels in the CTCs. From this group of genes, WNT2 (a member of a signaling pathway known for its role in embryogenesis and cancer) was selected for further investigation. Results showed that WNT2 was highly expressed in CTCs and metastases. These findings were in contrast to primary tumors, in which WNT2 was rarely expressed.

Through further studies, the Dream Team ultimately showed that WNT2 might be responsible for the CTC’s ability to escape “anoikis” – one of the body’s normal mechanisms to eliminate these cells as they circulate in the blood. If CTCs are not eliminated, they have an increased chance of establishing metastases.

The team also identified a drug that blocks a step in the WNT2 pathway, thereby

suppressing the ability of CTCs to survive in the bloodstream. This drug is not available for clinical use and further studies would be needed to test its efficacy in patients with pancreatic cancer. While most of the work was performed using a mouse model of pancreatic cancer, the team found that similar mechanisms appear to operate in CTCs from patients with pancreatic cancer.

This study sheds new light on how pancreatic cancer cells may metastasize, and identifies a potential drug target for interrupting the WNT pathway and limiting the chance for metastases to spread to other organs.