Researchers find tumor microbiome interactions may identify new approaches for pancreatic cancer treatment

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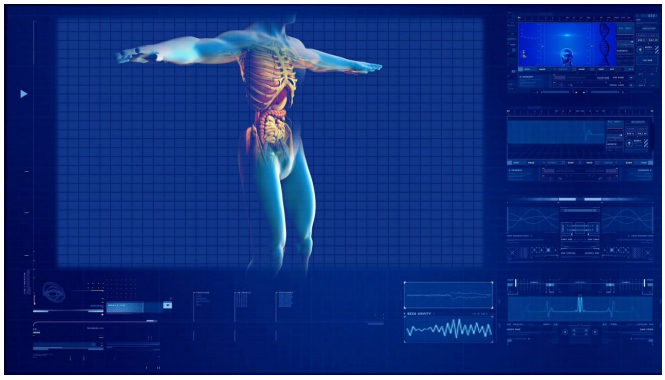

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Investigators from Rutgers Cancer Institute of New Jersey, the state's leading cancer center and only National Cancer Institute-Designated Comprehensive Cancer Center, together with RWJBarnabas Health, examined the microbiome of pancreatic tumors and identified particular microorganisms at single cell resolution that are associated with inflammation and with poor survival.

According to the researchers, these microorganisms may be new targets for earlier diagnosis or treatment of pancreatic cancer, which is the fourth leading cause of cancer death for both men and women in the United States. The findings are published in the online version of *Cancer Cell*.

Microbes are living things that are too small to be seen with the naked eye. We have more microbes living in our body than the total number of human cells, and can be found in organs like the pancreas, which at one time was considered microbe-free.

Subhajyoti De, Ph.D., principal investigator at Rutgers Cancer Institute and senior author of the study along with graduate student Bassel Ghaddar, a student in the MD/Ph.D. program at Rutgers Robert Wood Johnson Medical School, began exploring if there are microbes residing in pancreatic tumors, and if they have consequences for cancer progression or treatment. However, studying microbes in tumors is difficult, in part since every patient is different, and because microbial footprints are too subtle to detect reliably.

To explore further, the researchers teamed up with Martin Blaser, MD, Henry Rutgers Chair of the Human Microbiome at Rutgers University and world-renowned microbiome expert. The investigators developed a genomic approach called SAHMI (Single-cell analysis of Host-Microbiome Interactions) to identify microorganisms associated with individual human cells. Sifting through millions of RNA sequences using sophisticated software, they identified which ones likely represent human genes, and which ones are microbial in origin.

"This new technique allowed us to identify tumor-associated microbes and measure the activity of the host cells at the same time, which is a significant technical advance, and the results were stunning," notes Dr. De, who is also an associate professor of cancer systems biology at Rutgers Robert Wood Johnson Medical School.

Studying two independent groups of pancreatic tumors, the team found that some had bacteria that associated with specific cell-types within the tumor, which were essentially absent in normal pancreatic tissues. These bacteria were predominantly located within tumor cells, and their abundance correlated with cancer-related cell activities. The specific signatures of the microbes that were found predicted particularly aggressive cancer

progression and poor prognosis.

The microbial footprints within the pancreatic tumors raised the question of whether the immune cells that were present were responding to the cancer or to the microbes. The study findings suggested that the immune responses were mostly responding to the microbes in the tumor and not to the cancer cells.

"Our observations provide a new view about why pancreatic cancers are so difficult to treat," notes Dr. Blaser, who is also a research member at Rutgers Cancer Institute and professor of epidemiology and biostatistics at Rutgers School of Public Health. "But better understanding these interactions may identify new approaches for therapies."

More information: Subhajyoti De, Tumor microbiome links cellular programs and immunity in pancreatic cancer, *Cancer Cell* (2022). DOI: 10.1016/j.ccell.2022.09.009. www.cell.com/cancer-cell/fullt … 1535-6108(22)00438-X

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