Dr. Rachael Guenter: "Targeting Proteins on the Surface of Pancreatic Cancer"

Pancreatic ductal adenocarcinoma (PDAC) is the most common form of pancreatic cancer and one of the deadliest cancers. Pancreatic cancer is particularly difficult to treat because it is often discovered only after it has grown or spread to other organs. Even when pancreatic cancer is detected earlier, current treatments are often unable to completely eliminate the disease. New approaches are urgently needed to better detect pancreatic tumors and selectively target cancer cells for treatment.

Our research focuses on a protein called **calreticulin** (**CALR**). CALR normally resides inside cells, where it performs several important functions. However, when cancer cells experience certain types of stress, CALR can move from inside the cell to the outer surface of the cancer cell. This creates an opportunity: a protein that is normally hidden inside the cell becomes exposed and accessible for targeting. Importantly, we have found that this process can be triggered in pancreatic cancer. Our laboratory has generated strong = evidence demonstrating that chemotherapy increases the amount of CALR displayed on the surface of pancreatic cancer cells. We propose to take advantage of surface CALR for better tumor detection and delivery of therapy.

To capitalize on this discovery, our team has developed a custom-made molecule that binds specifically to CALR. This CALR-binding molecule can be linked to a small amount of radioactive material, allowing us to track where it travels in the body using specialized imaging. In our studies in mice with pancreatic tumors, the radioactive CALR-binding molecule successfully traveled to and accumulated within the tumors, demonstrating that surface CALR can be used to locate pancreatic cancer in a living organism. This approach could ultimately provide a new strategy for both detecting and treating pancreatic cancer. Radioactive labels used for imaging could help physicians identify tumors or monitor how they respond to treatment. In the future, the same CALR-binding molecule could potentially be paired with therapeutic forms of radiation to deliver treatment directly to cancer cells while limiting exposure to healthy tissues.

By combining chemotherapy-induced CALR exposure with a molecule designed specifically to recognize CALR, this work has the potential to establish a new platform for more precise pancreatic cancer detection and targeted therapy.