Obesity has long been identified as a risk factor for pancreatic cancer, and how to leverage that knowledge for prevention and treatment has been elusive. Mandar Deepak Muzumdar, MD, is in the process of changing that.

Dr. Muzumdar has uncovered hormonal activity associated with obesity that creates targets for drug development. He was a lead author of a paper published in the journal Cell in May 2020 that revealed the role of the popular hormone cholecystokinin (CCK) made within the pancreas itself in accelerating tumor progression in pancreatic ductal adenocarcinomas in mice. Dr. Muzumdar’s discovery opens the possibility of more effective drugs in the battle against pancreatic cancer—as well as a new promising strategy of employing endocrinology and genetics in concert to explore the mechanisms driving obesity-related cancers.

The paper is the result of intensive work since his arrival at Yale Cancer Center three years ago. But his interest in this area started much earlier than that to a degree. Dr. Muzumdar was a medical student at Stanford. “On my clinical oncology rotation, one of the things that impressed upon me was to learn the risk factors of different cancer types,” he said. “I never quite made sense why it would matter, because at that point the patient had already been diagnosed with cancer. It was not clear that knowing the risk factors would really change their treatment.”

As his studies continued, obesity was getting increasing attention as a risk factor in pancreatic and other cancers. But there was scant knowledge about exactly how obesity was contributing to malignancies. “I conceived this project to study why this was,” Dr. Muzumdar said. “I was fortunate to go where the science led us and to find collaborators to help us start the journey.”

“We also had a very diverse array of trainees who were involved in the project. I think training the next generation of scientists in cancer biology is really important. It taught me in the fact that we were not afraid to involve so many trainees to make important discoveries,” he said.

His work showed that tumor progression could be slowed or stopped in mice with pancreatic tumors if they lost weight. Unfortunately, since pancreatic cancer is typically diagnosed in advanced stages in humans, that finding does not point to a treatment option. But Dr. Muzumdar said that the information will be important for doctors to use in counseling weight loss for patients who may have a high-risk for pancreatic cancer.

Late diagnosis is one of the major challenges of pancreatic cancer. There is no single lab that can do everything. Every lab has its expertise, and there’s relationships that are required between the disciplines to work together to accelerate discovery around cancer prevention and treatment.

“There is no single lab that can do everything. Every lab has its expertise, and there’s relationships that are required between the disciplines to effectively take advantage of the basic science,” Dr. Muzumdar said. “Collaboration helps us validate critical findings at the investigation. We are able to validate our findings for example, from our animal models in human biospecimens. We were able to follow these interesting findings in human specimens and validate that they were present where we thought they would be.” Based on these findings, Dr. Muzumdar believes that targeting CCK or other hormones made within the pancreas may become an important strategy in pancreatic cancer prevention or even treatment.

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Dr. Muzumdar is an Assistant Professor of Medicine (Medical Oncology) and Genetics. He received the KRAS gene, which has mutations in more than 90 percent of pancreatic cancer patients, to look larger in his investigations. “A few years ago, we tried to test whether KRAS was a good target in pancreatic cancer. Instead of drugs, which weren’t available, we used genetic tools to eliminate KRAS in pancreatic cancer cells, and through those studies we found that over half of the pancreatic cancer cell lines that we eliminated KRAS in could not survive starvation.”

This led him to think about linking “beyond the gene” to other activity within the pancreas and ultimately to CCK. The investigation reinforced Dr. Muzumdar’s belief in “translational science” as endocrinology became important in his own work. He is the leader of the Yale Pancreatic Cancer Collaborative (see feature article), which aims to help scientists from various disciplines work together to accelerate discovery around cancer prevention and treatment.

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