Sylvester Pancreatic Cancer Researcher  Dr. Nagaraj Nagathihalli Awarded Florida Department of Health Grant

The Florida Department of Health has awarded Nagaraj Nagathihalli, Ph.D., an associate professor at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine, a $583,200 grant to study tobacco risk, tumor progression, and therapeutic options for pancreatic cancer.

Nagaraj Nagathihalli, Ph.D.

A leading cancer biologist, Dr. Nagathihalli has been working to identify driving cellular and molecular mechanisms related to how tobacco promotes pancreatic cancer progression and aggressiveness, and to develop new therapeutic strategies to reduce the poor outcomes associated with this disease.

Tobacco use has reached epidemic proportions worldwide and emerged as a leading cause of many malignancies, including esophageal, oral, breast, colon, and pancreatic carcinomas. Carcinogenic compounds from tobacco are quickly absorbed into the bloodstream and cause pancreatic injury by a series of oncogenic events that culminate in progressive tumorigenesis.

"Despite such a high prevalence of tobacco-associated pancreatic cancer in the population, mechanistic understanding
of how tobacco consumption precedes pancreatic neoplasia remains limited,” said Dr. Nagathihalli, principal investigator on the study and associate professor in the DeWitt Daughtry Family Department of Surgery at the Miller School. “Ingesting tobacco smoke triggers inflammatory and immune responses resulting in inflammation and fibrosis of the pancreatic parenchyma, providing a milieu amenable to the aggressive progression of pancreatic neoplasia and to evade therapeutic intervention.”

Nipun Merchant, M.D.

High Burden in of Pancreatic Cancer in Florida

The incidence of pancreatic cancer in the U.S. is rapidly increasing, and the burden is particularly high in Florida. Despite being the 12th most common cancer diagnosed, pancreatic cancer will soon overtake colorectal cancer as the second leading cause of cancer death in the US.

The health impact of this project is fivefold: 1) testing and targeting molecular pathways in experimental animal models that recapitulate tobacco smoking; 2) pharmacologic identification of novel, clinically important mechanistic targets; 3) identifying therapeutic avenues to potentiate immunotherapy efficacy; 4) cross-validation using human pancreas cancer samples; and 5) testing the translational potential for treatment using targeted inhibitors combined with immunotherapy.

“Dr. Nagathihalli’s previous work identified the molecular pathways that are activated with tobacco smoking and promote neoplastic progression and are associated with poor prognosis
in patients with pancreatic cancer,” said investigator Nipun Merchant, M.D., chief of the Division of Surgical Oncology and director of the Sylvester Pancreatic Cancer Research Institute. “The exact contribution of these molecular pathways associated with smoking-induced pancreatic neoplasia remains poorly understood. Therefore, the studies in this proposal will advance therapeutic options and are specifically designed for tobacco-associated pancreatic cancer.”

Dr. Nagathihalli and the team at the Sylvester Pancreatic Cancer Research Institute are working to bring change to the treatment of pancreatic cancer.

**Therapeutic Strategies for Improving Outcomes**

Specific combination therapeutic strategies have yet to be explored in treating pancreatic cancer and other malignancies. Dr. Nagathihalli said that the experimental design in this grant has the potential for near-immediate clinical implementation. The team believes that the studies will improve survival outcomes for tobacco-associated patients with pancreatic cancer by developing novel combinations of chemo and immunotherapies.

Wael El-Rifai, M.D., Ph.D.

“Although every cancer is different, it is essential that the scientific community integrate the lessons we have learned from other tobacco-related cancers into therapeutic approaches. Both immune stimulation and curtailing immune
Evasion are crucial to improve outcomes for pancreatic cancer patients, who are uniquely susceptible due to their specific smoking-induced mechanism,” Dr. Nagathihalli said.

“Successful completion of these studies can determine whether a personalized approach for tobacco-associated pancreatic cancer can be utilized to advance progress toward cures and improve survival of Floridians,” said Wael El-Rifai, M.D., Ph.D., associate director of basic science and co-leader of the Tumor Biology Program at Sylvester and professor and associate vice chair of the DeWitt Daughtry Family Department of Surgery.

“We are extremely excited about this opportunity that’s been given to us by the state of Florida. These studies are critical to our having a better understanding of pancreatic cancer in tobacco-smoking populations,” Dr. El-Rifai said.

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