

UNC research trio teams up to fight cancer drug resistance

The V Foundation awards \$600,000 grant to UNC Lineberger to track kinase activity in head and neck, lung and esophageal cancers.

A dynamic team of cancer researchers at UNC Lineberger Comprehensive Cancer Center have been funded by The V Foundation for Cancer Research to focus on finding new treatments for cancers of the head, neck, lung and esophagus while better understanding why these cancers can become resistant to new therapies.

The research team will be led by Ben Major, PhD, assistant professor of cell biology and physiology, Neil Hayes, MD, MPH, associate professor of medicine, and Gary Johnson, PhD, Kenan Distinguished Professor and chair of the Department of Pharmacology. The V Foundation, one of the nation's leading cancer research foundations, awarded \$600,000 to the UNC Lineberger team over a period of three years.

"Most patients with the types of cancers being studied in this grant – head and neck, lung and esophageal – are initially diagnosed with advanced disease, with over 80 percent of lung cancer patients and 90 percent of esophageal cancer patients dying of the disease," said Hayes, a medical oncologist who, in addition to his cancer genetics research, also treats patients at the N.C. Cancer Hospital.

While very few new treatments for these types of cancers are available to patients currently, exciting advances have been made in the development of targeted, kinase inhibitor therapies. Kinases are proteins expressed in human tissues that play a key role in cell growth, particularly in cancer. Of the 518 known human kinases, over 400 are expressed in cancers. Efforts have been made to develop kinase inhibitors as targeted cancer treatments, but most metastatic cancers eventually become resistant to these treatments.

The research team will track kinase activity in 50 tumor samples both prior to and following treatment with a combination of kinase inhibitor therapies. Matching both the genomic profile of the tumor with the kinase activity will then offer the researchers a glimpse into why cancer cells begin to resist these therapies, and further study how combination therapies might help block resistance.

"By defining the tumor kinase activity before and after therapy along with the overall kinome-level response to therapy, we hope to identify certain kinase signatures that can be targeted to accelerate the development of new drugs," said Johnson, who developed the technology to track kinase activation in real-time.

Together with Major, the two researchers have refined the kinome technology since its initial discovery in 2012 for use in small volume, clinical samples.

"With this new technology, we can measure both the presence and activity of 70-80 percent of all kinases simultaneously, allowing us to see how cancers evade treatment," said Major.

The grant is funded through The V Foundation's Translational Clinical Research grant program and meant to facilitate the transition of projects from the laboratory to the clinic.

"We are excited to bring together translational scientists with patient-centered research to care for our patients with some of the harder to treat cancers," said Jason Akulian, MD, MPH, clinical assistant professor, Division of Pulminology & Critical Care Medicine. "This is exactly the kind of team science we can all support."

Translational researchers seek to apply basic knowledge of cancer and bring the benefits of the new basic-level understandings to patients more quickly and efficiently.



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Neil Hayes, MD, MPH; Ben Major, PhD; Gary Johnson, PhD