Meet the Researcher

Luke Wilkins, MD

"This funding from the American Cancer Society will have a direct impact on my pre-clinical research developing novel, image-guided cancer therapies. With this project and future clinical trials, I hope to change the treatment paradigm of my patients."

The Rector and Visitors of the
University of Virginia
Charlottesville, VA

Grant Term:
7/1/2019 – 6/30/2023

Grant Award:
$792,000.00

Preclinical Transarterial Embolization for Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer deaths worldwide. Due to increasing obesity rates and increasing rates of hepatitis B and C, HCC is increasing in incidence. Most HCC patients are ineligible for liver transplant or surgery and require some other therapeutic treatment. When the blood supply to the tumor is occluded this creates low levels of oxygen (hypoxia) within the tumor that are, in theory, lethal for the tumor cells. However, this is not the case as the treatment is not considered curative and there are high rates of residual untreated tumor and tumor recurrence. A small minority of patients experience a complete response to treatment and only few patients become eligible for a curative liver transplant. A major improvement in TACE is needed to improve catheter-based treatments for HCC.

Dr. Wilkins theorizes that cells of HCC survive embolization through both changing their method of metabolism and achieving inadequate levels of hypoxia. There is prior research showing that a majority of HCC cells may survive embolization by employing glycolytic metabolism. Glycolytic metabolism can function without the need for oxygen. Dr. Wilkins' recently published results show that a natural compound called caffeic acid (CA) is lethal to cellular functions that are active in both hypoxic and normoxic cellular environments. When combined with small particles (embolization) it causes extensive tumor regression. Dr. Wilkins hypothesizes that this enhanced effect to embolization is because the two treatments are synergistic and affect both methods of metabolism in the HCC cell.

The objective of this project is to test if small particles loaded with caffeic acid will perform better than small particles alone in treating tumors in a large animal model (Marmota monax, woodchuck) of HCC. The woodchuck tumors develop spontaneously in diseased liver and are the closest analog to human HCC. They will be treated using the exact methods as done in current clinical practice. Improvements in catheter-based treatment for HCC will transform clinical practice as more patients will be cured through embolization or have improved chances at survival to curative liver transplant. The proposed research is innovative because it utilizes a novel agent and delivery system that is synergistic with the hypoxic environment created by occluding the tumor blood flow. The woodchuck model is the closest analog to human HCC and an accurate model of embolization. This will allow for effective translation into a clinical trial.

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