

Title: Targeted Therapeutics for Gastric Cancer

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ABSTRACT

With rising mortality rates, the burden of gastric cancer in PR is becoming a public health priority. Yet, very few studies have been conducted to characterize this health disparity. Moreover, very few therapeutic options exist for gastric cancer, where the 5-year survival rate is less than 20%. Therefore, the GOAL of this proposal is to reduce the GAP IN KNOWLEDGE on biomarkers and therapies for gastric cancer by profiling gastric cancers from Puerto Ricans and testing new targeted therapeutics. The LONG TERM GOAL of our research is to increase the therapeutic options for gastric cancer, especially in Hispanic patients. The HYPOTHESIS is that targeting novel biomarkers: p21-activated kinase (PAK) and its regulatory non-coding RNAs (ncRNAs) is a rational strategy to cure gastric cancer. The RATIONALE stems from a large body of data identifying PAK isoforms as prognostic markers in gastric cancer, and the relevance of ncRNAs as key regulators of cancer. The Dharmawrdhane group at the UPR MSC is developing small molecule inhibitors targeting PAK signaling, and has characterized a number of experimental therapeutics, including our patented (US8884006B2) drug EHop-016 and its more efficient derivative EHop-167. Therefore, a major objective of this proposal is to test EHop-016 and EHop-167 as anti gastric cancer therapeutics. SPECIFIC AIM 1 will develop novel patient derived xenografts from Puerto Rican gastric cancer patients, collected through our collaborator Dr. Marcia Cruz at the UPRCCC, to characterize the gastric cancer tissues and test the efficacy of the new drugs. SPECIFIC AIM 2 will profile the ncRNA (both microRNAs and long ncRNAs) in gastric cancer tissues from Puerto Ricans and non-Hispanic whites to identify novel biomarkers associated with Puerto Rican gastric cancer. Aim 2 will be conducted at the UTMDACC by the co-leader Dr. George A Calin, an expert in ncRNA technology. Therefore, we expect to demonstrate the validity of targeting PAK and also identify unique ncRNAs dysregulated in Hispanic (Puerto Rican) gastric cancer. This study will lead to the development of targeted therapeutics: EHop-016 and derivatives that can be used independently, or in combination with ncRNA-based therapeutics.