Scientific Abstract

Gastric Interception Research Team:

"SU2C Gastric Cancer Interception Research Team: Early Detection and Interception ofDiffuse and Intestinal Gastric Cancer"

[This abstract was provided by the scientists when their application was accepted.]

[This abstract was provided by the scientists when their application was accepted.]
Background: Gastric cancer (GC) is the third-leading cause of cancer death worldwide. Current screening based on conventional endoscopy cannot reliably distinguish precancerous gastric lesions. Thus, developing novel early detection and interception strategies is a high unmet need.

Objective: To leverage the molecular events that underpin development of GC to develop novel tissue imaging and blood-based biomarkers for effective early detection and interception.

Rationale: We have successfully developed imaging probes targeting tumor-associated proteases, capsule imaging characterizing microscopic architecture, and circulating biomarkers for early detection of colorectal, esophageal, and pancreatic cancers in humans. In parallel, we have demonstrated the ability to apply this technology in our novel genetically engineered mouse models (GEMM) that faithfully recapitulate major TCGA GC subtypes. This provides a compelling rationale to translate these imaging and "liquid" biopsy approaches to the challenge of early detection and interception of GC.

Aims:
1) Discover and optimize molecularly specific imaging agents and novel circulating biomarkers for early stage GC using mouse models recapitulating the major TCGA GC subtypes.
2) Translate preclinical findings to humans by assessing the feasibility of molecular endoscopic or capsule imaging across the spectrum of gastric premalignancy and refine circulating biomarkers within cohorts of individuals undergoing routine GC screening and surgery for early-stage disease.
3) Demonstrate the feasibility of a molecular and/or capsule imaging platform for detection of GC and validate circulating tumor markers in locally advanced GC patients enrolled in a clinical trial.

Design: Blood and tissue from GEMM will be comprehensively profiled for circulating tumor DNA (ctDNA), circulating tumor cells (CTC), and the exosome landscape according to GC subtype and stage of lesion. Novel molecular imaging probes that target tumor-associated proteases resulting in release of a near-infrared fluorescent fluorophore as well as capsule-based optical coherence tomographic imaging will be performed at multiple time points during gastric tumorigenesis in mice and humans. Biomarkers identified in GEMM will be validated in humans using blood and tissue from diverse cohorts that encompass both environmental (Korea) and genetic (CDH1/hereditary diffuse GC) risk. The most promising imaging and blood-based biomarkers will then be validated in an already planned clinical trial of GC patients.

Clinical Impact/Significance: Our proposal will advance clinical practice through novel imaging and blood-based early detection tools that can be applied cost effectively (e.g., unsedated capsule imaging) for broad screening of populations at environmental risk (e.g., Korea) or in a targeted manner (e.g., molecular endoscopic imaging and liquid biopsy) for surveillance of well-defined populations at genetic risk (e.g., individuals with CDH1).