

## Scientific Abstract

## SU2C-Torrey Coast Foundation Gastroesophageal Cancer Research Team:

"Therapeutics for Gastroesophageal Adenocarcinoma: Application, Translation and Discovery"

Outside of anti-PD1/PDL1/HER2 therapies in selected patients there has been no improvement in outcomes in gastroesophageal carcinoma (GC). The landscape of cancer therapeutics includes three broad modalities: biologic/cellular therapies targeting surface antigens; molecular therapies directed at intracellular targets required for cancer cell growth and immunomodulators. This Research Team addresses the first two of these areas with the goal of discovering new targets and therapeutics in order to launch new clinical trials. The Team will tackle their goals via two aims:

Aim 1: Defining and targeting the cell surface of gastroesophageal carcinoma: The Team will systematically discover single and combination surface targets for biotherapeutics using proteomics and computational mining and, in parallel, generate novel Claudin 18.2 binders for a new CAR-T trial in GEA.

Aim 2: Functional genomic approaches to identify therapeutic targets in gastroesophageal carcinoma: Current functional genomic studies (e.g., CRISPR) are missing paralog drug targets such as CDK4/6. Using a dual CRISPR paralog library and new GEA patient-derived models, the Research Team will elucidate paralogous gene dependencies in GEA cancer.