Dissertation Defense - Kelly Arias Cardenas, PhD Biosciences

All are invited to attend the defense. For more information please contact Graduate Coordinator at

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Candidate: Kelly Arias Cardenas
Program: PhD, Biosciences

Date: Wednesday April 12th, 2022

Time: 2:00 PM

Meeting Location: https://gmu.zoom.us/j/96352358096?pwd=UVY5OG0vY3F1THdHcldIV2RIcVNnQT09

Title: Targeting CEACAM5/6 With a Novel Dual Specific Antibody-Drug Conjugate as a Therapeutic Strategy in Gastrointestinal Cancers

Committee Chair: Dr. Alessandra Luchini

~~**Committee Co-Chair:** Dr. Cohava Gelber~~

Committee Members: Dr. Lance Liotta, Dr. Mariaelena Pierobon

ABSTRACT:
Carcinoembryonic antigen cell adhesion molecule (CEACAM) family members 5 and 6 are tumor-associated antigens frequently upregulated in epithelial cancers, including pancreatic ductal adenocarcinoma (PDAC), where they contribute to invasion, metastasis, survival, resistance to chemotherapy, and immune escape. CT109 is a novel humanized antibody with dual specificity for both CEACAM5 and 6, mediated by binding to a shared glycoepitope. CT109 exhibits a high affinity to both CEACAMs. To further develop CT109, in vitro and in vivo characterization of antibody-drug conjugates (ADCs) was performed. CT109 bound to both cell surface and recombinant CEACAM5 and CEACAM6 on immunoblots. CT109 exhibited remarkable high tissue specificity in IHC and high expression prevalence in PDAC and colorectal cancer (CRC). CT109 was internalized in antigen-expressing, but not in non-expressing, PDAC cells with a half-maximal localization to low pH compartments after 2.3-9.6 hours. In vitro, the CT109-SN-38 and auristatin ADCs exhibited robust dose and antigen-dependent cell killing. In vivo, CT109-SN-38 mediated specific tumor-killing, resulting in reduced tumor growth rates and volumes (through day 50, $p = 0.02$) and reduced tumor burden below baseline in a subset of mice (3/10 mice in the high dose group).