Tomas Lama-Diaz, PhD
Columbia University Irving Medical Center

Abstract:
Cancer risk increases when cells accumulate DNA damage that exceeds their capacity for accurate repair. Under normal conditions, cells use specialized repair systems, commonly known as the DNA damage response, to detect and correct DNA lesions, thereby protecting the genome from harmful mutations. However, inherited or somatic mutations in key repair genes such as BRCA1 and BRCA2 compromise DNA repair and markedly increase the likelihood of developing breast, ovarian, prostate, and pancreatic cancers.

These same genetic defects also create unique vulnerabilities in cancer cells that can be therapeutically exploited. In 2005, researchers discovered that tumors lacking functional BRCA1 or BRCA2 become highly dependent on another DNA repair protein, PARP1. PARP inhibitors block this protein's activity, selectively killing BRCA-mutant cancer cells. These drugs are now widely used to treat BRCA-related cancers and have substantially improved outcomes for many patients.

Unfortunately, many cancers eventually develop resistance to PARP inhibitors, limiting how long these drugs remain effective. To address this challenge, the proposed research will combine large-scale genetic screens and cutting-edge gene-editing tools to (1) identify new BRCA-specific vulnerabilities targetable with additional drugs or in combination with PARP inhibitors, and (2) elucidate the genetic determinants and molecular mechanisms underlying sensitivity and resistance to PARP inhibitors. Through this approach, we aim to uncover new therapeutic candidates for breast cancer, support the design of more effective drug combinations, and characterize genetic variants associated with treatment response.

Bio:
Dr. Lama-Diaz received his undergraduate degree from the University of Santiago de Compostela in Spain. Afterward, he completed his master's and doctoral studies at the Center for Research in Molecular Medicine and Chronic Diseases (CIMUS) under the supervision of Dr. Miguel Gonzalez Blanco. He is currently a postdoctoral scientist at the Irving Cancer Research Center (ICRC), working in the Department of Genetics and Development at Columbia University Irving Medical Center. As a member of Dr. Ciccia's laboratory, he applies CRISPR-based functional genomics to investigate the molecular mechanisms underlying synthetic lethality and therapy resistance in BRCA1-deficient tumors.