

ACS FELLOW NAME, DEGREE (working toward or received):

Daniella Obidj, B.A. Biological Sciences, Chemistry Minor, University of Maryland, Baltimore County

Certificate in Cancer Studies, Case Western Reserve University, expected May 2026

NAME OF SPONSORING INSTITUTION: Case Western Reserve University

FELLOWS MENTOR(S):

Ruth Keri, PhD: Professor, Department of Molecular Medicine, Pharmacology, Genetics and Genome Sciences, and General Medical Sciences—Oncology, Case Western Reserve University
Associate Director for Basic Research, Case Comprehensive Cancer Center
Member, Molecular Oncology Program, Case Comprehensive Cancer Center

DESCRIPTION OF THE FELLOWS' RESEARCH PROJECT AND PROGRESS:

I have participated in 3 different projects while an ACS Post-Bacc Fellow. My first project involved developing TMU27a (TMU), a first-in-class non-nucleoside inhibitor of ribonucleotide reductase (RNR). RNR is a rate-limiting enzyme for nucleotide pool maintenance. Although RNR overexpression correlates with poor survival in many cancers, gemcitabine is the only FDA-approved RNR inhibitor for solid tumors. Its nucleoside structure causes off-target effects, dose-limiting toxicities, and rapid resistance. My lab hypothesized that TMU's non-nucleoside design would overcome these limitations, effectively targeting proliferative cancers. My specific contributions to this study involved the generation of gemcitabine-resistant cell lines, demonstrating that TMU treatment reduces nucleotide pools, induces DNA damage and chromosomal instability, stalls replication forks, inhibits proliferation, and promotes cell death in vitro.

My second project involved enhancing Triple Negative Breast Cancer (TNBC) sensitivity to mTOR inhibitors via NIMA-Related Kinase 2 (NEK2) inhibition. mTOR inhibitors show limited efficacy in TNBC compared to other breast cancer subtypes, creating an unmet need for sensitization strategies. TNBC cells are particularly vulnerable during mitosis, where mTOR promotes survival. NEK2, a mitotic kinase highly expressed in TNBC, was targeted to boost mTOR inhibitor effects. We hypothesized that NEK2 inhibition induces mTOR pathway dependency and anti-apoptotic gene reliance, such that combining NEK2 and mTOR inhibitors increases chromosomal instability (CIN), driving cell death—especially in cells with low basal anti-apoptotic expression. My work explored the heterogeneity in responsiveness to this combination in different cell lines, including assessing anti-apoptotic protein levels and inhibition effects, synergistic mechanisms, and mitotic cell fates.

Recently, I started working on a project focused on YES1, a Src family kinase critical for centrosome homeostasis, bipolar spindle formation, and genome stability in TNBC. YES1 correlates with therapeutic resistance and poor outcomes in TNBC, representing a vulnerability for inducing lethal chromosomal instability. Prior lab data showed enhanced YES1 inhibitor efficacy in immunocompetent versus immunodeficient mice, without increased immune cell recruitment. We hypothesize YES1 inhibition drives tumor death via: (1) elevated cytosolic dsDNA activating cGAS-STING, recruiting resident immune cells for phagocytosis; and (2) direct necroptosis from cGAS-STING activation. My work has confirmed cGAS-STING pathway activation upon YES1 inhibition. Before leaving this program, I will determine if YES1 overexpression limits immune responses during cGAS-STING activation, elucidate the activation mechanism, and work on confirming the roles of resident immune cells in conveying enhanced tumor death in immunocompetent models.

CAREER DEVELOPMENT ACTIVITIES (E.G., INDIVIDUALIZED COURSEWORK OR WORKSHOPS

ATTENDED): Completing an IDP helped me start thinking about the goals I wanted to accomplish during my time in this program. Working with Dr. Keri, the IDP has helped me to take ownership of my progress. Examples include advocating for attending different conferences to present my work, working on my networking and presentation skills, requesting shadowing experiences, and designing a path to improving my MCAT scores. I discuss research and career goals every two weeks with Dr. Keri.

Courses taken:

BIOC 453 Cancer Therapeutics Pathways
PHRM 525 Topics in Cell & Molecular Pharmacology
PHRM 526 Grant Writing Tutorial
IBMS 500 Being a Professional Scientist
PATH 520 Hallmarks of Cancer
IBMS 453 Cell Biology I
IBMS 455 Molecular Biology I

I participated in several activities that increased my awareness of cancer research and clinical care. I attended the Jackson Laboratory Annual Short Course on Experimental Models of Human Cancer in Bar Harbor, ME. I took the On Demand Kaplan MCAT Preparatory Course for approximately 3-4 months, which resulted in an increase in my MCAT score compared to previous attempts (from 74th to 87th percentile). I shadowed Dr. Vincent Wu, a surgical breast oncologist at the Cleveland Clinic. I was also able to meet with many program leaders, including Alex Huang (Director of the CWRU MSTP program), Tom McKenzie (Assistant Director of the CWRU School of Medicine Office of Admissions), Justin Lathia (Co-Leader of the Molecular Oncology Program at the Case Comprehensive Cancer Center), Marvin Nieman (Vice Provost and Dean for CWRU Graduate Studies), and several others. I also completed 8 mock interviews to prepare for my MSTP interviews. Lastly, I helped mentor several undergraduates in the Keri Lab and served as a mentor for the ACS Summer Internship Program.

PUBS/MANUSCRIPTS CO-AUTHORED: (See instructions for more information):

My work on the first two projects described above will result in co-authorship on two papers as I provided data and images for several figures in both. I will also be a co-author on a review focused on the mitotic kinase, NEK2, in cancer, one of the main targets of my second project. I am writing several sections as a contributor to this review.

Manuscripts in Preparation:

Taylor L. Brzozowski, Kristen Weber-Bonk, Mary Vincent, Daniella Obidi, Hailey Brady, Eric Mosher, Chris Dealwis, Anthony Berdis, Derek Taylor, and Ruth Keri. "A novel class of non-nucleoside RNR inhibitors induce excessive genomic instability and cancer cell death without signs of overt toxicities."

Mary Vincent, Kristen Weber-Bonk, Daniella Obidi, Ananya Jain, and Ruth A. Keri. "NIMA Related Kinase 2 is a collateral vulnerability for mTOR inhibitor efficacy in TNBC cells that have low basal anti-apoptotic tone."

CONFERENCE PRESENTATIONS: (See instructions for more information):

Obidi, D. A Novel Class of RNR Inhibitors Induces Genome Instability and Cell Death Without Inducing Overt Toxicities in Multiple Cancer Models (2025, August 26) [**Selected for oral presentation**]. Great Lakes Breast Cancer Symposium, Pittsburgh, PA, USA.

Obidi, D. A Novel Class of RNR Inhibitors Induces Genome Instability and Cell Death Without Inducing Overt Toxicities in Multiple Cancer Models (2025, September 24) [Poster presentation]. ACS CICRT Post-Baccalaureate Fellows Meeting, Atlanta, GA, USA.

Obidi, D. A Novel Class of RNR Inhibitors Induces Genome Instability and Cell Death Without Inducing Overt Toxicities in Multiple Cancer Models (2025, October 28) [Poster presentation]. Case CCC Annual Retreat, Cleveland, OH, USA.

Obidi, D. A Novel Class of RNR Inhibitors Induces Genome Instability and Cell Death Without Inducing Overt Toxicities in Multiple Cancer Models (2025, November 20) [Poster presentation]. ABRCMS, San Antonio, TX, USA.

HONORS, AWARDS, FELLOWSHIPS, AND ANY OTHER SUPPORT RECEIVED DURING THE PERIOD OF TRAINING: I was awarded funding for the JAX/ACS Cancer Course. I was also invited to give an oral presentation at the Great Lakes Breast Cancer Symposium 2025 on my first project. Lastly, I was invited to speak about the impact of cancer research and volunteering as part of the National Storytelling Project with RadicalMedia.