ORSP 2026 Student Research Fellowship Program Project Application

Project Description:

Title: Pediatric Cancer Research: Determining the Role of Cellular Metabolism in Therapeutic Resistance

Principle Investigator: Hope C. Ball, Ph.D.; Associate Research Scientist (Akron Children's Hospital); Assistant Professor Department of Biomedical Sciences (NEOMED)

Abstract: Cancer is the second leading cause of death in the pediatric population. While adult cancers arise from genetic instability caused by repeated carcinogenic exposure, most pediatric cancers are caused by mutations or dysregulations in pathways governing normal development. Pediatric mutations are unique and demonstrate significant differences from their adult same-cancer counterparts. Because of this, findings from adult malignancies cannot be directly translated into effective pediatric therapies. While improvements in diagnostic and treatment strategies have improved patient outcomes, a significant number of cases are still compromised by therapeutic resistance. Therapy development is hampered both by unique pediatric mutations and because the underlying mechanisms of therapy resistance remain poorly understood.

Significance: Improvements in care have improved overall survival rates for many common childhood cancers, but overall survival for patients with bone and CNS tumors have not changed significantly. One reason for this is that patients with recurrent and/or metastatic disease often have tumors resistant to standard-of-care chemotherapies. These realities underscore the critical need for research to better understand therapy resistant mechanisms towards the goal of identifying novel targets for therapy, prevent metastatic spread, and improve chemotherapeutic efficacy.

Goals/Objectives: The goals of my research laboratory are to determine the underlying mechanisms that contribute to chemotherapeutic resistance in several common pediatric solid tumors (medulloblastoma, neuroblastoma, and osteosarcoma). Cellular metabolism in one way in which cancer cells hijack host resources and escape immune detection. These pathways are of particular interest for the development of novel therapeutics, and my goals are to elucidate cancer-specific mechanisms and/or biomarkers to further these research avenues.

Methods/Data Analysis: My laboratory utilizes both *in vitro* and *in vivo* methods. Fellows can expect to learn cell culture, RNA/DNA/protein isolation, gene expression (qPCR), Western blot, pathway modulation (by RNAi, overexpression vectors, and/or pharmacology), proliferation/viability assays, and data analysis (ANOVA, t-tests, relative expression (delta-delta Ct)).

Fellow's Contributions to Research: The data collected will be vital to improving the scientific understanding of the mechanisms underlying chemotherapeutic resistance in pediatric solid cancers. The Fellow will work alongside the PI and the Senior Technician to learn all necessary laboratory techniques towards the goal of becoming proficient and independent in these tasks. The Fellow will be directly involved with data collection and analysis, and will be responsible for preparing and presenting a poster at the annual NEOMED Student Research Fellowship Symposium. Additionally, the Fellow will be included on all posters, presentations, and publications that result from the work conducted in the laboratory during the Fellowship.

Student Fellow Training and Mentoring Plan:

Training/Mentoring Plan: Mentoring is an important part of any internship program. The training the Fellow will receive in the laboratory will advance their understanding of basic/translational research study design (including methodology, implementation, and data analysis) and improve their ability to write/critically evaluate published peer reviewed research, an ability critical not only to this fellowship, but to their future profession as a physician. To foster these skills, the Fellow will attend and participate in weekly lab meetings and journal clubs and may be asked to contribute to manuscripts in preparation for publication in peer reviewed journals.

Resources: The Fellow will have access to the PI and Senior technician who are skilled in molecular techniques and have experience teaching these techniques. The Fellow will also have access to hospital research meetings, access to clinical journals, and scientific and data analysis software.

Location: Research will take place in the Akron Children's Hospital Hematology/Oncology Molecular Research Laboratory located on the second floor of the RGE building at NEOMED.