

Summer Research Fellowship Proposal for 2020

FACULTY INFORMATION:

NAME: Meenakshisundaram Balasubramaniam, Ph.D.

DEPARTMENT: Geriatrics, College of Medicine.

LOCATION: Reynolds institute on Aging, UAMS

PROJECT INFORMATION:

TITLE: Structure based targeted screen for novel drug discovery for treating glioblastoma

LOCATION OF THE PROJECT: 4th floor of Reynolds institute on Aging, UAMS

BRIEF DESCRIPTION OF THE PROJECT: Glioblastoma multiforme (GBM) is one of the most aggressive human brain tumors, and accounts for more than 50% of the astrocytic tumors (Ref). GBM is characterized by rapid progression and short survival; at present there are no known cures. Many genes and its mutations were identified to play a critical role in disease progression including Isocitrate Dehydrogenase 1 (IDH1), KRAS, and BRAF. Targeting these proteins specifically (target-based) by small molecule inhibitors would help delay disease progression and improve survival. Most of the chemotherapy drugs that are currently in use shows toxicity and adverse side effects in patients. These adverse side effects and toxicity are often due to off-target interactions of chemotherapy drugs. Target specific drugs would minimize off-target interactions and its subsequent toxicity. Using computational modeling and simulations, we constructed three-dimensional structures for IDH, KRAS, and BRAF along with their mutated form. Comparing the mutated structures of each candidate proteins with their wild-type counter-part predicted regions/site that are unique for mutated form. Targeting such unique region/site by small molecules would be target specific, not affecting wild-type counterpart, with high efficacy and selectivity for cancer cells. Based on high-throughput computational screening of virtual small molecule library of 735,000 compounds against candidate proteins mentioned above, we picked top 15 novel target-specific molecules for experimental validation. We expect student to screen top predicted molecules for its efficacy (inhibiting cell progression) in cell-based screen (glioblastoma cell models).

STUDENT'S RESPONSIBILITIES-DUTIES IN THE PROPOSED PROJECT:

Maintaining cell culture models, treating cells with lead molecules and screening for efficacy such as cell killing.

ESTIMATED TIME FOR PROJECT COMPLETION: 6 to 8 weeks

DOES THE WORK INVOLVE ANIMAL RESEARCH? YES -----
NO ---X----