

YOU ARE INVITED TO ATTEND THE
DEFENSE OF THE DOCTORAL
DISSERTATION

**“PTCH1 Overexpression Mitigates Glioblastoma Growth:
Potential Therapeutic Strategy”**

By

Vibha Harindra Savanur
Cell Biology, Neuroscience, and Physiology PhD Program

B.E., Visvesvaraya Technological University, Karnataka, India - 2013
M.S., University of Minnesota, Minneapolis - 2015

Thesis Advisor:
Pranela Rameshwar, Ph.D.
Department of Medicine

Tibor Rohacs, Ph.D.
Department of Pharmacology

Friday, May 3rd, 2024
1:00 P.M.
MSB, H609b

Join Zoom Presentation:
<https://rutgers.zoom.us/j/95822058774?pwd=czNPTTdoWk9wTWV3bm9MTDlyWkwxUT09>

Meeting ID: 958 2205 8774
Password: 111426

ABSTRACT

The overarching goal of this thesis is to identify new targets to improve the survival of patients with glioblastoma multiform (GBM). This grade IV glioma is the most common and aggressive cancer in the central nervous system. GBM is treated by surgical resection, radiation, and the frontline DNA alkylating agent, temozolomide (TMZ), which crosses the blood-brain barrier (BBB). To date, the median survival for GBM patients is about 14.5 months with 5% patients surviving up to 5 years. Sonic Hedgehog (SHH) signaling is increased in GBM due to decreased expression of PTCH1; consequently, increasing SMO and Gli1. MicroRNA9 (miR9) suppresses PTCH1 translation in GBM, resulting in chemoresistance. This thesis tested the hypothesis that ectopic PTCH1 could mitigate SHH activation to decrease SMO and Gli, and this would lead to TMZ sensitivity. Using a lentivirus, I expressed PTCH1 or empty vector control (EV) in U118 and T98G cells. These cells were used in functional studies and RNA-Seq. The results indicated that continued expression of PTCH1 was critical to the behavior of GBM. Specifically, there were enhanced cell proliferation, differentiation, and increased TMZ sensitivity. Interestingly, maintaining PTCH1 on GBM cells mitigated the effects of exogenous SHH that could be released from brain cells. This thesis developed a method to isolate GBM cell subsets, including stem cells by stably transfecting with SORE-6 GFP under the control of tandem repeats of OCT4a and SOX2 response elements. These latter studies will be able to determine how overexpressed PTCH1 could influence the stem cell subsets, since this population can resist most treatments and initiate tumor recurrence. Overall, this study supported future screens for small molecules to maintain PTCH1 in GBM to combine with available drugs.