

April 6, 2015

Final Studentship Progress Report for Summers 2013/2014 - Mr. Rajas Tipnis.

Lab of Dr. Sachin Katyal, University of Manitoba and Manitoba Institute of Cell Biology at CancerCare Manitoba

**Project Title: Inhibition of the DNA single strand break repair pathway in the treatment of malignant brain tumours.**

Over the past two summers, Rajas has had a very educational and productive research experience. In pursuing the research goals specified in his Brain Tumour Foundation of Canada Studentship, Rajas has exceeded expectations by developing expertise in performing advanced cell culturing techniques and DNA damage repair assays.

During this time, Rajas has made some key inroads in identifying ways to target pediatric medulloblastoma (MB) cells through modulation of DNA repair pathways. As most frontline cancer chemotherapeutics in some way target the cell's genome to induce cell death, there is a great deal of interest to harness the ability to modulate the tumour cell's DNA repair activity in order to improve therapeutic efficacy. Rajas has performed numerous cell based assays to track DNA damage repair activity in human MB cell lines. Using genetic techniques, Rajas inhibited the DNA single-strand break repair (SSBR) factors, XRCC1 and TDP1, in brain tumour cell lines and showed an increased susceptibility for these genetically modified lines to generate augmented DNA damage upon application of commonly used chemo/radiotherapy. He also found that co-inhibition of these genes acted to synergize the formation of these breaks. Furthermore, as recent data has showed that ATM also participates in DNA SSBR, he found that further inhibition of ATM with XRCC1 or TDP1, could elicit an even greater genotoxic response, thus leading to increase tumour cell death. Rajas then took this data another step forward and used combinations of well-known inhibitors of ATM and the DNA SSBR pathways and showed that this synergized genotoxicity could be achieved pharmacologically, a validation of his genetic data and representing a more feasible approach with promising applicability in the treatment of childhood medulloblastoma.

Rajas is a very keen scientist who wishes to continue this research in my lab. He has committed to returning to my lab in the summer of 2015, wherein he has secured competitive funding for his research activities. Furthermore, he will continue with this project through the 2015-2016 school year as an undergraduate honours research project student. He will further develop his study by examining the synergy involved in ATM and DNA SSBR and how these can be harnessed to augment anti-tumour therapeutic responses. It is his goal to better understand these repair factors and how inhibition of SSBR may lead to better tumour treatment paradigms.

I would like to take this opportunity to once again thank the Brain Tumour Foundation of Canada for their financial support of Rajas and the research project in my lab. Furthermore, I also would like to acknowledge the family of Taite Boomer, who helped make this Studentship stipend possible.

If you have any questions, please do not hesitate to contact me.

Best,

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