



**INDIAN INSTITUTE OF TECHNOLOGY DELHI
DEPARTMENT OF BIOCHEMICAL ENGINEERING &
BIOTECHNOLOGY**

2018-19 Seminar Series

Wednesday, 19th September, 2018



Dr. Reshu Gupta
Senior Research Scientist,
Entrinsic Health Solutions, USA

Title: Role of uPA/uPAR and cathepsin B shRNA and circulating anoctamin-1 RNA as anti-tumor agents and predictor of radiation induced gastrointestinal toxicity

Urokinase-type plasminogen activator system (uPA, uPAR) and cathepsin B regulates protease activity and gene expression within the cell. In cancer, these proteases are frequently over-expressed in comparison to normal tissues where their expression is limited. Cell-signaling initiated by these proteolytic cascades promotes cancer cell proliferation, migration, angiogenesis, invasion, metastasis, epithelial-mesenchymal transition, stem cell-like properties and therefore survival of cells. Their overexpression also allows cancer cells to “escape” from the cytotoxic effects of targeted anticancer drugs. Several earlier studies have revealed that these proteolytic networks play affirmative roles in various aspects of tumorigenesis; however, there are very few studies which show the pathways affected by their down regulation. Therefore, my investigation uses this approach to examine the therapeutic significance of RNAi mediated simultaneous down regulation of these proteolytic networks either alone or in combination with irradiation in malignant meningiomas and medulloblastomas. I investigated that inhibition of these proteases significantly reduced angiogenesis as compared to control treatment, inhibits TGF- β 1-driven invasion and survival of meningioma cells by downregulation of XIAP and pSMAD-2 expression, significantly induces Chk1-mediated G2/M cell-cycle arrest and permanent arrest G2/M phase and subsequent apoptosis both in vitro and in vivo. These studies present role of uPA/uPAR and cathepsin B shRNA as potential therapeutic agents for brain tumor treatment, where they can be used either alone or with radiation. I also discovered that circulating RNA specific for Ano1, a calcium-activated chloride channel, has great promise as a point-of-care biodosimeter following intentional or accidental radiation exposure and predictor of acute GI toxicity in prostate cancer patients. Similar to prostate cancer, the criteria to assess radiation toxicity in oral cancer is cytological assessment of the oral cavity, however, these methods are labor, expertise intensive, cost effective and require long preparation times. Therefore, there is an acute need for the identification of radiation-specific biomarkers that can serve both as a biodosimeter for radiation exposure and as a predictor of radiation-induced toxicity in oral cancer patients. Circulating lncRNAs may serve as a novel class of biomarkers for radiation exposure, alterations in long non-coding RNAs, have been reported in cells/tumors subjected to radiation exposure, implying that they play an important role in cellular stress response to radiation. While the use of lncRNAs as radiation biomarkers has been reported, the integrated use of lncRNAs to accurately determine radiation doses is novel and has not been published. Therefore, in my future proposal I would like to evaluate role of circulating long non-coding RNAs (lncRNAs) as a biodosimeter and indicator of radiation induced toxicity in oral cancer.

All are welcome

Seminar will be held in DBEB Seminar room at [Block I, Room 223](#) at **3:30 pm**

For additional information, contact Seminar coordinator Dr. Preeti Srivastava at preeti@dbeb.iitd.ac.in or Dr. D. Sundar at sundar@dbeb.iitd.ac.in