Department of Biological Sciences
Graduate seminar

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Date &Time: **January 30, 2018 at 4:00p.m** Venue: **L8, LHC**

Deciphering the role of SNARE proteins in breast cancer cell invasion.

The SNARE family proteins are one of the most intensively studied elements of protein machinery involved in intracellular trafficking.SNAREs found on the vesicle (v-SNARE) and target (t-SNARE) membranes form the "SNARE complex" to drive the docking and fusion of different cellular compartments[1]. It facilitates cellular trafficking of various cargoes like Matrix Metalloproteinases, Integrin, Transferrin, LDL, etc., for normal functioning of the cell. Amongst the members of the SNARE superfamily, identifying SNARE proteins which are involved in delivering cargoes for cancer cell invasion can lead to the development of novel therapeutics[2]. In this study, we have used siRNA based knockdown approach coupled with various assays such as Gelatin degradation assay, Matrigel invasion assay,and Invadopodia formation assay which led us to narrow down from 14 candidates, involved in endocytic and recycling pathway, to 4, namely STX2, STX7, VAMP3,and VAMP7. Our preliminary data suggest that STX7 resides in early endosome (EEA1) as well as in recycling compartments (Rab4 & Rab11). Because of its combined presence in early and recycling compartment, we hypothesized that STX7 may have a role in trafficking of certain cargoes towards the plasma membrane which will help in breast cancer cell invasion. Cargoes enroute to this pathway were tracked via Immunofluorescence. It is found that a significant population of Integrin, MT2MMP, EGF and Transferrin are co-localizing with STX7. We could see STX7 co-localizing with invadopodial marker, cortactin. In separate set of experiments we have seen STX7 near the degradation spot. However, to find specific STX7-cargoes responsible for cell invasion, comparative proteomics will be carried out with enriched surface proteomes from wild type and STX7 depleted cells. Interacting partners of STX7 that facilitates the final step of fusion will be identified via Immunoprecipitation followed by Mass spectrometry.

References:

[1] Jahn R, Scheller RH(2006). SNAREs-engines for membrane fusion ,Nat Rev Mol Cell Biol. Sep;7(9):631-43.

[2] Meng J, Wang J(2015).Role of SNARE proteins in tumourigenesis and their potential as targets for novel anti-cancer therapeutics.Biochim Biophys Acta. Aug;1856(1):1-12.