



## **L4H Seminar VIVEK MALHOTRA 'Remodelling Secretory Compartments to Generate Transport Carriers for Collagen Export'**

VIVEK MALHOTRA  
Intracellular Compartmentation group  
Centre for

November 19, 2014

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Wednesday, November 19, 2014, 12:00. Seminar Room

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COPII vesicles are known to export secretory cargoes from the endoplasmic reticulum (ER) in eukaryotic cells. However, the most abundant secretory cargo, i.e., the collagens, is too big

to fit into the generic COPII vesicles of 60-90 nm in average diameter. Do cells employ a different class of carriers to export collagens or specific mechanism that uses the same COPII machinery to regulate the size of the COPII carriers commensurate with the size of the cargo? We identified a protein, TANGO1, which is anchored at the ER exit site, and required for the export of collagen VII.

Hyper secretion of collagen VII results in the development of cylindromas ( large tissues that grow on the face and head of patients), and defects in secretion of collagen VII is associated with epidermolysis bullosa, a debilitating skin disorder for which there is no therapy.

The SH3 like domain of TANGO1 binds collagen VII in the lumen of the ER. TANGO1 binds COPII subunits Sec23/Sec24 via the proline rich domain (PRD) in the cytoplasmic face of the ER. TANGO1 thus connects collagen VII with the COPII machinery. Another protein called cTAGE5 binds TANGO1 and recruits Sec12 to ER exit sites. This reaction thus brings more Sec23/Sec24 that engage additional TANGO1-cTAGE5-cargo complexes. These interactions concentrate Procollagen VII at ER exit sites. Membrane fusion proteins SLY1 and ER localized Syntaxin 18 are then engaged at this site for fusion of membranes from a downstream compartment such as ERGIC or Golgi. As a result, the Procollagen VII enriched ER patch grows into a large bud. TANGO1-cTAGE5-Sec12-Sec23/Sec24 remain at the neck of the growing bud. Upon loading a given amount of Procollagen VII, TANGO1 separates from Procollagen VII and from Sec23/Sec24, which promotes recruitment of Sec13/Sec31 that triggers fission of a mega Procollagen VII containing transport carrier from the ER. Imaging these membrane domains is one the key issues for us and I will discuss our hypothesis and current findings on the mechanism of TANGO1 dependent regulated export of collagen VII.

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**Hosted by Prof. Maria Garcia-Parajo**