

Understanding determinants of protein trafficking : A new perspective on COPII vesicular transport

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Abstract

The early secretory pathway is highly conserved among all the metazoans and is considered crucial for several cellular processes including development and function of the immune, neuronal, endocrine and skeletal systems. This pathway is tightly regulated and contributes to the trafficking of a considerable fraction of the whole proteome in and around the urbane environment of a cell. It involves designated export machinery, consisting of COPII coat proteins involved in sorting of the cargoes in membrane bound vesicles emanating from the endoplasmic reticulum (ER). The flexibility of the coat machinery to accommodate diverse size and shaped cargoes in order to meet the sophisticated demands of the cell is long-debated and is still under consideration. Some post-translational modifications or protein-protein interactions of the coat proteins are speculated to contribute to the coat conformational changes resulting in different size transport vesicles, but the mechanism involved in lugging large cargo, e.g. collagen remains to be determined. The flux of collagen export and transport from the ER can also be tuned in response to environmental changes and cellular requirements. There are numerous human skeletal and connective tissue disorders associated with the defects in the early secretory pathway which involve aberrations in COPII protein subunits or accessory proteins, which in turn perturbs the ability of collagen to sort correctly in trafficking machinery. Some of the pathological conditions associated with these diseases results from collagen deposition defect. My seminar and proposed work here would provide framework to advance our basic understanding of the early secretory pathway involved in collagen transport and its emerging connection with human skeletal diseases.