Molecular Mechanisms of Intracellular Transport: From Biology…to Physics

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ABSTRACT: Vesicular traffic links the different intracellular compartments of eukaryotic cells and allows for the exchange of macromolecules. A large number of proteins that function directly or indirectly in vesicular traffic, estimated to represent about 10-20% of the human "proteome", have been identified. Among them, small GTPases of the Rab family play a key regulatory role. We will illustrate this role for three Rab GTPases (Rab1, Rab6 and Rab11) associated with compartments of the biosynthetic/secretory pathway.

The complexity of intracellular transport makes useful the development of model membranes. We describe here experimental systems based on lipid giant unilamellar vesicles (GUVs), which are attached to kinesin molecules. These systems give rise to thin membrane tubes and to complex tubular networks when incubated *in vitro* with microtubules and ATP. This assay was used to investigate lipid sorting during tube formation. The GUVs have been made of various compositions of DOPC/cholesterol/sphingomyelin. As shown, the lipids can be dynamically sorted into growing tubes, and a coupling based on phase separation exists between lipid sorting and the fission of tubes into small vesicles. This assay was recently used to reconstitute the binding of COPI coats (involved *in vivo* in transport between Golgi and the endoplasmic reticulum). The presentation will illustrate the role of proteins whose activity is sensitive to membrane curvature and the importance of membrane tension in tube formation.

KEYWORDS: Vesicular transport, membrane curvature & tension, unilamellar vesicles, membrane tubes, Rab GTPases

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