Making a raft with oligomers

Epithelial cells differentially segregate proteins to their apical and basolateral surfaces. For some apical localization events, association of glycosylphosphatidylinositol (GPI)-anchored proteins with detergent-resistant rafts is necessary but not sufficient. Now, on page 699, Paladino et al. show that the key for proper protein sorting may be the formation of high molecular weight aggregates of apically targeted GPI-anchored proteins as they segregate into rafts in the Golgi.

The researchers separated rafts on sucrose gradients. The rafts containing apical proteins, like PLAP and GFP-GPI, had a high concentration of protein when compared with rafts with basolaterally targeted proteins. Mutations of GFP-GPI that impaired formation of high molecular weight complexes caused mis-targeting of the protein to the basolateral surface. Using pulse-chase experiments, the researchers found that oligomerization occurred as the protein-laden rafts made their way through the trans-Golgi network.

The team hypothesizes that oligomerization of the apically targeted proteins in the Golgi helps them to form large rafts that then pinch off on their way to the apical surface. The new hypothesis contradicts work by Polishchuk et al. (Nat. Cell Bio. 2004. 6:297–307). In their paper, Polishchuk et al. proposed that apical and basolateral proteins exit the trans-Golgi network together in vesicles targeted to the basolateral membrane, and that the apical proteins are subsequently resorted and transcytosed to the apical membrane. Paladino et al. didn’t see any trafficking of apical proteins to the basolateral surface and suggest that the difference in the results might result from differing culture conditions.

If oligomerization is driving apical segregation, the question remains as to what induces oligomerization. Paladino et al. are currently testing one possibility: that glycosylation or other protein modifications are used to gather together the protein.