

EHBP1L1 coordinates Rab8 and Bin1 to regulate apical-directed transport in polarized epithelial cells

The highly conserved Rab guanosine triphosphatase (GTPase) Rab8 plays a role in exocytosis toward the polarized plasma membrane in eukaryotic cells. In murine Rab8-deficient small intestine cells, apical proteins are missorted into lysosomes. In this study, we identified a novel Rab8-interacting protein complex containing an EH domain-binding protein 1-like 1 (EHBP1L1), Bin1/amphiphysin II, and dynamin. Biochemical analyses showed that EHBP1L1 directly bound to GTP-loaded Rab8 and Bin1. The spatial dependency of these complexes at the endocytic recycling compartment (ERC) was demonstrated through overexpression and knockdown experiments. EHBP1L1- or Bin1-depleted or dynamin-inhibited small intestine organoids significantly accumulated apical membrane proteins but not basolateral membrane proteins in lysosomes. Furthermore, in EHBP1L1-deficient mice, small intestine cells displayed truncated and sparse microvilli, suggesting that EHBP1L1 maintains the apical plasma membrane by regulating apical transport. In summary, our data demonstrate that EHBP1L1 links Rab8 and the Bin1-dynamin complex, which generates membrane curvature and excises the vesicle at the ERC for apical transport.

