Epsin 1 is involved in recruitment of ubiquitinated EGF receptors into clathrin-coated pits

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Epsin consists of an epsin NH2-terminal homology (ENTH) domain that promotes interaction with phospholipids, several AP-2 binding sites, two clathrin binding sequences and several Eps15 homology domain binding motifs. Epsin additionally possesses ubiquitin-interacting motifs (UIMs) and has been demonstrated to bind ubiquitinated cargo. We therefore investigated whether epsin promoted clathrin-mediated endocytosis of the ubiquitinated EGF receptor (EGFR). By immunoprecipitation, we found that epsin 1 interacted with ubiquitinated EGFR and that functional UIMs were essential for complex formation. Furthermore, RNAi-mediated knock down of epsin 1 was found to inhibit internalization of the EGFR, while having no effect on endocytosis of the transferrin receptor. Additionally, upon knock down of epsin 1, translocation of the EGFR to central parts of clathrin-coated pits was inhibited. This supports the contention that epsin 1 promotes endocytosis of the ubiquitinated EGFR.