# Assembly of ESCRT machinery on membranes and disassembly by Vps4 AAA-ATPase

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ESCRT complexes (endosomal sorting complexes required for transport) promote efficient sorting of ubiquitinated transmembrane proteins to lysosomes *via* multivesicular bodies (MVBs) [1]. In addition to their role in endosomal protein sorting, ESCRTs also function in cytokinesis and viral maturation and budding [2]. Many enveloped viruses use short peptide motifs present within their L-domains (late assembly domains) to recruit components of the host ESCRT machinery and use them in a Vps4-dependent fashion to facilitate viral budding.

Our goal is to understand the mechanisms of the assembly and disassembly of the host endosomal sorting machinery. We have combined X-ray crystallography, electron microscopy and protein engineering to determine the architecture of the multicomponent ESCRT complexes and the links that join one ESCRT complex to another. We have also uncovered the structural basis for the essential link between the ESCRT machinery and the Vps4 AAA-ATPase which plays a critical role in the final steps of ESCRT function. ESCRTs are cytosolic proteins that are only transiently recruited to their targets. While the targeting to the sites of viral budding is mediated by the viral PTAP- and YPXnL-peptide motifs, ESCRT targeting to endosomal membranes is mediated by a network of interactions with phosphoinositides [3] and ubiquitinated membrane proteins. An emergent property of the assembly of yeast ESCRT-I/II supercomplexes on membranes is the ability to dramatically deform membrane morphology. *In vitro,* subunits of ESCRT-III complexes can self-assemble into filaments and large sheets. We have designed chimeric ESCRT-III subunits that readily form filaments that can be disassembled by the ATPase activity. The disassembly of ESCRT-III lattices by the Vps4 ATPase may be a driving force in membrane fission, which is a step common to MVB formation, viral budding and cell abscission [4,5].

**References**

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