Mechanisms of exosome biogenesis and protein budding
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The prevailing paradigm of exosome biogenesis posits that exosomal proteins and lipids bud at endosome membranes, generating vesicle-laden endosomes that release their internal vesicles upon fusion with the plasma membrane. However, vesicles and proteins also bud from the plasma membrane, making it unclear whether cells possess two separate mechanisms of vesicle and protein budding, or a common mechanism that occurs at two sites. Using a variety of experimental systems and techniques, we explored the relative contribution of the endosome and plasma membranes to vesicle secretion and protein budding. Our results fail to support the endosome-centric model of exosome biogenesis, point to the plasma membrane as the primary site for vesicle secretion and protein budding, and provide additional support for the hypothesis that retrovirus budding is mediated by a normal, non-viral processes of vesicle secretion.