**Figure S1** A cartoon showing the domain organisation of full-length myosin VI and a schematic and sequence alignment of C-terminal region of the tail. (a) The cartoon depicts the domain organisation of myosin VI highlighting the globular C-terminal tail with the relative positions of the splice inserts (LI: large insert, SI: small insert), the binding sites for Dab2 and GIPC/optineurin (positions 1184aa (W) and 1107-1109aa (RRL) respectively) and the PIP2 binding site. Black arrowheads (1 and 2) indicate the tryptic cleavage sites and black lines show the positions of domains 1 and 2. The amino acid (aa) numbering refers to the chicken sequence. (b) An alignment of the human (H), chicken (C) and mouse (M) myosin VI C-terminal tail sequences (aa 1017 – end) using ClustalW from [www.ch.EMBnet.org](http://www.ch.EMBnet.org). The large and small inserts (LI and SI) and the RRL, WWY, and lipid (KSKNKPR) binding sites are shown in bold along with the phosphorylatable TINT sequence. Arrowheads 1 and 2 mark the trypsin cleavage sites. Predicted secondary structure for the chicken myosin sequence obtained by a consensus of 8 prediction algorithms is shown: “c” is random coil, “e” is extended sheet, “h” is α helix and a blank space indicates no consensus.
Figure S2 Possible roles for myosin VI in the early stages of clathrin mediated endocytosis. We speculate that at (1) Dab2 is bound via its N-terminal phosphotyrosine (PTB) motif to the cytoplasmic tail of a LDL receptor and is bound to PIP_2 (P) in the plasma membrane. Myosin VI (MD denotes its motor domain and 1 and 2 the domains in the C-terminal tail) is recruited to the plasma membrane by binding to Dab2 and also to PIP_2 (P). Possibly by interacting with newly polymerised actin filaments (initiated by the WASP/Scar/PIP_2 and Arp2/3 complexes), myosin VI could cluster the receptors and then generate sufficient force to pull the membrane inwards to form a nascent clathrin coated pit at (2). The clustering of myosin VI in such a ‘pit’ might favour dimerisation or multimerisation (possible CT tail interactions indicated by double headed arrow) and the resulting myosin VI dimers (multimers) together with the endocytic machinery (AP-2, clathrin and accessory proteins) and the actin filament network could be involved in the formation of clathrin coated vesicles, their uncoating and then subsequent delivery into the cell. At this stage it should be stressed that multiple myosin VI monomers might also be able to accomplish the same tasks. A recent relevant review by Lois Weisman explores possible molecular mechanisms for membrane-cargo transport by myosin V.

Supplementary references