

P018 Vps4 in receptor trafficking, receptor signalling and cell-cell communication

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Many types of cancer are associated with up-regulated signalling from growth factor receptors. To maintain a normal level of cell divisions down-regulation of these receptors is important. The receptors are down-regulated by endocytosis, followed by sorting into the lumen of the multivesicular bodies (MVBs) and degradation in the lysosomes. The signalling is turned off by sorting the receptors into the lumen of MVBs. Studies in the yeast *Saccharomyces cerevisiae* have shown that the AAA-type ATPase Vacuolar protein sorting 4 (Vps4) is required for efficient transport of biosynthetic and endocytic cargo from MVBs to the lysosome-like vacuoles. Vps4 is conserved throughout evolution and exists in humans (*Homo sapiens*), yeast and fruit fly (*Drosophila melanogaster*) among other species. We are interested in the role of Vps4 in receptor trafficking, receptor signalling and cell-cell communication in *Drosophila melanogaster*. By creating a fly line expressing a dominant negative form of Vps4, locked in the ATP-state, we can study the “loss of function” effect in clones of cells in various tissues. Preliminary results from such analyses show that ubiquitinated cargo and Hrs accumulate in large endocytic structures. This indicates that Vps4 is required for normal receptor sorting.