The molecular mechanism of the BMP feedback regulator pentagone

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BMP signalling is required in all organisms for the control of tissue growth and morphogenesis. We focus on the regulation and function of BMP signalling in the wing precursor of the model organism *Drosophila melanogaster*. The lab has previously identified and characterised Pentagone (Pent), a secreted feedback regulator of BMP signalling in Drosophila. Transcription of *pentagone* is repressed by BMP signalling, and Pentagone in turn promotes spreading of the BMP ligand Decapentaplegic through the wing precursor. Wing precursors that are *pent* mutant have defects in growth and patterning which are due to deficiencies in BMP signalling. In addition to BMP patterning defects, *pent* mutant wings also have phenotypes that appear to be due to a reduction in Wingless signalling, a Drosophila Wnt protein. This leads us to hypothesise that Pent exerts its function through factors that are common to both the BMP and Wnt pathways in the wing precursor. Chief among these are two glycophosphatidylinositol anchored heparan sulphate proteins (glypicans), Dally and Dally like (Dlp). Pent genetically interacts with Dlp, antagonizing phenotypes caused by over-expression of Dlp. Pent physically interacts with both Dally and Dally like, and when in high levels causes endocytosis and degradation of Dally and Dlp. This internalisation of Dally requires Rab5, but seems to be independent of clathrin. Similarly, internalisation of endogenous Pent also requires Rab5 but not clathrin. These data lead us to hypothesise that Pent regulates the membrane localisation of glypicans, and we are not planning experiments to directly test this hypothesis.