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Bearded family members inhibit Neuralized-mediated endocytosis and signaling activity of Delta in Drosophila.

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Résumé

Endocytosis of Notch receptor ligands in signaling cells is essential for Notch receptor activation. In *Drosophila*, the E3 ubiquitin ligase Neuralized (Neur) promotes the endocytosis and signaling activity of the ligand Delta (DI). In this study, we identify proteins of the Bearded (Brd) family as interactors of Neur. We show that Tom, a prototypic Brd family member, inhibits Neur-dependent Notch signaling. Overexpression of Tom inhibits the endocytosis of DI and interferes with the interaction of DI with Neur. Deletion of the Brd gene complex results in ectopic endocytosis of DI in dorsal cells of stage 5 embryos. This defect in DI trafficking is associated with ectopic expression of the single-minded gene, a direct Notch target gene that specifies the mesectoderm. We propose that inhibition of Neur by Brd proteins is important for precise spatial regulation of DI signaling.