CDB SEMINAR

Speaker: Martin Baron

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http://www.wtccmr.man.ac.uk/gl/mb-ri.html

Title: " Regulation of the Notch receptor by Suppressor of deltex "

Date: Tuesday, February 24

Time: 16:00 P.M.～17:00 P.M.

*This seminar will start immediately after the previous one by Dr.Matsuno

Place: 7th floor Conference Room of Building A, CDB

Summary

The Notch receptor regulates many cell fate decisions in diverse organisms from nematodes to mammals. Notch signalling is initiated by ligand-dependent cleavages that result in the release of the soluble intracellular domain of Notch. The latter translocates to the nucleus and activates the transcription factor Suppressor of Hairless. Signalling by Notch is normally kept under tight regulatory control. Sorting of membrane bound receptors within the endosomal pathway is linked to regulation of signal activation in a number of signalling pathways. The relationship between Notch receptor trafficking and signal regulation is however poorly understood. Suppressor of deltex is a *Drosophila* Nedd4 family E3 ubiquitin ligase protein, which localises at the cell surface and negatively regulates the Notch signalling pathway. We show *in vivo* that Su(dx) can limit signalling induced by Notch and that Su(dx) function is partially overlapping with that of the related DNedd4 protein. We show that Su(dx) interacts with Notch at the cell surface and directs its subsequent trafficking within the early and late endosomes. We further show that Notch endocytosis is associated with both down-regulation and signal activation. These alternative signalling outcomes are correlated with differential Notch localisation within specific endosomal domains. We propose that Su(dx) interacts transiently with Notch at the apical adherens junction and predetermines the availability of Notch for signalling, by regulating its subsequent trafficking destinations. Intersections between trafficking routes may provide key points at which other signals can modulate Notch activity.

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