Specificity of cell signalling: the case of Notch.

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There is a fundamental question at the field of cell signalling: how can the activation of the same pathway in different tissues or under different physiological conditions lead to so many different responses? We are investigating this question from the perspective of Notch signalling. Utilising an assay to precisely control the triggering of the Notch pathway, we have combined the data from mRNA expression profiling and ChIP-chip analysis against \textit{Suppressor of hairless} from three different \textit{Drosophila} cell lines and wing disc tissues to uncover the primary Notch target genes in different cellular contexts. Additionally, we have assayed chromatin dynamics and cooperating transcription factor recruitment that contribute to the specificity of Notch target gene selection. We describe Twist as the specificity factor in muscle precursor cells. Cooperation with other signalling pathways adds another layer of complexity to the Notch regulome and we use the interactions between the Notch and EGFR pathways to illustrate this point. We also describe the identification of feed-forward regulatory loops as a common theme amongst Notch target genes that act to modulate the onset and duration of the Notch signal. Currently we are investigating how the metabolic status of a cell can influence Notch target gene selection and conversely how Notch signalling regulates cellular metabolism, thus creating a regulatory cycle that governs Notch signaling under both physiological and pathological conditions.