Integration of signalling pathways in epithelial patterning

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Control of cell differentiation during development is accomplished by signalling pathways that establish spatial patterns of gene expression in tissues. How genes in the nuclei of signal-receiving cells differentially interpret such signals and how they integrate multiple inductive signals is still an open question. Our recent studies of BMP morphogen signaling in Drosophila revealed a simple logic in gene regulation by this pathway. By analysing two direct target genes of the pathway that are differentially regulated upon signalling (i.e. repressed versus activated), we identified two DNA motifs implementing these opposing functions. The two motifs are very similar to each other as they both contain binding sites for Smad proteins, the signal mediators of the pathway. Nevertheless, the motifs differ at specific nucleotide positions that affect co-factor recruitment and ultimately transcriptional outcome.
Using tools and knowledge derived from these studies, we now seek to understand how BMP signaling interacts with other signaling pathways during cell fate allocation processes. We will present recent findings from our studies on signal integration during epithelial patterning in Drosophila oogenesis. By identifying and analyzing *cis-regulatory modules* (*CRMs*) of *broad* (*br*), a key patterning gene co-regulated by BMP and EGF signaling, we establish that the spatiotemporal dynamics of *br* expression do not solely depend on dynamic changes in inductive signals but also on the dynamic utilization of different *CRMs*. We suggest that such multi-*CRM* regulation of gene expression dynamics is a common feature of patterning networks.