A "blimp" of time

By Xiaowei Zhuang group

http://dx.doi.org/10.1101/273151

The development of a multicellular organism requires an extremely accurate spatiotemporal regulation of gene expression (Wilczynski *et al*., 2012). In order to understand the whole process, many of the transcription factors required for the development of organs have already been identified and their expression pinpointed spatially. However, the mechanisms through which they coordinate downstream gene expression in time remain poorly understood.

The tracheal tube maturation of *Drosophila melanogaster*, which is a model commonly used to study epithelial organ development, involves the timely and spatially regulated deposition of a chitinous apical extracellular matrix. One of the main genes involved in the process is the gene B-Lymphocyte Inducing Maturation Protein-1 (Blimp-1), a downstream effector of the mid-embryonic ecdysone hormone pulse (Ng *et al*., 2006). Blimp-1, which has a homologous in humans called Prdm1 (Huang, 1994), is a transcriptional repressor that exerts a function in tracheal system morphogenesis during embryonic development. The big question is how does this transcription factor regulate the downstream tube maturation events over time.

In an attempt to address part of this question, Öztürk-Çolak and colleagues started by tracing the Blimp-1 expression during embryogenesis, having detected the protein throughout the several stages of tube maturation. Deleting Blimp-1 in embryos leads to inflated tubes, altered cell morphology and early chitin deposition, when compared with wild-type embryos (see **Figure 1**). Using an opposite approach, they increased the Blimp-1 expression in one end of the larvae and found that this increase led to a delay in the chitin deposition. Taken together, these results suggest a central role for Blimp-1 in dictating the timing of chitin deposition in the dorsal trunk.

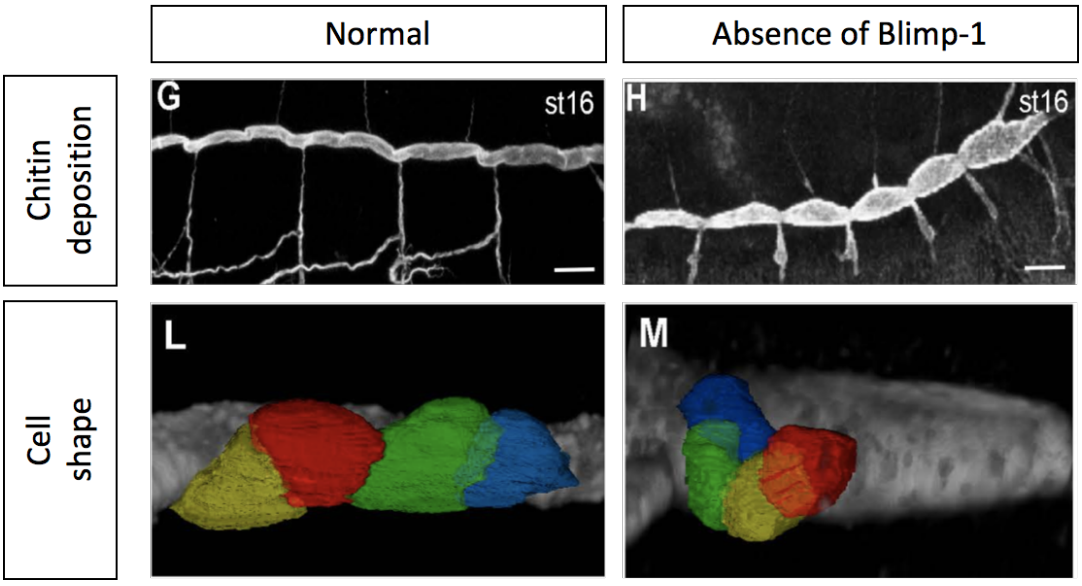

Figure 1 - Deletion of Blimp-1 affects chitin deposition and cell shape in embryo cells.

In order to understand the involvement of Blimp-1 in the regulation of its downstream targets, the authors analysed the levels of several key proteins for tube maturation. Obtained data suggest that Blimp-1 directly regulates the levels of these proteins in tracheal cells during tube maturation, acting as a transcriptional repressor in the correct timing of the expression of the respective genes. More particularly, they show evidence for the presence of a new player in this cascade of events: they observed Blimp-1 to be repressing the kinase Btk29A. This repression disappears at later embryonic stages, enabling the signalling to regulate the cytoskeleton inside the cell.

Overall, these results show Blimp-1 as an hormone-responsive element, modulating chitin deposition during the temporal regulation of tubulogenesis. Shedding light on these processes may be helpful to understand the underlying physiology/pathology in clinically relevant tubular-deficiency diseases and unravel how cells assemble in well organized and complex organs with three dimensional tubular architecture.

References:

Huang S. 1994. Blimp-1 is the murine homolog of the human transcriptional repressor PRDI-BF1. Cell. 15;78(1):9.

Ng T, Yu F, Roy S. 2006. A homologue of the vertebrate SET domain and zinc finger protein Blimp-1 regulates terminal differentiation of the tracheal system in the Drosophila embryo. Dev Genes Evol. 216(5):243-52.

Wilczynski B, Liu YH, Yeo ZX, Furlong EE. 2012. Predicting spatial and temporal gene expression using an integrative model of transcription factor occupancy and chromatin state. PLoS Comput Biol. 8(12):e1002798.