Muscles from Ectoderm: Possible Cases of *in vivo* Reprogramming

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Differentiated cells can be transformed into different cell types by a process termed cell-fate reprogramming. For example, the forced expression of transcription factors can directly change fibroblasts into neurons or into induced pluripotent stem cells. However, very little is known about the natural mechanisms of reprogramming during animal development. During *C. elegans* development, the founder cell AB gives rise to predominantly ectodermal cells. However, a few cells break this lineage pattern. For example, the left intestinal muscle cell, the anal depressor muscle cell, the sphincter muscle cell, and the body wall muscle ABprpppppaa are derived from AB. We hypothesize that these changes in lineage are caused by *in vivo* reprogramming events. To test this hypothesis, we are using genetic screens to identify the machinery that controls the development of these ectoderm-derived muscle cells, determining the mechanisms by which these cell fates are established, and profiling the epigenetic changes that occur during these cell-fate decisions.

The *C. elegans* homolog of Twist, CeTwist (encoded by *hlh-8*), is required for the development of the intestinal muscles and the anal depressor cell (Corsi *et al*., Development, 2000). Twist is a basic helix-loop-helix transcription factor that is required for the epithelial-mesenchymal transition (EMT), which is a natural transformation in cell lineage important for animal development. Thus, the development of the intestinal muscle cells and the anal depressor cell bear similarity to EMT in both their striking change in lineage and in their genetic requirements. Identifying the machinery that controls the development of ectoderm-derived muscle cells might reveal new factors that can reprogram cell fate as well as factors involved in EMT.

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