Cytoplasmic NOTCH and membranal β-catenin link cell fate choice to EMT during myogenesis.

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How cells in the embryo coordinate epithelial plasticity with cell fate decision in a fast changing cellular environment is largely unknown. In chick embryos, skeletal muscle formation is initiated by migrating neural crest cells that, in passing, trigger myogenesis in selected epithelial somite progenitor cells, which rapidly translocate into the nascent muscle to differentiate. Here, we uncovered at the heart of this response a signalling module encompassing NOTCH, GSK-3β, SNAIL1 and WNT. This module transduces the activation of NOTCH from neural crest cells into i) an inhibition of GSK-3β activity by non-transcriptional NOTCH signalling; ii) a SNAIL1-induced epithelial to mesenchymal transition (EMT) leading to iii) the recruitment of membranal β-catenin to trigger WNT/β-catenin signalling and myogenesis independently of WNT ligand. Our results intimately associate the initiation of myogenesis to a change in cell adhesion and may reveal a general principle for coupling cell fate changes to EMT in many developmental and pathological processes.

Distinct stem cell populations establish skeletal muscles during development: insights into disease

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Skeletal muscles are heterogeneous in design and function. Some of these differences are rooted in their origins: cranial vs. somitic derived. The gene regulatory network in distinct anatomical locations provides some insight into this modular design. For example, extraocular muscles are Tbx1-independent, whereas cardiopharyngeal mesoderm skeletal muscles (ex. facial, esophagus and laryngeal muscles) are Tbx-1 dependent. The esophagus links the oral cavity to the stomach and facilitates the transfer of bolus through striated and smooth muscle contractions. Using multiple genetic tracing and mouse mutants, we demonstrate that esophagus striated muscles (ESM) are not derived from somites as generally thought, but are of cranial origin. We identify Tbx1 and Islet1 as key regulators thereby demonstrating that ESM is a third derivative of cardiopharyngeal mesoderm, in addition to heart and head muscles. Several unique features of the ESM including temporal specification points to this muscle as unique in developmental origins and function. Notably, ESM are absent in chick, and Islet1 appears to be a critical determinant distinguishing the mammalian and avian programs. These findings have important implications for understanding the etiology of esophageal dysfunctions including dysphagia manifested in congenital disorders such as DiGeorge syndrome and they underscore the importance of investigating the multilineage potential of cardiopharyngeal mesoderm. In addition, they provide important insights into interpreting clinical manifestations of diseases that affect only a subset of muscles.

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Abstract missing