Cell Fate Determining Molecular Switches and Signaling Pathway in Pax7-expressing Somitic Mesoderm

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Pax7-expressing progenitor cells in the somitic mesoderm differentiate into multiple lineages, such as brown adipose tissue, dorsal dermis, as well as muscle in the dorsal trunk and the diaphragm [1]; however, the key molecular switches that determine and control the process of lineage commitment and cell fate are unknown. Lineage tracing studies have already shown that while $Pax7^+$ cells marked at embryonic day 9.5 (E9.5) can develop into brown adipose, dermis, and muscle, the $Pax7^+$ cells at later developmental time points have limited lineage potency to brown fat and muscle (at E10.5), then to muscle only (at E12.5). The regulatory mechanism of this lineage restriction is not fully understood. To probe the mechanisms behind mesoderm development, $Pax7^{CE}/ROSA26^{YFP}$ embryos were tamoxifen-induced at E9.5 to label $Pax7^+$ cells for lineage tracing and harvested at later time points for analysis. The YFP-labelled cells which belonged to the Pax7 lineage were enriched by fluorescence-activated cell sorting (FACS) and subject to single-cell RNA profiling. We observed that a subpopulation of cells differentiates into the myogenic lineage, showing Myf5 expression as early as E12.5, whereas the rest of the population is fibroblast-like and has high collagen expression. This fibroblast-like population appears to be the early stage of the adipocyte and dermal lineages. Cells at E14.5 have distinct myogenic populations that express Myod1 and Myog; we also identified other populations with Ebf2 or Twist2 expression, which could belong to brown adipose or dermal lineage, respectively. Further analysis of their gene expression patterns confirms the important role of Notch signaling in the myogenic populations. Finally, we identified novel surface markers for these subpopulations, which will enable enrichment and sorting of these newly identified cell types for further functional evaluation.

References:

[1] C. Lepper, C. Fan, genesis 48 424–436, (2010).