CDB SEMINAR

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15:00~16:00 C1F CDB Auditorium

Cellular and molecular mechanisms of lineage segregation during mesoderm development

Summary

Understanding the basis of cell specification and the transition from initial patterning to subsequent growth during tissue development are of fundamental significance. The somite-derived dermomyotome generates a variety of derivatives including striated muscle, dermis and vascular cell types (smooth muscle and endothelium) in a spatial and temporally-regulated fashion. Hence, the epithelial dermomyotome is an excellent system to investigate mechanisms that account for lineage segregation and morphogenesis during ontogeny. Based on single cell lineage analysis in ovo, we previously reported that the avian dermomyotome is composed of both multipotent as well as fate restricted progenitors. Subsequently, we showed that the orientation of cell divisions plays a pivotal role in fate choices. LGN-dependent early planar divisions are required for proper allocation of progenitors into either dermomyotome or myotome while late perpendicular divisions are necessary for the normal balance between muscle and dermis production.

Next, we asked what are the mechanisms underlying dermomyotome development into muscle, and in particular, the transition from a first phase of progenitor differentiation into myofibers, that set a basic muscle architecture, ensued by a growth phase composed of proliferative Pax7-positive progenitors. We report that Sonic hedgehog (Shh) promotes terminal differentiation of dermomyotome-derived progenitors throughout the patterning phase in both avians and mice. An in vivo reporter of Shh activity combined with mouse genetics enabled us to characterize a spatio-temporal sequence of epaxial myotomal maturation and the existence of both positive and negative Shh activities operating on distinct cell subsets. Following this sensitive period, the dermomyotome becomes refractory to Shh; a block localized upstream of Smoothened signaling. The end of responsiveness to Shh coincides, and is thus likely to enable, the transition into the growth phase of the muscle primordium.

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