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Single-cell transcriptomics of human embryos identifies multiple sympathoblast lineages with potential implications for neuroblastoma origin

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Abstract

Characterization of the progression of cellular states during human embryogenesis can provide insights into the origin of pediatric diseases. We examined the transcriptional states of neural crest– and mesoderm-derived lineages differentiating into adrenal glands, kidneys, endothelium and hematopoietic tissue between post-conception weeks 6 and 14 of human development. Our results reveal transitions connecting the intermediate mesoderm and progenitors of organ primordia, the hematopoietic system and endothelial subtypes. Unexpectedly, by using a combination of single-cell transcriptomics and lineage tracing, we found that intra-adrenal sympathoblasts at that stage are directly derived from nerve-associated Schwann cell precursors, similarly to local chromaffin cells, whereas the majority of extra-adrenal sympathoblasts arise from the migratory neural crest. In humans, this process persists during several weeks of development within the large intra-adrenal ganglia-like structures, which may also serve as reservoirs of originating cells in neuroblastoma.

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