A single-cell transcriptomic atlas of the developing chicken limb

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Through precise implementation of distinct cell type specification programs, differentially regulated in both space and time, complex patterns emerge during organogenesis. Thanks to its easy experimental accessibility, the developing chicken limb has long served as a paradigm to study vertebrate pattern formation. Through decades' worth of research, we now have a firm grasp on the molecular mechanisms driving limb formation at the tissue-level. However, to elucidate the dynamic interplay between transcriptional cell type specification programs and pattern formation at its relevant cellular scale, we lack appropriately resolved molecular data at the genome-wide level. Here, making use of droplet-based single-cell RNA-sequencing, we catalogue the developmental emergence of distinct tissue types and their transcriptome dynamics in the distal chicken limb, the so-called autopod, at cellular resolution.; Using single-cell RNA-sequencing technology, we sequenced a total of 17,628 cells coming from three key developmental stages of chicken autopod patterning. Overall, we identified 23 cell populations with distinct transcriptional profiles. Amongst them were small, albeit essential populations like the apical ectodermal ridge, demonstrating the ability to detect even rare cell types. Moreover, we uncovered the existence of molecularly distinct sub-populations within previously defined compartments of the developing limb, some of which have important signaling functions during autopod pattern formation. Finally, we inferred gene co-expression modules that coincide with distinct tissue types across developmental time, and used them to track patterning-relevant cell populations of the forming digits.; We provide a comprehensive functional genomics resource to study the molecular effectors of chicken limb patterning at cellular resolution. Our single-cell transcriptomic atlas captures all major cell populations of the developing autopod, and highlights the transcriptional complexity in many of its components. Finally, integrating our data-set with other single-cell transcriptomics resources will enable researchers to assess molecular similarities in orthologous cell types across the major tetrapod clades, and provide an extensive candidate gene list to functionally test cell-type-specific drivers of limb morphological diversification.
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