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The adult human testis transcriptional cell atlas

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Abstract

Human adult spermatogenesis balances spermatogonial stem cell (SSC) self-renewal and differentiation, alongside complex germ cell-niche interactions, to ensure long-term fertility and faithful genome propagation. Here, we performed single-cell RNA sequencing of ~6500 testicular cells from young adults. We found five niche/somatic cell types (Leydig, myoid, Sertoli, endothelial, macrophage), and observed germline-niche interactions and key human-mouse differences. Spermatogenesis, including meiosis, was reconstructed computationally, revealing sequential coding, non-coding, and repeat-element transcriptional signatures. Interestingly, we identified five discrete transcriptional/developmental spermatogonial states, including a novel early SSC state, termed State 0. Epigenetic features and nascent transcription analyses suggested developmental plasticity within spermatogonial States. To understand the origin of State 0, we profiled testicular cells from infants, and identified distinct similarities between adult State 0 and infant SSCs. Overall, our datasets describe key transcriptional and epigenetic signatures of the normal adult human testis, and provide new insights into germ cell developmental transitions and plasticity.