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The Dynamic Transcriptional Cell Atlas of Testis Development during Human Puberty

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Abstract

The human testis undergoes dramatic developmental and structural changes during puberty, including proliferation and maturation of somatic niche cells, and the onset of spermatogenesis. To characterize this understudied process, we profiled and analyzed single-cell transcriptomes of ~10,000 testicular cells from four boys spanning puberty and compared them to those of infants and adults. During puberty, undifferentiated spermatogonia sequentially expand and differentiate prior to the initiation of gametogenesis. Notably, we identify a common pre-pubertal progenitor for Leydig and myoid cells and delineate candidate factors controlling pubertal differentiation. Furthermore, pre-pubertal Sertoli cells exhibit two distinct transcriptional states differing in metabolic profiles before converging to an alternative single mature population during puberty. Roles for testosterone in Sertoli cell maturation, antimicrobial peptide secretion, and spermatogonial differentiation are further highlighted through single-cell analysis of testosterone-suppressed transfemale testes. Taken together, our transcriptional atlas of the developing human testis provides multiple insights into developmental changes and key factors accompanying male puberty.