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Single-cell analysis of human testis aging and correlation with elevated body mass index

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Abstract

Aging men display reduced reproductive health; however, testis aging is poorly understood at the molecular and genomic levels. Here, we utilized single-cell RNA-seq to profile over 44,000 cells from both young and older men and examined age-related changes in germline development and in the testicular somatic cells. Age-related changes in spermatogonial stem cells appeared modest, whereas age-related dysregulation of spermatogenesis and somatic cells ranged from moderate to severe. Altered pathways included signaling and inflammation in multiple cell types, metabolic signaling in Sertoli cells, hedgehog signaling and testosterone production in Leydig cells, cell death and growth in testicular peritubular cells, and possible developmental regression in both Leydig and peritubular cells. Remarkably, the extent of dysregulation correlated with body mass index in older but not in younger men. Collectively, we reveal candidate molecular mechanisms underlying the complex testicular changes conferred by aging and their possible exacerbation by concurrent chronic conditions such as obesity.

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