Single-cell RNA sequencing analysis reveals sequential cell fate transition during human spermatogenesis

With the support by the National Natural Science Foundation of China, the joint research team led by Zhao XiaoYang (赵小阳) from the South Medical University, Tang FuChou (汤富酬) and Qiao Jie (乔杰) from Peking University published their latest progress in human spermatogenesis in *Cell Stem Cell* (2018, 23(4): 599—614).

Infertility occurs in 10%—15% of all couples, and male factors contribute to approximately 50% of the cases. The investigations on germ-cell fate transition, differentiation mechanisms of spermatogenesis, and molecular diagnosis of male infertility could provide new insights into *in vitro* spermatogenesis, definite marker genes of human testicular germ cells, and powerful candidate genes associated with the occurrence of male infertility.

Spermatogenesis is the complex yet highly ordered process of the continuous supply of spermatozoa. The maintenance of spermatogonial stem cells (SSCs), their preparation for differentiation, and subsequent commitment to meiosis and spermiogenesis are the key events of spermatogenesis. Previous studies have revealed the transcriptional signatures of human germline cells. However, the developmental landscapes of human spermatogenesis after puberty remain largely undefined.

In the present study, scientists performed scRNA-seq of 2854 individual testicular cells from donors with normal spermatogenesis (donors with normal fertility or obstructive azoospermia [OA]) using a modified scRNA-seq method. Combined with the virtue of bioinformatic strategies, the 2854 testicular cells were defined as three spermatogonia subtypes, seven spermatocyte subtypes, and four spermatid subtypes in the context of their step-wise development. Further analyses identified several stage-specific marker genes of human germ cells such as *HMGA1*, *PIWIL4*, *TEX29*, *SCML1*, and *CCDC112*. Moreover, with the present scRNA-seq datasets of normal spermatogenesis as the reference, they identified altered gene expression patterns in the testicular cells of one NOA patient via scRNA-seq analysis, providing a new platform for further diagnosis and investigation of male infertility.

This work allows for the reconstruction of transcriptional programs inherent to the sequential cell fate transition during human spermatogenesis and has implications for deciphering male-related reproductive disorders.

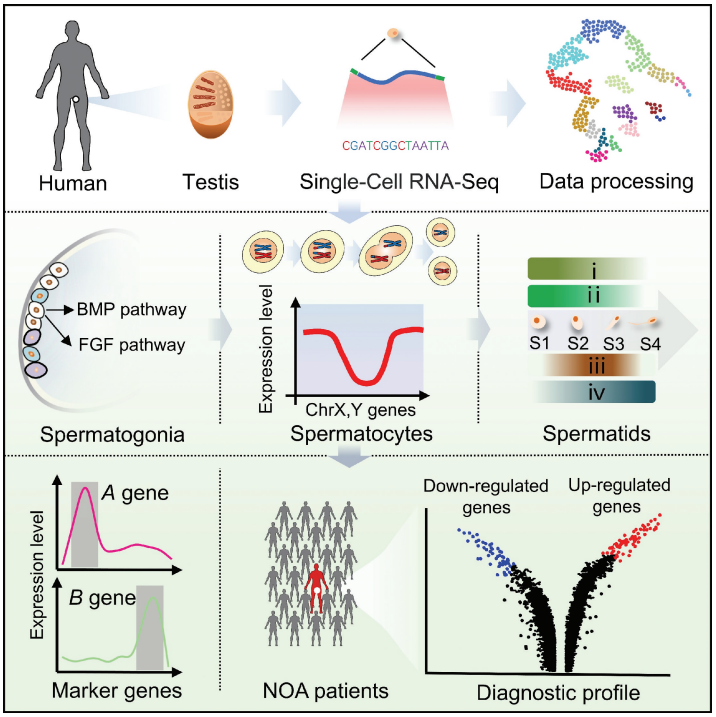

Figure Chinese scientists first revealed the landscapes of human spermatogenesis and male infertility via scRNA-seq analysis.