

Brief Communication

Distribution characteristics of mitochondria-rich segments in the epididymis

Qiuru Huang*, Jiaxin Li*, Jun Yu

Institute of Reproductive Medicine, Medical School of Nantong University, Nantong 226001, Jiangsu, PR China.

**Equal contributors.*

Received August 6, 2023; Accepted August 18, 2023; Epub August 20, 2023; Published August 30, 2023

Abstract: The epididymis is a highly specialized tissue that plays vital roles in sperm maturation and storage. The spatio-temporal repertoire of epididymal cells and their gene expression in the epididymis remain less characterized. With the help of single-cell RNA sequencing (scRNA-seq), Shi et al., reveal a spatio- and segment-specific distribution pattern of mitochondria that adds another layer of complexity to our understanding of the epididymis. They unexpectedly find a higher abundance of mitochondria and mitochondrial transcription in the corpus and cauda compared to the caput of epididymis, which are believed to be responsible for providing the energy necessary for sperm maturation and motility.

Keywords: Epididymis, caput, corpus, cauda, single-cell RNA sequencing, mitochondria

The epididymis is a highly specialized tissue in the male reproductive system that plays crucial roles for sperm maturation and storage [1, 2]. It contains a convoluted tubule that can be divided into several segmented regions with unique cellular composition and functions. A comprehensive understanding of spatio-temporal landscape of epididymal cells and their specific segments are vital to decode the molecular mechanisms that underlying sperm development and function.

Single-cell RNA sequencing (scRNA-seq) is a powerful tool that allows for the detailed profiling of gene expression in thousands of individual cells. With the widespread application of single-cell RNA sequencing, the physiological functions of mammalian male reproductive organs, have been intensively analyzed. Green et al., provided a single-cell transcriptome atlas of somatic cells and different stage of germ cells from the adult mouse testis [3]. Guo et al., utilized scRNA-seq to profile the gene expression patterns of individual cells isolated from human testicular tissue [4]. Wang et al., identified distinct cell populations corresponding to different stages of human spermatogenesis by analyzing the scRNA-seq data [5]. However, the spatio-temporal repertoire of epididymal cells

and their gene expression in the epididymis are still less characterized.

By applying this technique to the mouse epididymis, several groups have succeeded in generating a comprehensive cell atlas for mouse epididymis and the caput segment of human epididymis [6-8]. The identification of principal cells, myoid cells/fibroblasts, clear/narrow cells, macrophages/monocytes, basal cells, halo/T cells, endothelial cells, and sperm, have been made along with noteworthy observations. In particular, Shi et al., have made a significant contribution to this field [7]. They not only deciphered the cell compositions and gene characteristics, but also revealed a spatio- and segment-specific distribution pattern of mitochondria that adds another layer of complexity to our understanding of this organ. The validity of these results has been reinforced by both scRNA-seq datasets and histological and molecular validation. These studies represent a significant advancement in our understanding of the epididymis and provide a solid foundation for future research in this area.

Mitochondria play crucial roles in energy production that is involved in the regulation of spermatogenesis, sperm production, and mul-

Epididymal mitochondria-rich segments

tiple sperm functions [9, 10]. It was unexpected to find a higher abundance of mitochondria and mitochondrial transcription in the corpus and cauda compared to the caput of epididymis. In the context of the epididymis, these mitochondria-rich segments are believed to be responsible for providing the energy necessary for sperm maturation and motility.

The application of scRNA-seq to the epididymis has provided valuable insights into the spatio-temporal landscape of epididymal cells and their specific mitochondria-rich segments. This knowledge is essential for understanding the molecular mechanisms underlying sperm development and function, and may have implications for the development of new strategies to improve male fertility.

Disclosure of conflict of interest

None.

Address correspondence to: Jun Yu, Institute of Reproductive Medicine, Medical School of Nantong University, Nantong 226001, Jiangsu, PR China. E-mail: yujun9117@126.com

References

- [1] Breton S, Nair AV and Battistone MA. Epithelial dynamics in the epididymis: role in the maturation, protection, and storage of spermatozoa. *Andrology* 2019; 7: 631-643.
- [2] Cornwall GA. New insights into epididymal biology and function. *Hum Reprod Update* 2009; 15: 213-27.
- [3] Green CD, Ma Q, Manske GL, Shami AN, Zheng X, Marini S, Moritz L, Sultan C, Gurczynski SJ, Moore BB, Tallquist MD, Li JZ and Hammoud SS. A comprehensive roadmap of murine spermatogenesis defined by single-cell RNA-seq. *Dev Cell* 2018; 46: 651-667, e10.
- [4] Guo J, Grow EJ, Mlcochova H, Maher GJ, Lindskog C, Nie X, Guo Y, Takei Y, Yun J, Cai L, Kim R, Carrell DT, Goriely A, Hotaling JM and Cairns BR. The adult human testis transcriptional cell atlas. *Cell Res* 2018; 28: 1141-1157.
- [5] Wang M, Liu X, Chang G, Chen Y, An G, Yan L, Gao S, Xu Y, Cui Y, Dong J, Chen Y, Fan X, Hu Y, Song K, Zhu X, Gao Y, Yao Z, Bian S, Hou Y, Lu J, Wang R, Fan Y, Lian Y, Tang W, Wang Y, Liu J, Zhao L, Wang L, Liu Z, Yuan R, Shi Y, Hu B, Ren X, Tang F, Zhao XY and Qiao J. Single-cell RNA sequencing analysis reveals sequential cell fate transition during human spermatogenesis. *Cell Stem Cell* 2018; 23: 599-614, e4.
- [6] Rinaldi VD, Donnard E, Gellatly K, Rasmussen M, Kucukural A, Yukselen O, Garber M, Sharma U and Rando OJ. An atlas of cell types in the mouse epididymis and vas deferens. *Elife* 2020; 9: e55474.
- [7] Shi J, Fok KL, Dai P, Qiao F, Zhang M, Liu H, Sang M, Ye M, Liu Y, Zhou Y, Wang C, Sun F, Xie G and Chen H. Spatio-temporal landscape of mouse epididymal cells and specific mitochondria-rich segments defined by large-scale single-cell RNA-seq. *Cell Discov* 2021; 7: 34.
- [8] Leir SH, Yin S, Kerschner JL, Cosme W and Harris A. An atlas of human proximal epididymis reveals cell-specific functions and distinct roles for CFTR. *Life Sci Alliance* 2020; 3: e202000744.
- [9] Durairajanayagam D, Singh D, Agarwal A and Henkel R. Causes and consequences of sperm mitochondrial dysfunction. *Andrologia* 2021; 53: e13666.
- [10] Vertika S, Singh KK and Rajender S. Mitochondria, spermatogenesis, and male infertility - an update. *Mitochondrion* 2020; 54: 26-40.