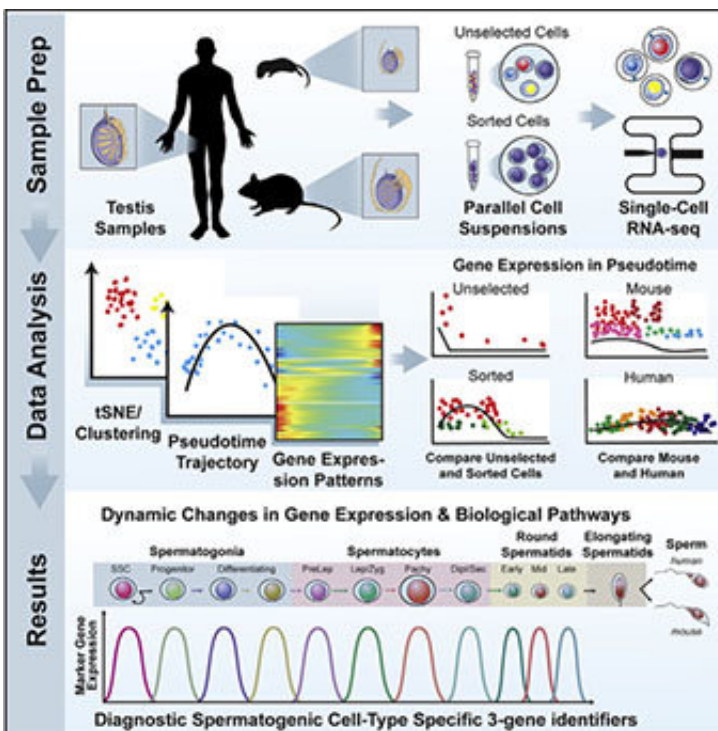


Research team constructs world's most comprehensive digital roadmap to unlock male infertility

November 7 2018, by Milady Nazir



Credit: University of Texas at San Antonio

Millions of couples who have trouble conceiving may get relief from new research led by scientists at The University of Texas at San Antonio. The researchers have developed a high-resolution genetic map showing how men produce sperm cells. Their effort could help address genetically based challenges with male fertility, a major cause of

conception problems.

The researchers' findings reveal detailed information about which [genes](#) are turned on or off in stem [cells](#) that ultimately grow into [sperm cells](#). This data could give doctors crucial insight into the development of sperm in a patient, a perspective that was lacking up until now.

UTSA researcher Brian Hermann says the new knowledge could be a game changer for uncovering what can go wrong in men who suffer from infertility.

"We took a new, cutting-edge approach down to the level of [individual cells](#) to understand all the changes in which genes are used to make sperm in the testicles. That previously had not been possible and impedes progress toward a cure for male infertility," said Hermann, a biology professor and director of the UTSA Genomics Core.

The findings appear in the November 6 edition of the scientific journal, *Cell Reports*. Professors Hermann and John R. McCarrey led the group, which included researchers at UTSA and across the country.

Together, the team built a comprehensive digital library of the cell types required for sperm production in mice and men. They examined more than 62,000 cells and identified 11 different gene expression profiles; their work even uncovered rare and new cells for which little data was previously reported. The research, which began in early 2014, was supported by the Kleberg Foundation, the Hurd Foundation and the National Institutes of Health (NIH).

According to the NIH, reproduction issues in males contribute to at least half of infertility cases among couples. Many cases of male infertility are treated with medication. Some even require surgical procedures. Yet, in almost half of these same cases, the reasons for [male infertility](#) are

unknown.

UTSA's digital roadmap was constructed using the sequencing of genes expressed in [germ cells](#). The researchers used high-tech machines which allow scientists to examine tens of thousands of individual cells and produce the library of genes expressed in each cell in one to two days. The method also employed cutting-edge bioinformatics, data analytics that decode gene expression data generated from the cells.

UTSA's individualized approach to profiling gene expression at the single-cell level is what makes this work different. Previous methods have relied on analyzing groups of cells, but when they are bundled together in experiments, the differences among the individual cells are averaged and therefore obscured. Hence, UTSA's new approach provides important data that can help uncover the biology underlying how sperm are produced and what may go wrong in men who suffer from infertility.

"This is how we find the needles in the haystack," said Hermann. "We weren't previously able to separate different cells with different functions, so in order to understand exactly how they are different, we looked at individual single cells, instead of the typical way of grabbing them all in bulk as a group."

UTSA's new digital gene expression library offers many scientific applications. It could help improve clinical diagnoses in men with [infertility](#) because their [gene expression](#) "signatures" will be different than those in the normal men now described in this new database. The UTSA resource can also provide a foundation to help innovate the next generation of male contraception and to even potentially develop sperm outside the body.

The researchers are hopeful that the methodology can also be applied to

other biological processes in the body in order to uncover new information on which to base novel approaches to diagnose, treat or prevent a wide variety of diseases.

"It's been a dream for decades to take the most primitive cells in the testis and convert them into sperm in a petri dish, yet this has never worked," said Hermann. "If anyone is going to generate [sperm](#) cells in a dish, they'd want to know how similar those cells are to those that occur naturally in the body. The data we have generated now provides a reference library for comparison."

More information: Brian P. Hermann et al, The Mammalian Spermatogenesis Single-Cell Transcriptome, from Spermatogonial Stem Cells to Spermatids, *Cell Reports* (2018). [DOI: 10.1016/j.celrep.2018.10.026](#)

Provided by University of Texas at San Antonio

Citation: Research team constructs world's most comprehensive digital roadmap to unlock male infertility (2018, November 7) retrieved 1 May 2024 from <https://phys.org/news/2018-11-team-world-comprehensive-digital-roadmap.html>

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