

Researchers find new genetic information behind urogenital track anomalies

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About one in every 100 babies is born with some kind of developmental anomaly in the urogenital tract. In most cases abnormalities are mild, but sometimes life-long and even life-threatening disease develops.



Infertility is another important aspect that associates with urogenital anomalies. Therefore understanding how those features occur is instrumental in developing future treatments.

To date, diseases which scientist understand the best are those caused by mutations in the proteins involved. However, in many diseases such mutations are not found, and the disease is "idiopathic" or referred as without a known cause, and maybe triggered by e.g. environmental factors.

Classically scientists have studied such cases by injecting many copies of the gene of interest into fertilized egg of an experimental animal. However, the major problem with this technique is that scientist have almost no control over where in the genome the gene lands, and what <u>cell</u> <u>types</u> start to produce the encoded protein.

By employing an unconventional genome engineering trick that increased GDNF production 3-6 times, scientists revealed that ureter, which allows urine produced by kidneys to enter bladder, length is regulated by GDNF levels, and that tubes connecting testicles to <u>reproductive organs</u> are misplaced when there is too much GDNF, resulting in infertility in males.

GDNF is a secreted <u>protein</u> which signals growth and survival for many types of cells. In females, too much GDNF resulted in imperforated vagina or lack of vaginal opening, resulting in infertility.

The researchers were able to trace some of those defects back to altered stem cell behavior in the developing urogenital block and identified some signaling pathways involved. Collectively these findings provide new information on altered stem cell behavior in the developing kidney.

The research was started at the Institute of Biotechnology, HiLIFE,



University of Helsinki, and performed in collaboration with the group of Dr. Satu Kuure and Professor Hannu Sariola.

Dr. Jaan-Olle Andressoo is currently an Associate Professor of Translational Neuroscience at the Faculty of Medicine, University of Helsinki.

Dr. Satu Kuure is director of GM-unit core facility at HiLIFE and principal investigator of STEMM research program at Faculty of Medicine, University of Helsinki.

The results of this study were published in Scientific Reports.

More information: Hao Li et al. Development of the urogenital system is regulated via the 3'UTR of GDNF, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-40457-1

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