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New mechanism for male infertility discovered

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A new study led from Karolinska Institutet in Sweden links male infertility to autoimmune prostatic inflammation. The findings are published in the journal *Science Translational Medicine*.

Involuntary childlessness is common, and in half of all cases attributable to infertility in the man. Although male infertility has many possible causes, it often remains unexplained.

In the present study, the researchers have discovered a reason for reduced fertility in people with autoimmune polyendocrine syndrome type 1 (APS1), which increases the risk of developing autoimmune disease (caused by the immune system attacking and damaging healthy cells) and which is often used as a model for autoimmune disease in general.

Infertility is common in people of both sexes with the disease. While infertility in women with APS1 is caused by autoimmune action against the ovaries, what gives rise to the corresponding infertility in men has never been ascertained. Keen to investigate whether male fertility could be explained by an autoimmune reaction against some part of the male reproductive organs, the researchers behind this new study examined the immune system of 93 men and women with APS1.

"We found that the immune system in a large group of patients reacted to a protein formed only in the prostate, namely the enzyme transglutaminase 4," says lead investigator Dr Nils Landegren at

Karolinska Institutet's Department of Medicine in Solna. "What we found was that it was only men who reacted to transglutaminase 4 and that the immune reaction first appeared at the onset of puberty once the prostate gland had matured. Interestingly, previous studies on mice have shown that transglutaminase 4 plays an important part in male fertility."

To better understand their findings, the team examined the animal model for APS1 (i.e. mice with the same genetic defect as human patients with the syndrome) and found that male mice spontaneously developed an inflammatory disease in their prostate glands - a so-called prostatitis - and reacted to transglutaminase 4.

"The finds are important as they point to a new disease mechanism for male infertility, but more work needs to be done to understand the significance of autoimmune prostatitis to infertility in the male population at large," says Dr Landegren.

More information: 'Transglutaminase 4 as a prostate autoantigen in male subfertility', N. Landegren, D. Sharon, A. K. Shum, I. S. Khan, K. J. Fasano, Å. Hallgren, C. Kampf, E. Freyhult, B. Ardesjö-Lundgren, M. Alimohammadi, S. Rathsman, J. F. Ludvigsson, D. Lundh, R. Motrich, V. Rivero, L. Fong, A. Giwercman, J. Gustafsson, J. Perheentupa, E. S. Husebye, M. S. Anderson, M. Snyder, O. Kämpe, *Science Translational Medicine*, Vol 7 Issue 292 292ra101 (2015), online 17 June 2015. stm.sciencemag.org/lookup/doi/ … scitranslmed.aaa9186

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