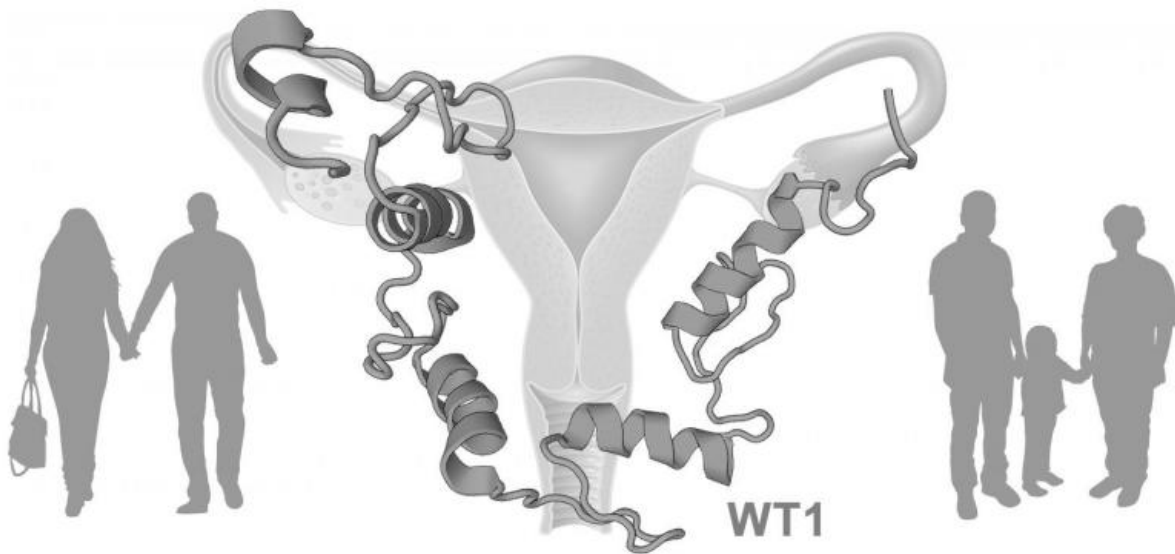


Researchers find gene Wt1 to impact women's fertility

March 28 2017



Researchers from the Leibniz Institute on Aging (FLI) in Jena/Germany found the gene WT1 to control female fertility. Credit: Graph: Kerstin Wagner/FLI; Source: toropova1964, La Gorda/www.fotolia.com

It has been estimated that more than 80 million people in the world have an unfulfilled desire to have children. But for every 10th couple, the reasons therefor remain unclear. Now, researchers from the Leibniz Institute on Aging (FLI) in Jena/Germany have, together with clinical partners, found a new gene mutation that obviously leads to infertility in women. The mutated gene WT1 plays an important role in the early

embryonic development controlling proteins (especially proteases) that are needed for the successful nidation in mother's womb. The astonishing results were recently published in the journal *Human Molecular Genetics*.

For many couples, starting an own family remains an unfulfilled dream. According to estimations, this is true for about 80 million people worldwide. Some fight for years to have own children; some stay childless without any medical indication. Now, researchers from Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena/Germany in collaboration with clinical partners discovered a formerly unknown gene mutation that could at least partly explain unwanted childlessness. The study's results were recently published in the journal *Human Molecular Genetics*.

Newly discovered mutation of gene WT1

In collaboration with the Sophien and Hufeland Hospital Weimar and the Heidelberg University Women's Hospital, researchers from FLI's research group of Christoph Englert investigated samples of women younger than 40 years that suffer from unwanted childlessness. In one out of eight women, the gene WT1 showed a previously unknown mutation in one of its two alleles. "This result was really surprising", explains Dr. Abinaya Nathan, who is the study's first author. "Up to now, WT1 was only known as [tumor suppressor gene](#) important for the development and maintenance of organs like heart or kidney". But which role does this gene play with regard to fertility?

Conserved gene function

To answer this question, the researchers from Jena conducted mouse experiments. What they found was that mice lacking one Wt1 copy had

far less offspring than healthy wild type mice. Moreover, the researchers discovered that it is Wt1's activity in the ovary that regulates fertility. After ovulation, the ovary is responsible for guiding the ovule into the womb. The ovary is also the place where fertilization takes place. If the ovule was inseminated, it travels down the fallopian tube to the womb, while dividing and developing continuously. "This process has to be strictly regulated", explains Professor Christoph Englert, who leads a research group at the FLI. "If the embryo develops too quickly, a tubal pregnancy may occur; if the embryo develops too slowly, nidation into the womb won't be successful. Hence, the communication between mother's ovary tissue and the ovule is a highly important prerequisite for a successful pregnancy", continues Prof. Englert.

Wt1 – Interacting with proteases

FLI's researchers showed that so-called "proteases" are essential for this communication. They degrade proteins and "pre-digest" the embryo to prepare it for nidation. "Usually, these proteases are only active in the womb", Professor Englert explains. "However, if the Wt1 gene is mutated, protease Prss29 already becomes active in the ovary, harming the embryo in a way that it cannot attach itself anymore to the uterine wall and finally is rejected. This could be the reason why these women cannot become pregnant even though there has been no clinical indication so far".

"Results for mice and humans are very similar, showing that this function of the Wt1 gene is highly conserved in mammals", Dr. Verena Holschbach from the Heidelberg University Women's Hospital emphasizes. "The new WT1 [gene mutation](#), which we have found, causing the premature activation of proteases already in the ovary, offers completely new approaches to help childless couples to fulfill their desire to have children", the researchers conclude. The next steps will be even broader clinical patient screenings and a more detailed examination

of how to alter the womb milieu.

More information: Abinaya Nathan et al. The Wilms tumor protein Wt1 contributes to female fertility by regulating oviductal proteostasis, *Human Molecular Genetics* (2017). [DOI: 10.1093/hmg/ddx075](https://doi.org/10.1093/hmg/ddx075)

Provided by Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)

Citation: Researchers find gene Wt1 to impact women's fertility (2017, March 28) retrieved 20 March 2024 from

<https://medicalxpress.com/news/2017-03-gene-wt1-impact-women-fertility.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--