

Press Release  
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## Researchers Find Gene *WT1* to Impact Women's Fertility

It has been estimated that more than 80 million people in the world have an unfulfilled desire to have children. But for every 10<sup>th</sup> 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*.

**Jena.** 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* (<https://doi.org/10.1093/hmg/ddx075>).

### 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.

### **Publication**

Nathan A, Reinhardt P, Kruspe D, Jörß T, Groth M, Nolte H, Habenicht A, Herrmann J, Holschbach V, Toth B, Krüger M, Wang ZQ, Platzer M, Englert C. The Wilms tumor protein Wt1 contributes to female fertility by regulating oviductal proteostasis. *Human Molecular Genetics* 2017, DOI: 10.1093/hmg/ddx075.

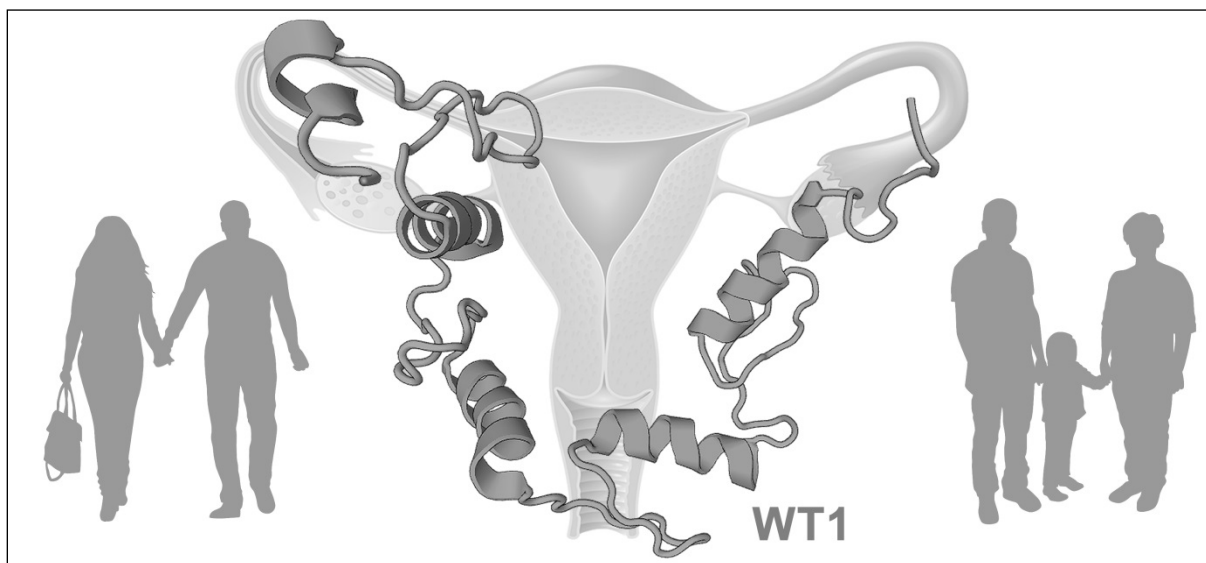
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## Pictures



**Pic 1:** Researchers from the Leibniz Institute on Aging (FLI) in Jena/Germany found the gene *WT1* to control female fertility.

[Graph: Kerstin Wagner/FLI; Source: © toropova1964, © La Gorda/www.fotolia.com]

## Background information

The **Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)** is the first German research organization dedicated to biomedical aging research since 2004. More than 330 members from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit [www.leibniz-fli.de](http://www.leibniz-fli.de).

The **Leibniz Association** connects 91 independent research institutions that range in focus from the natural, engineering and environmental sciences via economics, spatial and social sciences to the humanities. Leibniz Institutes address issues of social, economic and ecological relevance. They conduct knowledge-driven and applied basic research, maintain scientific infrastructure and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer to policy-makers, academia, business and the public. Leibniz Institutes collaborate intensively with universities – in the form of “WissenschaftsCampi” (thematic partnerships between university and non-university research institutes), for example – as well as with industry and other partners at home and abroad. They are subject to an independent evaluation procedure that is unparalleled in its transparency. Due to the institutes’ importance for the country as a whole, they are funded jointly by the Federation and the Länder, employing some 18,600 individuals, including 9,500 researchers. The entire budget of all the institutes is approximately 1.7 billion EUR. See [www.leibniz-association.eu](http://www.leibniz-association.eu) for more information.