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Press release
September 28, 2018

New function of "kidney-gene" – *WT1* plays a role in the central nervous system and controls movement

The *WT1* gene fulfills a central role in the development of a healthy, proper functioning kidney. Mutations in *WT1* lead to impairments in kidney development and cause Wilms tumors, a pediatric kidney cancer. Researchers of the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) in Jena have now discovered a further important function of *WT1*. It is also active outside the kidneys in the central nervous system and is involved in controlling movement. If the gene is missing in the spinal cord, locomotor aberrancies occur. The results have now been published in *Life Science Alliance*.

Jena. Transcription factor WT1 (Wilms tumor 1) has been known for nearly 30 years and it is significantly involved in the development of a healthy and properly functioning kidney. Impairments in the developmental process lead to kidney cancer in children. The gene is also responsible for maintaining kidney function. Recently, even an association between unexplained childlessness and mutations of *WT1* has been demonstrated.

Researchers of the Leibniz Institute on Aging – Fritz Lipmann Institute (FLI) und the Institute of Zoology and Evolutionary Research of the Friedrich Schiller University Jena (FSU) together with colleagues of the University Uppsala, Sweden and the Helmholtz Zentrum München have now discovered another important role of the *WT1* gene: It is also active outside the kidney in the central nervous system and is involved in the differentiation of spinal cord neurons that control rhythmic movements. The results have now been published in the journal *Life Science Alliance*.

"This result was completely surprising for us, because we thought we already knew the *WT1* gene quiet well after all those years of research", tells Prof. Christoph Englert, Group Leader at FLI. "Until now, the Wilms tumor suppressor gene *WT1* was known as an important gene for the development and maintenance of various organs, such as kidneys and heart. But it was new to us, that it also influences our movements." But what function does this gene play in the central nervous system?

Loss of WT1 changes movements

The researchers analyzed in which areas of the spinal cord and brain the *WT1* gene is active. They examined mice that lacked the gene. "A loss of the gene changes the motor processes; the mice show problems with the coordination of their legs, which lead to a changes in their walk", tell Dr. Danny Schnerwitzki, first author of the study.

The intestine, respiration and our walk are controlled and regulated by neural networks that work like circuits. Neurons of the brain and spinal cord are also involved in these processes. "We were able to show that the *WT1* gene controls a certain group of neurons that is responsible for locomotion", says Dr. Schnerwitzki about the results. They show that the development of certain neurons in the spinal cord depends on WT1 expression and that a loss of *WT1* is linked to locomotion.

WT1 controls neuron specification

“In a second step, we investigated the development of neurons as a function of *WT1* expression and performed locomotion analyses of *WT1* knockout mice”, says Prof. Englert. The researchers used molecular biological and electrophysiological approaches as well as a special X-ray method developed at the Institute of Zoology and Evolutionary Research of FSU to visualize changes in locomotion. “Our data indicate that the gene not only contributes to the coordination of locomotion, but is also required for proper differentiation of spinal cord neurons during embryogenesis”, says Englert.

Also in Zebrafish, the researchers found WT1 in neurons of the spinal cord. This indicates that the function of the gene is evolutionarily conserved. In fish, the gene seems to be responsible for controlling their swimming movement.

The study does not only demonstrates the previously undescribed importance of WT1 in the development of spinal cord neurons, but also underlines its role in the circuits responsible for the functional implementation of locomotion in the neurons. “Studying patients with a *WT1* mutation could show us what differences in the role of WT1 humans in comparison to the model systems show and uncover its contribution to locomotor changes.”

Publication

Danny Schnerwitzki, Sharn Perry, Anna Ivanova, Fabio V Caixeta, Paul Cramer, Sven Günther, Kathrin Weber, Atieh Tafreshiha, Lore Becker, Ingrid L Vargas Panesso, Thomas Klopstock, Martin Hrabe de Angelis, Manuela Schmidt, Klas Kullander, Christoph Englert. Neuron-specific inactivation of Wt1 alters locomotion in mice and changes interneuron composition in the spinal cord. Life Science Alliance 2018, DOI: 10.26508/lsa.201800106

Videomaterial

X-ray fluoroscopy video shows skeleton of Wt1fl/fl control mouse running on a treadmill.
http://movie.life-science-alliance.org/video/10.26508/lsa.201800106/video-1
X-ray fluoroscopy video shows skeleton of Nes-Cre;Wt1fl/fl mouse running on a treadmill.
http://movie.life-science-alliance.org/video/10.26508/lsa.201800106/video-2
Video shows newborn Wt1fl/fl pup performing air-stepping after tail pinch.
http://movie.life-science-alliance.org/video/10.26508/lsa.201800106/video-3
Video shows newborn Nes-Cre;Wt1fl/fl pup performing air-stepping after tail pinch.
http://movie.life-science-alliance.org/video/10.26508/lsa.201800106/video-4

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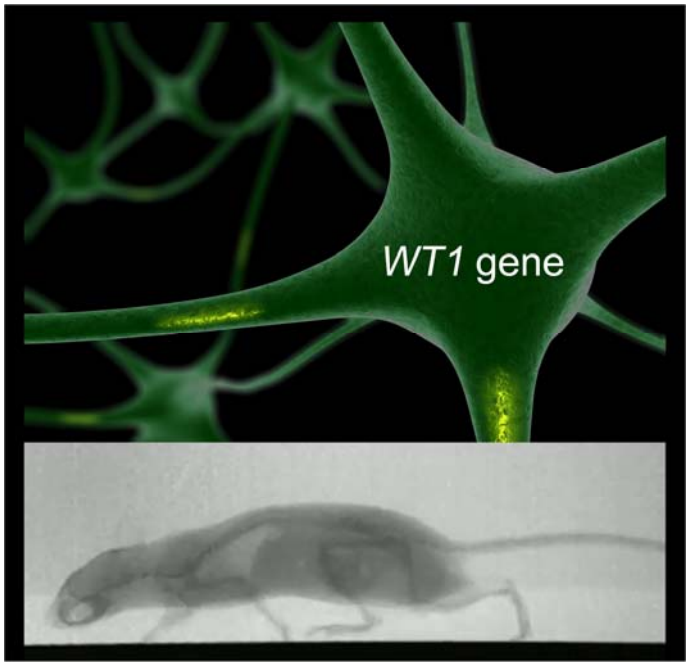
Leibniz Institute on Aging –
Fritz Lipmann Institute

Picture



Picture:

Gene WT1 appears also outside of the kidney in the central nervous system, it is needed for neuro specification and locomotor control. (Picture: Kerstin Wagner / FLI; Source: u.a. http://movie.life-science-alliance.org/video/10.26508/lsa.201800106/video-2, www. panthermedia.net)

Background information

The **Leibniz Institute on Aging – Fritz Lipmann Institute (FLI)** – upon its inauguration in 2004 – was the first German research organization dedicated to research on the process of aging. More than 330 employees from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit www.leibniz-fli.de.

The **Leibniz Association** connects 93 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 19,100 individuals, including 9,900 researchers. The entire budget of all the institutes is approximately 1.9 billion EUR. See www.leibniz-association.eu for more information.