PRESS RELEASE

Fat cells under false command

Researchers in Bonn are investigating how cellular antennas regulate the development of precursor cells in fat tissue

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Bonn, August 20 – Too much fat can be unhealthy: how fat cells, so-called adipocytes, develop, is crucial for the function of the fat tissue. That is why a team led by researchers from the University Hospital Bonn (UKB) and the University of Bonn investigated the influence of primary cilia dysfunction on adipocyte precursor cells in a mouse model. They found that overactivation of the Hedgehog signaling pathway causes abnormal development into connective tissue-like cells instead of white fat cells. Their findings have now been published in The EMBO Journal.

White adipose tissue stores energy and regulates important metabolic processes in the body. "It constantly grows or shrinks, depending on how much energy we consume or burn. Specialized 'stem cell-like' precursor cells play a key role in this process because they have the ability to form new fat tissue," says corresponding author Prof. Dagmar Wachten, co-director of the Institute of Innate Immunity at the UKB. She is also a member of the ImmunoSensation2 Cluster of Excellence and the Transdisciplinary Research Areas (TRA) "Modeling" and "Life & Health" at the University of Bonn. Unlike mature fat cells, the precursor cells have a small structure called a primary cilium. Primary cilia act as a kind of antenna, which receives signals from the environment and regulates specific signaling pathways. Thereby, they control whether these cells develop into fat cells or connective tissue-like cells. Prof. Wachten sums up: "The regulation of these precursor cells is crucial for the health of white adipose tissue in obesity. We therefore wanted to find out how cilia control the development of precursor cells into fat cells."

Fat tissue shows early remodeling processes – even before obesity

The Bonn researchers investigated different subgroups of precursor cells in the adipose tissue of mice whose cilia function is impaired by a genetic disorder called Bardet-Biedl syndrome (BBS). People with BBS often suffer from obesity, and mice with BBS also show increased body weight. The research team found that when an important cilia protein (BBS8) is missing, changes in white adipose tissue occur even before the onset of obesity. The stem cell-like precursor cells decrease in number because they increasingly transform into connective tissue-like cells. These are found, among other places, in scar tissue, where they contribute to tissue hardening. However, their function in adipose tissue in the lean state is still unclear.

Overactivation of the Hedgehog signaling pathway drives maldevelopment

"We have identified the Hedgehog signaling pathway as a key factor in the malformation. Its activation is normally strictly regulated by primary cilia", says co-first author Katharina

Sieckmann, a doctoral student at the University of Bonn in Prof. Wachten's working group at the UKB. Alumna of the team and co-first author Nora Winnerling adds: "If cilia function is disrupted, as in BBS, this pathway becomes overactive and drives the cells in an undesirable direction: away from their actual function in forming fat cells. Thus, the Hedgehog signaling pathway controls cell fate in white adipose tissue."

These results show that cilia actively influence the fate of fat precursor cells in the adipose tissue and, thus, whether healthy adipose tissue is maintained. "These mechanisms could play a central role in the development of obesity. This discovery opens up new possibilities for targeted intervention in fat cell regulation and, in turn, for the development of more targeted therapies against pathological changes during obesity," says Prof. Wachten.

Participating institutions and funding:
This study was conducted as part of the DFG Collaborative Research Center SFB1454 "Metaflammation and Cellular Programming" and the Research Group FOR5547 “Primary cilia dynamics”. Prof. Wachten is spokesperson for the Collaborative Research Center 1454 and co-spokesperson for the Research Group 5547. In addition to the UKB and the University of Bonn, the Universities of Mainz and Münster as well as the German Center for Degenerative Diseases (DZNE) are involved in the research work.

Publication: Katharina Sieckmann, Nora Winnerling et al.: BBS8-dependent ciliary Hedgehog signaling governs cell fate in the white adipose tissue; The EMBO Journal; DOI: https://doi.org/10.1038/s44318-025-00524-y

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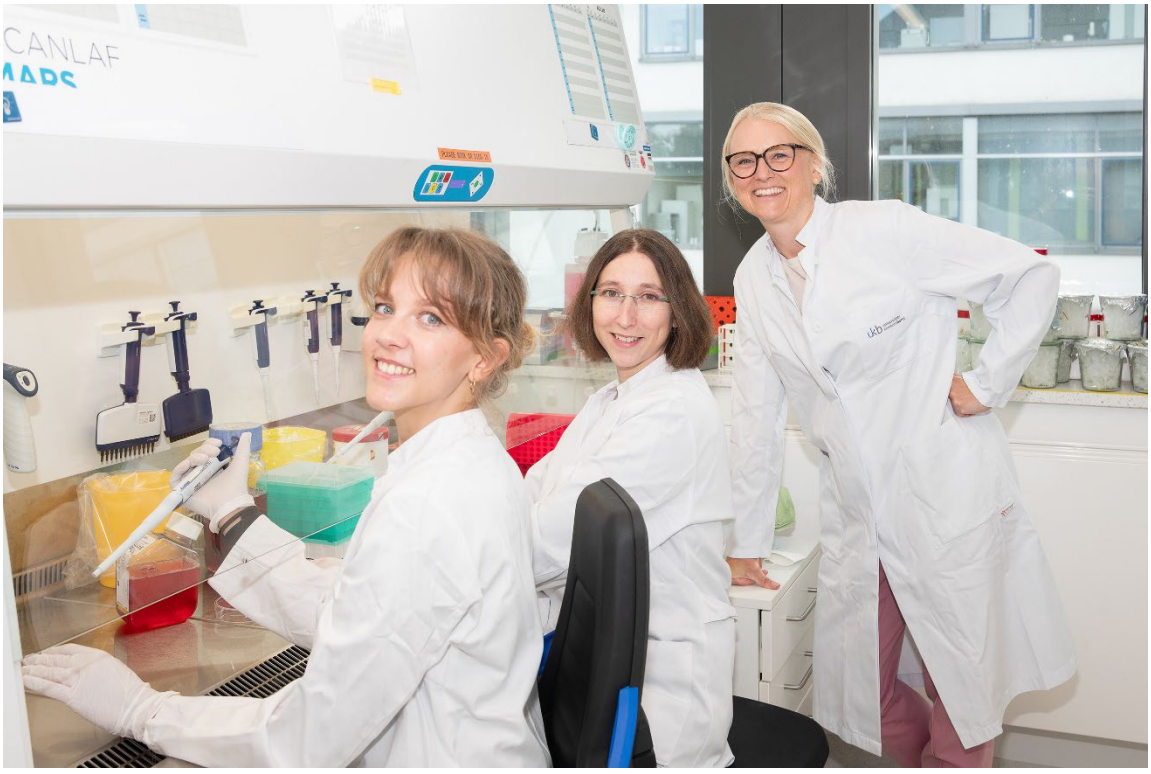

Caption: Fat cells under false command:
(from left) Katharina Sieckmann, Nora Winnerling, and Prof. Dagmar Wachten are investigating how cellular antennas regulate the development of precursor cells in fat tissue.

Image credits: University Hospital Bonn (UKB) / Rolf Müller

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About Bonn University Hospital: The UKB treats around 550,000 patients per year, employs approximately 9,900 staff, and has total assets of €1.8 billion. In addition to 3,500 medical and dental students, more than 600 people are trained in numerous healthcare professions each year. The UKB ranks first among university hospitals (UK) in North Rhine-Westphalia in the Focus hospital list, was able to raise nearly €100 million in third-party funding for research, development, and teaching in 2024, and has the second-highest case mix index (case severity) of any university hospital in Germany. The F.A.Z. Institute has awarded the UKB first place among university hospitals in the category “Germany's Training Champions 2024.”