Immune cells regulate body weight

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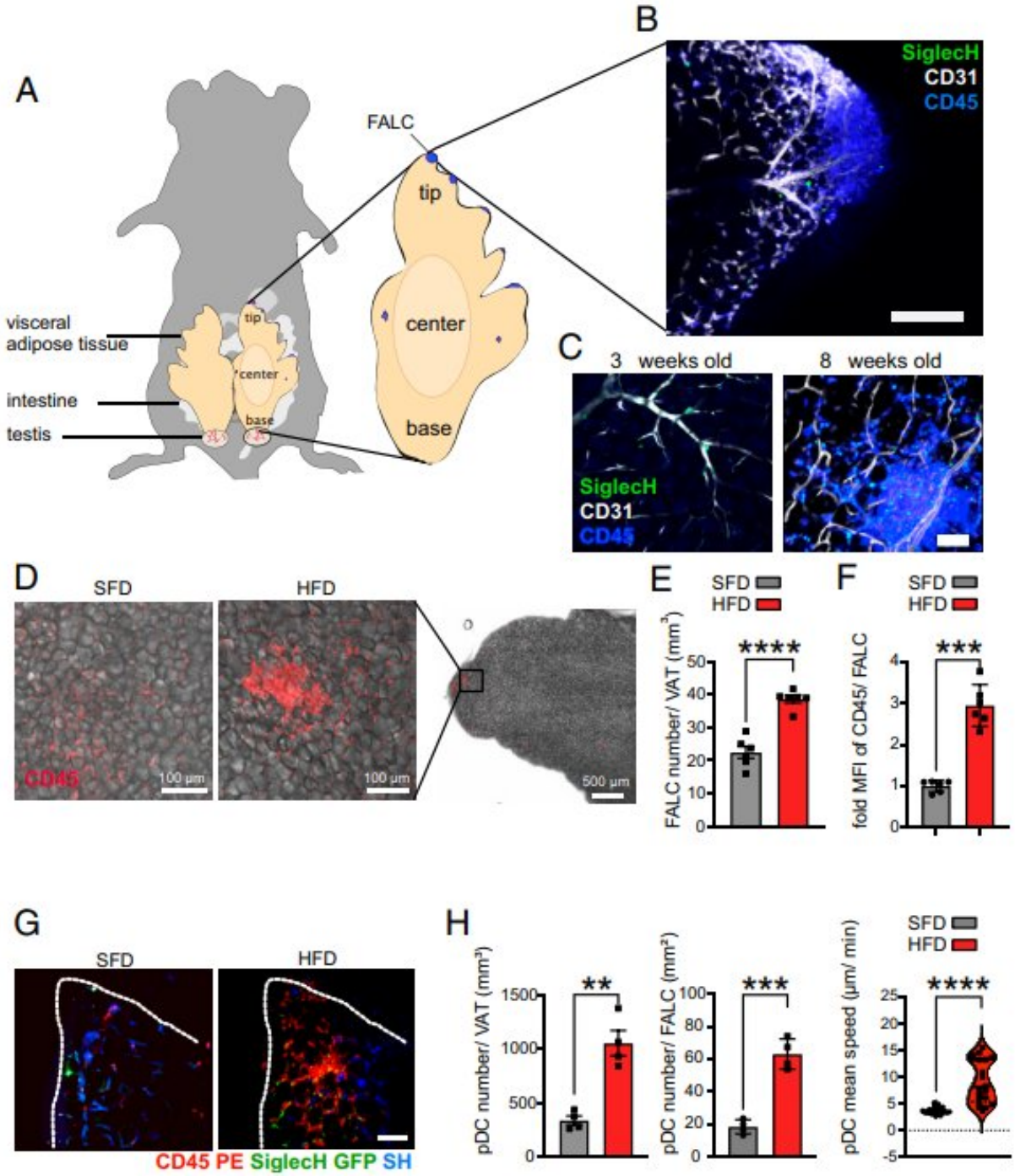

Diverse distribution of pDCs within the VAT. (A) VAT anatomy of the mouse and localization of fat-associated lymphoid clusters (FALCs). Male VAT was separated in the tip area (facing the liver), in the center part, and in the base part, which is attached to testis and epididymis. Confocal microscopy of FALC structures within VAT from chow-treated male mice. (B) VAT was stained for SiglecH (pDCs, green), CD31 (endothelia cells, white), and CD45 (hematopoietic cells, blue). Scale bar, 100 mm. (C) Representative images of VAT of 3-wk-old (left image) and 8-wk-old male mice (right image) stained for SiglecH (green), CD31 (white), and CD45 (blue). Scale bar, 50 mm. (D) Representative images of VAT of SFD or HDF mice, showing the adipocyte tissue in bright field (gray) and CD451 cells (red). Scale bars, 100 mm. (E) Number CD451 FALCs was quantified per volume of VAT from mice fed with a SFD (gray) and a HFD (red). Each dot represents total number of FALCs of one mouse. (F) The maximal MFI of CD45 was measured on the threedimensional projection images of FALCs, the mean intensity of SFD samples was set as 1, and the MFI of HFD FALCs was calculated accordingly. (G) Representative images of the VAT showing CD451 cells (red) at the tip of VAT, transferred SiglecH-GFP pDCs (green), and the adipose tissue labeled in blue by the second harmonic generation (SH). Images were acquired by multiphoton microscopy. Scale, 100 mm. (H) Left, After 3 wk of SFD and HFD, numbers of pDCs were quantified in relationship to the volume of VAT. (Middle) FALCs were visualized by three-dimensionalmaximum projection using Imaris (Bitplane) and numbers of pDCs were quantified per 1 mm2 . Right, Mean migratory speed of pDCs was measured by in vivo multiphoton microscopy after 3 wk of a HFD and compared with SFD. n 5 45 mice in each group. Statistical analyses were performed using a Student t test. Values represent mean ± SEM. **p The Journal of Immunology (2022). DOI: 10.4049/jimmunol.2100022

Obesity is among the biggest health challenges of the 21st century, according to the World Health Organization (WHO). Almost 60% of Germans are considered overweight, while 25% are obese. Moreover,

being overweight often triggers severe secondary diseases such as diabetes, arteriosclerosis, or heart attacks.

Immunological processes determine the course of this disease. As part of a new study, a group of LMU researchers led by Dr. Susanne Stutte and Professor Barbara Walzog has shown that a high-caloric diet, even for a period of only three weeks, has drastic effects on the immune system.

"A particular kind of immune cells known as plasmacytoid dendritic cells (pDCs) begins to accumulate in the visceral adipose tissue," explains Stutte. This adipose tissue is located inside the abdomen and surrounds internal organs. With high caloric diet, small clusters of immune cells form tertiary lymphoid structures inside this fat, resulting in fatal immune responses.

"Now, these pDCs in visceral fat are in a constant state of alarm and release type-I interferon," explains Walzog. This interferon usually mediates the control of infections, but here it triggers the metabolic syndrome: the metabolism derails and inflammatory markers rise. When the migration of pDCs into the fat is blocked, weight gain is reduced and the metabolic condition improves considerably.

The results of this study, published in *The Journal of Immunology* and which was carried out in collaboration with Harvard Medical School in Boston, could now contribute to the development of new approaches toward a therapeutic intervention of the metabolic syndrome.

More information: Susanne Stutte et al, High-Fat Diet Rapidly Modifies Trafficking, Phenotype, and Function of Plasmacytoid Dendritic Cells in Adipose Tissue, *The Journal of Immunology* (2022). DOI: 10.4049/jimmunol.2100022

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