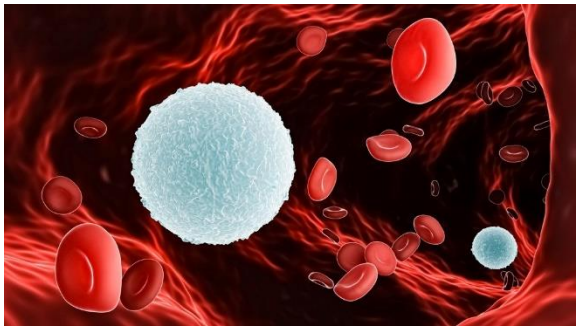
In Obesity White Blood Cell Type Identified as Important Contributor to Inflammation

Researchers explored neutrophil involvement in visceral adipose tissue (VAT) inflammation in obesity.



Study

In the present study, researchers investigated the role of VAT neutrophils in systemic metabolism disruption and insulin resistance related to obesity.

The study included 96 lean or obese patients from the Ohio State University's Center for Minimally Invasive Surgery in Columbus, Ohio. The researchers collected blood and fecal samples from the participants. They performed enzyme-linked immunosorbent assays (ELISA) to assess plasma biomarker levels. They amplified the bacterial 16S ribosomal ribonucleic acid (rRNA) gene from VAT or stool samples of obese and non-obese individuals.

The researchers explored the transcriptional profile of VAT neutrophils in human obesity and their potential link to gut bacterial translocation. To establish a causal relationship between gut microbiota changes and VAT neutrophilia, they administered human feces from lean and obese individuals into microbiome-depleted C57BL/6 mice. They collected epididymal VAT (eVAT), spleen, liver, and lung samples for flow cytometry, gene expression analysis, and 16S sequencing.

A group of lean, metabolically healthy patients additionally consumed an additional 1,320 kcal/day from fast-food restaurants, with more than 50% total fat and more than 10% saturated fat. The researchers quantified neutrophil abundance as a percentage of the cluster of differentiation 45-expressing (CD45+) cells in the stromal vascular fraction (SVF) using flow cytometry.

To investigate the potential for bacterial translocations driving recruitment of neutrophils to visceral adipose tissues, the researchers developed human-microbiota avatar mice by depriving the murine microbiota using broad-spectrum antimicrobials and antifungals and recolonizing with stool from obese or non-obese human subjects or control saline. They fed mice high-fat diets (HFD) or regular chow over five days, after which they sampled several tissues, including VAT, for immunological analysis.

The researchers investigated whether the VAT-isolated neutrophil expression might be detected elsewhere in the body. They developed a custom-signature technique for detecting VAT-isolated neutrophil (VIN)-type neutrophils in other transcriptome datasets. They used it to access publicly

accessible tumor-biopsy RNAseq data [from the Genotype-Tissue Expression Project (GTEx) and the Cancer Genome Atlas (TCGA) dataset] to examine VIN-type neutrophils.

Findings

Obese individuals showed higher circulating leptin, insulin, and triglycerides, decreased adiponectin, and higher insulin resistance. They were older, had higher neutrophil abundance, and reported increased plasma zonulin and lipopolysaccharide-binding protein. Obese individuals showed Streptococcaceae and Ruminococcaceae more prevalent in their gut microbiomes. The team noted Marvinobryantia enrichment in lean VAT and Pseudomonas enrichment in VAT obtained from HFD mice gavaged with the fecal microbiome of obese individuals. Obese humans with increased neutrophilic recruitment in their visceral adipose tissues showed proteobacteria enrichment.

HFD caused bacterial translocation into the liver, leading to VAT neutrophil accumulation and pro-inflammatory T cell changes among obese humans and mice. Only mice fed a high-fat diet and feces from obese individuals exhibited higher VAT neutrophil counts. A VAT-isolated neutrophil signature was related to overall survival in obesity-related cancers, associated with elevated insulin, leptin, triglycerides, decreased adiponectin, and advanced age.

Transcriptome analysis revealed that VAT neutrophils have more inflammation- and activation-related genes than peripheral blood (PB) neutrophils. VAT neutrophil proportion is correlated with adipocyte interleukin-1 beta (IL-1β), IL-8, nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3 (NLRP3), and leptin (LEP) gene expression. Females with obese VAT had more neutrophils than lean individuals.

Human VAT neutrophils showed distinct gene expression related to inflammation, chemotaxis, extracellular matrix production, reactive oxygen species, growth factors, and apoptosis. These upregulated genes indicate partial neutrophil activation, while increased genes related to bactericidal activity suggest bacterial contact.

The VIN-type signature, distinct from PB neutrophils, was distinguished by pro-inflammatory mediators like IL-1β, IL-8, plasminogen activator, urokinase receptor (PLAUR), nicotinamide phosphoribosyl transferase (NAMPT), prostaglandin-endoperoxide synthase 2 (PTGS2), protein phosphatase-1 regulatory subunit 15A (PPP1R15A), triggering receptor expressed on myeloid cells 1 (TREM1), and superoxide dismutase (SOD).

Conclusion

The study findings showed that neutrophils have a crucial role in persistent low-grade inflammation in VAT from obese individuals and are associated with insulin resistance and cancer survival. The findings indicate that VAT neutrophils and bacteria might be therapeutic targets for treating inflammatory obesity consequences such as insulin resistance and colon cancer.

Source:

https://www.news-medical.net/news/20240703/White-blood-cell-type-identified-as-important-contributor-to-inflammation-in-obesity.aspx