Discovery of new immune process that regulates inflammation in human fat may help manage obesity

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Irish and German scientists have just identified how specific immune cells can work together in fat to cause inflammation that leads to weight

gain and obesity. Their work pinpoints new avenues to exploit the regulation of that inflammation in fat tissue, thereby suggesting new ways to manage obesity.

There is a global epidemic in obesity in adults and children, with obese people predisposed to develop diabetes, cardiovascular disease, and cancer. New therapies are needed to help tackle this issue.

In their research, the scientists identified how "checkpoint proteins" and immune cells alter inflammatory cells within the fat tissue to cause obesity. In people with obesity (Body Mass Index BMI> 30 kg/m^2) these changes in checkpoint expression in the visceral fat was predictive of the person's weight.

The scientists then showed that modifications in the so-called immune checkpoint proteins of mice on a Western "high fat" diet were linked to dramatic reductions in the development of obesity and diabetes.

The study, just published in the leading international biomedical journal *Science Translational Medicine,* was led by Professor Padraic Fallon from Trinity College Dublin's School of Medicine, and Dr. Christian Schwartz, a former EMBO Fellow in Trinity and now a Principal Investigator at the University Hospital Erlangen.

Prof. Fallon commented that "this new process of checkpoint regulation of cells in visceral fat of obese individuals advances our understanding of how the immune system controls diet-induced weight gain that can lead to conditions such as obesity and type 2 diabetes."

"Our discovery has broader impacts on addressing how obesity influences co-morbidity with other diseases, as shown in the COVID-19 pandemic, where obese individuals that are infected with SARS-CoV-2 are more likely to develop severe disease that requires intensive care and

also have an increased risk of mortality."

Dr. Schwartz commented that "in our study, we analysed the function of immune checkpoints on specific cells and it is fascinating to see that a small change on one of many cell populations in the fat has such an impact on the outcome of the disease. Only through our basic research efforts using pre-clinical models, were we able to gain access to patients' samples and link our findings to human disease. It will be interesting to investigate now how we can manipulate this checkpoint on specific cell populations of interest to help people with obesity."

More information: Christian Schwartz et al, Innate PD-L1 limits T cell-mediated adipose tissue inflammation and ameliorates diet-induced obesity, *Science Translational Medicine* (2022). DOI: 10.1126/scitranslmed.abj6879

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