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Naturally occurring peptide may tackle the "root cause" of obesity-related diseases

Obesity typically occurs when a person eats more calories than they need for their daily activity. It results in a build-up of fatty tissue around all organs. In lean people, fat tissues work closely with hormones to maintain tissues in a healthy, anti-inflammatory state. In obesity this is lost, and the fat takes on a different personality that drives inflammation throughout the body. As such obese individuals are a greater risk of developing other diseases, such as type-2-diabetes. There is an urgent need to find new drugs for people at risk of developing these diseases, but who are struggling to reduce their weight through diet and exercise alone.

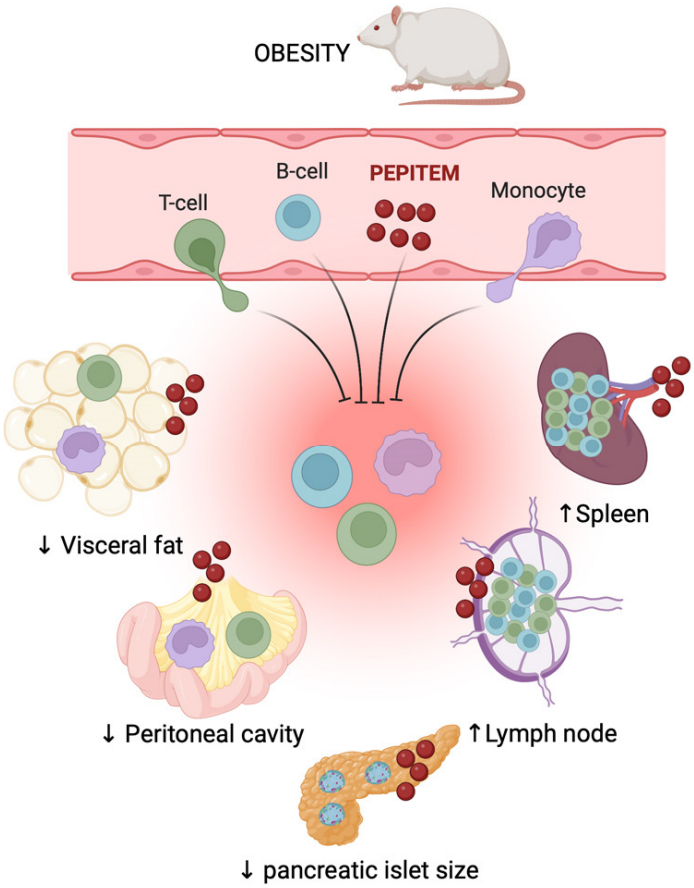

Fig. 1. PEPITEM reverse obesity induced inflammation by decreasing immune cell migration to peripheral tissues and increasing numbers in lymphoid tissues

Using an animal model of obesity, we examined the effect of a novel immunopeptide, PEPITEM, on the ability of immune cells to enter a variety of tissues, including the fat, peritoneal cavity (a thin membrane that contains the stomach, liver, and gut), spleen and lymph nodes[1]. When we treated mice with PEPITEM at the same time as putting them on high fat diet (i.e., before they are obese), we saw that PEPITEM reduces the

number of specific types of immune cells (T-cells and macrophages) in visceral fat and in the peritoneal cavity[1]. When we therapeutically treat obese mice with PEPITEM, we observe a similar reduction in the numbers of immune cells in these tissues. In contrast, PEPITEM therapy increased the numbers of certain immune cells (T-cells and B-cells) within the spleen and inguinal lymph node when compared to untreated obese controls. These data suggest that PEPITEM can reverse the pro-inflammatory effects of a high-fat obese diet, altering immune cell entry into a variety of tissues across the body to minimise systemic damage.

Obese patients are at greater risk of developing type 2 diabetes, which causes the growth of the number and size of insulin-producing cells of the pancreas leading to more insulin to being produced. We also examined the number and size of these insulin-producing cells in mice fed a high fat diet. Prophylactic or therapeutic treatment with PEPITEM reduced the size of insulin-producing cells[1], suggests that PEPITEM may offer a new therapy that could halt the onset of type-2-diabetes in obese individuals.

As an endogenous molecule (akin to insulin), therapeutic administration of PEPITEM or PEPITEM-based drugs may provide the opportunity to re-establish control over both local and whole body (systemic) metabolic and inflammatory processes underlying pathogenesis of obesity, and if given early enough could prevent the onset of obesity-associated diseases. Many of our current therapeutic strategies for obesity-associated chronic inflammatory diseases target the symptoms of the disease: excessive weight, elevated pro-inflammatory cytokine levels or pathogenic immune cell populations. PEPITEM represents a new strategic approach, focusing on restoring natural negative regulators of inflammation to act as a brake on the damage induced by obesity and its associated diseases.

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