Type I interferons fuel adipose inflammation in obesity

When people get fat the visceral adipose tissue (VAT), fatty deposits inside the body that cling around the internal organs, get inflamed. This chronic low grade inflammation is termed metaflammation. Metaflammation has been found to contribute to eventual insulin resistance and high blood sugar in these people. But the mechanistic link between increased getting fat and this chronic inflammation in the visceral fat tissues remains largely unclear. In this study we discovered that in obese individuals deregulation of a specific adipokine, chemerin, contributes to innate initiation of metaflammation, by recruiting circulating plasmacytoid dendritic cells (pDCs) into visceral adipose tissue via chemokine-like receptor 1 (CMKLR1).

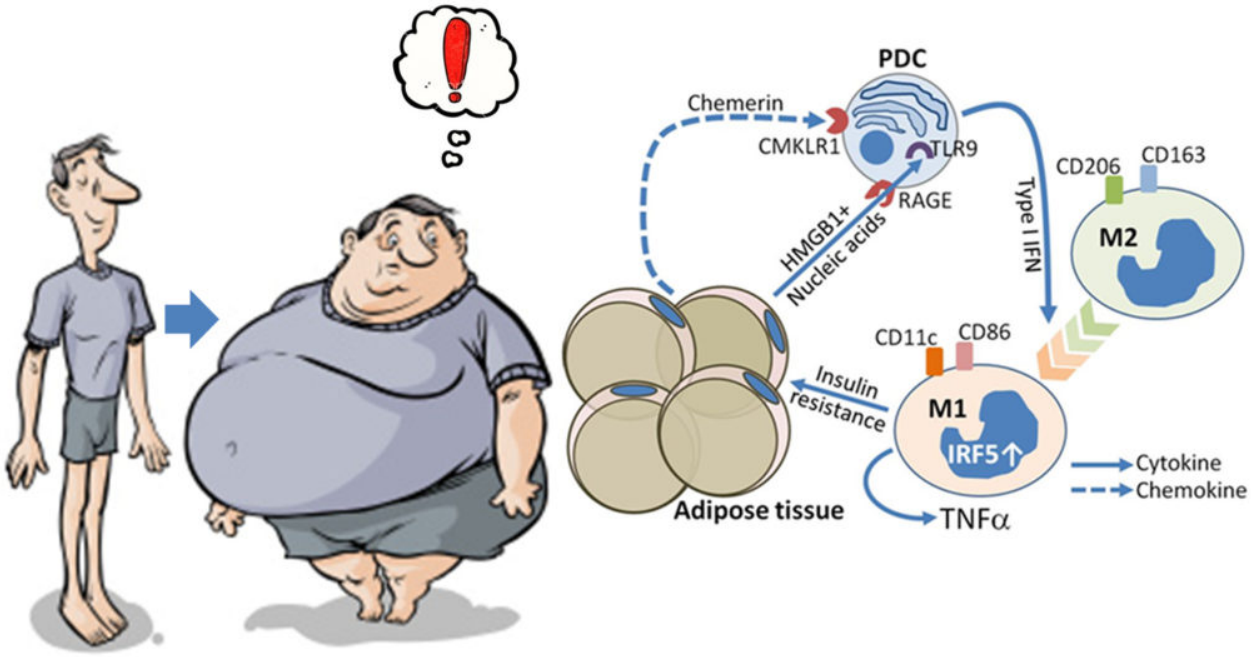

Fig. 1.

Adipose tissue-derived high mobility group B1 (HMGB1) protein, activates toll-like receptor 9 (TLR9) in the adipose-recruited pDCs by transporting extracellular DNA via receptor for advanced glycation endproducts (RAGE) and induces production of type I interferons. Type I interferons in turn help in proinflammatory polarization of adipose-resident macrophages. Interferon signature gene expression in VAT correlates with both adipose tissue and systemic insulin resistance in obese individuals, represented by ADIPO-IR and HOMA2-IR respectively, and defines two subgroups with different susceptibility to insulin resistance. Thus we revealed a hitherto unknown pathway that drives adipose tissue inflammation and consequent insulin resistance in obesity. This study was done in collaboration with bariatric surgeons from ILS Hospitals Kolkata, an

endocrinologist and a rheumatologist from Institute of Postgraduate Medical Education and Research Kolkata.

Dipyaman Ganguly
Ramanujan Fellow, Dept.of Science & Technology, Govt. of India
IICB-Translational Research Unit of Excellence (IICB-TRUE), Kolkata, WB, India
Division of Cancer Biology & Inflammatory Disorders
CSIR-Indian Institute of Chemical Biology, Kolkata, WB, India

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