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High-fat diet-induced obesity displays altered adipocyte differentiation in the absence of Interleukin-1 Receptor I (IL-1RI)

K.A.J. Mitchelson[1], J.C. Ralston[1], C.R. Strain[2], Y.M. Lenighan[1], E.B. Kennedy[1], G.M. Lynch[1], F.C. McGillicuddy[1], P.W. O'Toole[3] and H.M. Roche[1]

[1]*Conway Institute of Biomedical and Biomolecular Research and Institute of Food and Health, University College Dublin, Belfield, Dublin, Ireland,* [2]*Teagasc Food Research Centre, Moorepark, Fermoy, Cork, Ireland and* [3]*School of Microbiology, University College Cork, Cork, Ireland.*

High-fat diet (HFD)-induced obesity is associated with chronic low grade inflammation within adipose tissue where proinflammatory interleukin 1β (IL1β) expression is present[(1)]. Absence of IL-1 Receptor (*IL-1RI-/-*) protects against high-fat diet (HFD)-induced insulin resistance after 3 months HFD[(2)], but this protection was lost after 6 months HFD[(3)]. Wildtype (WT) mice were more glucose tolerant and insulin sensitive then IL-1RI-/- mice following 6 months HFD. Also, IL-1RI-/- mice showed a loss in adipose functionality, increased adipocyte hypertrophy and reduction in TNFα and IL-6 secretion from stromal vascular fraction (SVF). It was unknown if/how lack of IL-1RI disrupted pre-adipocyte differentiation. Additionally, it has been suggested that microbiome transfer can affect weight gain and phenotype in in mice with inflammation-induced disease. The purpose of this study was to determine how lack of IL-1RI altered adipogenetic potential and adipokine secretion in adipose tissue.

WT and IL-1R-/- mice were fed a HFD for 6 months (45 % kcal). A subset of cages cohoused WT and IL-1R-/- mice to determine whether microbiome transfer can affect phenotype. Glucose tolerance (1·5 g/kg) and insulin tolerance (0·5 U/kg) were tested. We investigated PPAR-γ and FASN gene expression in preadipocytes and differentiated adipocytes, lipogenesis in preadipocytes and differentiated adipocytes and IL-6 secretion in adipose tissue organ culture in wildtype versus IL-1RI-/-. Pre-adipocytes were isolated and differentiated from adipose tissue. Adipogenic marker expression was measured by real time PCR. Oil Red O absorbance measured triacylglycerol (TAG) accumulation. IL-6 secretion from adipose tissue (AT) explants following IL-1β/TNFα stimulation was measured by ELISA. Statistical significance was determined through one – and two-way ANOVA for PCR and GTT/ ITT respectively and unpaired t-test for TAG accumulation.

IL-1RI-/- mice had increased body weight ($P \leqslant 0{\cdot}05$) and AT weight compared to WT but both groups had similar glucose tolerance. IL-1RI-/- had higher insulin resistance but this was not statistically significant. Higher glucose tolerance was seen in both IL-1RI-/- and WT mice when they were cohoused together. Analysis of adipogenesis showed *Fasn* expression was 11- fold higher in differentiated adipocytes from IL-1RI-/- mice compared to WT mice. Conversely, *Ppar-γ* expression was 37- fold higher in differentiated adipocytes from WT mice compared to IL-1RI-/- mice. TAG accumulation was 50 % lower in differentiated adipocytes from IL-1RI-/- compared to WT. Adipose tissue explants had higher IL-6 secretion from WT then IL-1RI-/-. The microbiomes impact was determined and will be presented. IL-1RI-/- mice may have an increase in AT weight but adipocyte differentiation is impaired and Il-6 secretion is lower. The number of mature adipocytes and their affiliated inflammation is decreased. IL-1RI-/- may protect from HFD induced inflammation through disruption of adipogenesis. Co-housed mice total weight gain indicates a microbiome transfer which could provide a mechanism linking the beneficial alteration to adipogenesis and reduction of inflammation with a decrease in amount of adipose tissue.

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