Adipocyte 2:4, 266–271; October/November/December 2013; © 2013 Landes Bioscience

Galectin-3 is a regulator of metaflammation in adipose tissue and pancreatic islets

Nada N Pejnovic[1,2], Jelena M Pantic[1], Ivan P Jovanovic[1], Gordana D Radosavljevic[1], Aleksandar Lj Djukic[2,3], Nebojsa N Arsenijevic[1], and Miodrag L Lukic[1,*]

[1]Center for Molecular Medicine and Stem Cell Research; University of Kragujevac; Kragujevac, Serbia; [2]Institute of Pathophysiology; Faculty of Medical Sciences; University of Kragujevac; Kragujevac, Serbia; [3]Center for Endocrinology, Diabetes and Metabolic Diseases; Clinical Center; Kragujevac, Serbia

The cells of the innate and adaptive immune systems have been implicated in the development of obesity-induced metaflammation and metabolic disorders including type 2 diabetes. Galectin-3, a β-galactoside-binding lectin, modulates immune/inflammatory responses and specifically binds to advanced glycation end products (AGE), modified lipoproteins, and endotoxin. In the recently published study we demonstrate proinflammatory changes in the visceral adipose tissue and pancreatic islets in galectin-3-deficient mice fed high-fat diet which also exhibited excess adiposity, hyperglycemia, insulin resistance and systemic inflammation compared with their diet matched wild-type controls. This was associated with the increased incidence of Type-1 T and NKT cells and pro-inflammatory $CD11c^{+}CD11b^{+}$ macrophages in the visceral adipose tissue. Severe insulitis, infiltration of macrophages expressing NLRP3 inflammasome and IL-1β, and enhanced accumulation of AGE were present within the pancreatic islets in obese $LGALS3^{-/-}$ mice. Moreover, increased caspase-1 dependent IL-1β secretion with increased expression of NLRP3 inflammasome and phospho-NFκBp65 were observed in $LGALS3^{-/-}$ peritoneal macrophages stimulated in vitro by lipopolysaccharide and/or saturated fatty acid palmitate. The amplified high-fat diet-induced obesity and hyperglycemia and exacerbated inflammation in adipose tissue and pancreatic islets in $LGALS3^{-/-}$ mice suggest an important role for galectin-3 in the regulation of adiposity, metaflammation and type 2 diabetes.

Keywords: galectin-3, obesity, type 2 diabetes, inflammation, insulin resistance, NLRP3 inflammasome, NFκB, IL-1β

Submitted: 03/20/13

Revised: 04/30/13

Accepted: 04/30/13

http://dx.doi.org/10.4161/adip.24881

*Correspondence to: Miodrag L Lukic; Email: miodrag.lukic@medf.kg.ac.rs

Commentary to: Pejnovic N, Pantic J, Jovanovic I, Radosavljevic G, Milovanovic M, Nikolic I, et al. Galectin-3 deficiency accelerates high-fat diet induced obesity and amplifies inflammation in adipose tissue and pancreatic islets. Diabetes 2013; 62:1932-44; PMID:23349493; http://dx.doi.org/10.2337/db12-0222.

Obesity and its strong association with insulin resistance and type 2 diabetes have initiated the investigations of the underlying mechanisms of these disorders. Obesity itself leads to an inflammatory response, termed metaflammation, in metabolic tissues including adipose tissue, pancreatic islets, liver, muscle, and brain. Metaflammation is a low-grade, chronic inflammatory response that is induced by excess nutrients and often leads to the development of insulin resistance and metabolic disorders.[1] The pathophysiology, inflammatory triggers, and molecular pathways that associate metaflammation, diet, and type 2 diabetes are incompletely understood. It has been postulated that the degree of adiposity, the nature of immune/inflammatory response, and the composition of gut microbiota are the most important factors associated with the obesity-related pathologies.[2]

Obesity-Induced Inflammation in Adipose Tissue

Obesity is associated with the increased infiltration of immune cells into the adipose tissue and enhanced tissue expression of pro-inflammatory cytokines. Although the signals involved in the activation and attraction of immune cells into metabolic tissues are not fully elucidated, it is believed that adipocytes initiate