Hellenic Diabetological Chronicles 32, 3: 131, 2019

Pancreatic fat accumulation, extracellular matrix expression and inflammation in healthy, pre-diabetic and diabetic individuals

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The last decade we studied many different fat depots in the body and focused on ectopic fat accumulation because there is increasing evidence that this fat is associated with the development of type 2 diabetes. Our group could demonstrate by magnetic resonance imaging (MRT) quantification in cooperation with the Dept. of Radiology that the amount of pancreatic fat is inversely associated with insulin secretion in subjects with prediabetes. It has been suggested that pancreatic fat reduction may help to improve beta-cell function during a lifestyle-intervention. This fat compartment seems to be a modulator of endocrine pancreas function. In our recent studies we characterized pancreatic adipose tissue both in vivo and in vitro. In histological sections we could detect pancreatic fat cell accumulation in the pancreatic parenchyma but we found significant inter-individual differences in the fat amount. Furthermore, we detected also many monocytes/macrophages infiltrating the parenchyma and even the islets.

In our in vitro studies we examined the crosstalk of human pancreatic fat cells with islets isolated from human pancreatic resections and characterized their pro-inflammatory potential. We found that islets augmented the inflammatory response of pre-adipocytes, the precursor cells of differentiated adipocytes. We showed also in vitro that plasma components of obese prediabetic humans, such as fatty acids (palmitate) and the hepatokine fetuin-A, stimulate the production of cytokines and chemoattractants in pancreatic fat cells which may trigger inflammation. Furthermore, extracellular matrix affects metabolic function in many tissues. Pancreatic β-cells function maybe also influenced by a specific microenvironment composed of ECM surrounding the islet. Thus, we examined also many extracellular matrix components, like collagens, elastin, fibronectin, laminin and growth factors, e.g. TGF-β. The extracellular matrix distribution and amount was examined histologically in human pancreatic resections and mRNA expression was studied in cell cultures. We observed that the amount of matrix proteins expressed by fat cells varies between non-, pre-, and diabetic individuals and that the crosstalk with the fatty liver by fetuin-A influences the extracellular matrix expression predominantly in fat cells from pre-diabetic subjects which might influence islet function additionally. However, also human islets express and secrete inflammatory factors and extracellular matrix proteins influencing fat cell function.

In summary these data show that pancreatic fat cells, immune cells, the surrounding extracellular matrix and the interactions with islets seem to play a pivotal role in diabetes and obesity predominantly in pre-diabetic patients with fatty liver.