

The aim of the present project is to examine the influence of atRA treatment on the PVAT browning, changing of adipokine secretion and its modulation of endothelium function in mice model of atherosclerosis. Atherosclerosis considered before as a lipid storage disease, is nowadays generally accepted as an inflammatory disease. Because of it is long-lasting process in humans, development of animal models in which more rapid changes occur can be useful for the study of atherosclerosis pathogenesis. One of the most relevant models are apolipoprotein E-deficient mice that show impaired clearing of plasma lipoproteins and develop atherosclerosis in a short time, which give insight into the human process.

However, the precise role of BAT in atherosclerosis development remains unclear. BAT activation by β_3 -adrenergic receptor stimulation protects from atherosclerosis. Since the brown adipose tissue has been found in adult humans, significant efforts are being pursued to identify the mechanisms that promote a phenotypic change of white adipocytes into brown-like cells. It seems that activation of BAT is a promising new therapeutic way to battle with hypertriglyceridemia, obesity and cardiovascular diseases. Therefore, it seems important to find the agents that favor the acquisition of brown adipocyte-like features into white (or "predisposed" brite/beige) adipocytes. All trans-retinoic acids enhance expression of UCP1 in both WAT and BAT of mice. Retinoic acid, the carboxylic acid form of vitamin A, displays agonist activity toward several nuclear hormone receptors. In the present study, we test the hypothesis that atRA would lead to the transformation of perivascular white fat cells into brite cells in mouse model of atherosclerosis.

Perivascular adipose tissue (PVAT) normally surrounds large arteries and plays a critical role in the regulation of vascular function especially by synthesis and secretion of adipokines. Both brown-like and white-like PVAT secrete various factors that may prevent or promote the development of cardiovascular diseases (CVDs) depending on the adipocytes phenotype and their bioactivity in the neighboring vasculature. Notably, in pathophysiological conditions, such as obesity, hypertension or diabetes, there is an increase of the levels of PVAT-derived vasoactive products that promote the infiltration of inflammatory cells. This situation may induce vascular smooth muscle cells and ECs dysfunction, resulting in the development of vascular diseases. Therefore, we hypothesize that treatment with atRA might cause browning of PVAT and change to favorable PVAT-derived adiponectin profile that could modulated ECs in mice model of atherosclerosis. To test this hypothesis we use the endothelial cell culture and incubate it with PVAT culture medium. We also examine the signaling pathway by which adipokines from PVAT might alert ECs by using inhibitors.

We conclude that we hypothesized that activation of BAT is a powerful therapeutic avenue to ameliorate hyperlipidemia and protect from atherosclerosis.