Adipose tissue – muscle interactions

Ken Walsh, Whitaker Cardiovascular Institute, Boston University School of Medicine, USA

It is recognized that adipose tissue functions as an endocrine organ and that obesity contributes to cardiovascular and metabolic disorders through alterations in the levels of adipocyte-derived cytokines (adipokines). To better understand the interplay between body composition, metabolic function and cardiovascular disease, we created a mouse model of inducible skeletal muscle growth that we refer to as the "MyoMouse". In this model we find that activation of Akt signaling in muscle leads to a modest 5% increase in lean muscle mass, due to the selective hypertrophy of glycolytic type IIb fibers. Glycolytic muscle fibers grow in response to strength training and they are the fibers that are selectively lost during the aging process. In young obese mice, we find that the modest growth of type II fibers results in a marked reduction in fat mass and improvements in multiple metabolic parameters. These improvements result from the ability of type II fibers to modulate the metabolic properties of remote, metabolically important tissues. More recently, we have found that modest increases in the Akt-mediated glycolytic fiber growth can improve cardiac function following myocardial infarction and reverse aspects of the physiological declines that are associated with aging and muscle-wasting diseases. Thus, we have used the MyoMouse as a research engine to isolate "myokines" and other secreted proteins that may mimic the benefits of lean muscle mass/exercise training, and have been testing their utility in various disease models. I will give an update on the secreted proteins identified to date and provide details on their mechanisms of action.