**The role of microvesicles in physical inactivity-induced vascular maladaptation.**

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Physical inactivity is rampant in Canadian society with 85% of adults (20-79 years of age) not meeting the recommended 150 minutes of physical activity per week. This inactivity may be due in part to the environmental changes associated with urban sprawl. Loss of accessible parks and poor city planning limit opportunities to spontaneously engage in frequent physical activity. Habitual physical inactivity is a major contributor to chronic diseases, particularly those afflicting the cardiovascular system. Recent studies using bed rest have demonstrated profound systemic physiological impairments from physical inactivity including muscle mass and strength decline, as well as increased insulin resistance contributing to type 2 diabetes mellitus. Although insulin resistance typically occurs as a result of muscle insensitivity or insulin unavailability, a process partially regulated by vasculature, the role of vascular maladaptation in inactivity-induced insulin resistance has yet to be determined. Vascular function is partially regulated by microvesicles, as the molecules they transport facilitate cell-to-cell communication leading to structural and functional changes of blood vessels and their component cells. Whether concentrations of microvesicles are altered by physical inactivity, and the subsequent role this has in vascular maladaptation, is the question I aim to address in the proposed research. Specifically, I hypothesize that abrupt physical inactivity will have negative systemic effects on physiological functions including muscle, blood vessels, and insulin action. Further, I hypothesize that alterations in microvesicle concentrations as a result of decreased activity will contribute to vascular maladaptation following inactivity. Physically active participants will undergo a 21-day inactivity intervention in which their daily step count will be reduced. A variety of functional assessments, including oral glucose tolerance testing, microvesicle quantification, and transcytosis assays, will be employed to assess metabolic, muscular, and vascular function. These will be completed throughout the inactivity period and comparatively between active and habitually inactive individuals. The results of this study may begin to determine the mechanisms by which physical inactivity leads to increased disease risk.