Dr. Matrougui - Focus Areas

Despite major therapeutic successes, the causes and mechanisms of cardiovascular diseases, in most cases, remain unknown. The investigation of the causes of hypertension are complicated by contradictory findings for parameters (e.g. sympathetic activity and plasma renin activity) that are thought to be important for blood pressure regulation. However, increased peripheral vascular resistance, an important determinant of blood pressure, has been consistently observed in animal models and humans hypertension. Peripheral resistance is primarily determined by the distal part of the arterial vasculature consisting of the small resistance arteries (arteries with diameters (150 m) and the arterioles (the arteries leading into the capillaries). Therefore, alterations in the neurohormonal (e.g. angiotensin II and bradykinin) and mechanical (pressure or shear stress) systems that regulate resistance artery tone may play an important role in pathogenesis and progression of cardiovascular disease. The control of resistance artery tone is dependent upon a complex a dynamic interaction between endothelial cells, smooth muscle cells and matrix-extracellular. Shear stress- and bradykinin-acetylcholine-induced vasodilation are mediated by activation of nitric oxide release from endothelial cells. Whereas, pressure-induced contraction, termed myogenic tone, and Ang 11-induced contraction are mediated by direct effect on the smooth muscle cells. Both cell types may contribute to structural remodeling of arterial walls that occurs in response to chronic mechanical and/or neurohormonal stress associated with cardiovascular disease.

To investigate the control of the tone of resistance arteries, we used both intact arteries and smooth muscle cell culture models (isolated from mouse resistance artery). Our laboratory has concentrated on elucidating the mechanism of intraluminal pressure and/or flow in the control of resistance artery function as well as the artery wall remodeling. Representative current projects include: (A)Mechanism involved in contraction/relaxation of smooth muscle cells of resistance arteries; (B)Signaling cascades under acute or sustained Ang II, high glucose and stress oxidative (hydrogen peroxide) in vascular smooth muscle cells isolated from mice resistance arteries; (C)Role of intraluminal flow and pressure on resistance artery remodeling in hypertension and diabetes; (D)Role of PYK2, MAP-Kinase and Akt on flow-induced dilation, myogenic tone and wall artery remodeling.