Research Progress Summary:

Research Progress for Professor Yu Huang’s team:
We have worked heavily on the pathological mechanism of endothelial dysfunction in diabetes and hypertension and identified several potential biomarkers that impact vascular function in diabetes and diet-induced obesity. For example, we highlight the importance of uncoupling protein 2 in maintaining vascular function in diabetes and obesity. We demonstrate the molecular signalling cascade responsible for osteocalcin-induced transformation of vascular fibroblasts into myofibroblasts, a potential relevance of this bone hormone in the development of vascular remodelling and atherosclerosis in hypertension and diabetes. We also suggest the potential clinical application of calcitriol, the active form of vitamin D to preserve vascular function in hypertension and oestrogen deficiency, equivalent to menopause in women.

Research Progress for Professor Xiaoqiang Yao’s team:
Endothelium-derived hyperpolarizing factors (EDHFes) regulate vascular tone, blood perfusion and blood pressure. EDHF mechanisms are impaired in hypertension and diabetes mellitus. Among many EDHF mechanisms, the one involving endothelial cell KCa2.3 and KCa3.1 is the most important, regulating vascular tone in a variety of vascular beds. In this
study, we uncovered the physical and functional coupling of TRPV4 to KCa2.3 in endothelial cells. This type of physical association may allow Ca2+ entry through TRPV4 to stimulate neighbouring KCa2.3 in subcellular microdomains, causing endothelial cell hyperpolarisation. In addition, we found an important role of TRPV4-KCa2.3 signalling pathway in the control of local blood perfusion and blood pressure. A reduced TRPV4-KCa2.3 signalling may be an underlying reason for the impaired EDHF responses in diabetic rat models. In the future, it would be interesting to investigate the pathological role of impaired TRPV4-KCa2.3 signalling in human diabetes mellitus.
Recognitions:

Grants and Consultancy

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Publications:


Osteocalcin induces Ang II production which acts as an autacoid in the fibroblasts to activate PKCδ/TLR4/ROS/COX-2 signalling cascade to mediate fibroblast transformation. TLR4 stimulation further up-regulates TLR4 expression. OC, osteocalcin; ACE, angiotensin converting enzyme; Ang II, angiotensin II; AT1R, angiotensin II type 1 receptor; PKCδ, protein kinase Cδ; TLR4, toll-like receptor-4; ROS, reactive oxygen species; COX-2, cyclooxygenase-2; α-SMA, α-smooth muscle actin.

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