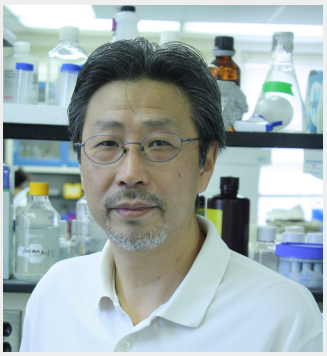
PAGE MORTON HUNTER DISTINGUISHED SEMINAR SERIES

VASCULAR STEM CELLS IN VEIN GRAFT REMODELING

Vein graft (VG) failure is associated with VG intimal hyperplasia, which is characterized by abnormal accumulation of vascular smooth muscle cells (SMCs). However, precise source of the neointimal SMCs and mechanism of the neointimal SMCs accumulation remain poorly understood. Herein we tracked down the fate of endothelial cells (ECs), vascular SMCs, and vascular stem cells (VSCs) expressing stem cell antigen 1 (SCA1) in VG remodeling and clarified their relative contributions to VG intimal hyperplasia. We demonstrated that after transplantation, most of the donor venous cells including ECs, SMCs, and VSCs die within 3 days, and the recipient arterial SCA1+VSCs are recruited to repopulate mainly the adventitia in VGs. The pre-existing mature SMCs, but not ECs, are the major cellular source of neointima cells. SCA1+VSCs do not differentiate into neointimal SMCs, but paracrine enforce media SMC dedifferentiation into neointimal SMCs. In addition, a unique subset of recipient adventitial SCA1+VSCs expressing cyclin-dependent kinase 8 (CDK8) is activated and migrates to the adventitia of VGs. Activation of CDK8 intensifies ISGylation in the SCA1+VSCs, which drives the VSC-mediated paracrine enforcement of SMC dedifferentiation, resulting in intimal hyperplasia toward VG failure. There findings uncover a novel intercellular communication between adventitial VSCs and medial SMCs in VG remodeling towards VG failure and CDK8 is a promising target for the treatment of VG failure.

Taixing Cui, M.D.



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Dr. Taixing Cui is a tenured professor at University of Missouri School of Medicine. He received his MD and completed his medical residency and fellowship in nephrology in China. He received his PhD and started his research career as an assistant professor in Japan. He then moved to US, starting with a research instructor at Morehouse School of Medicine, a research assistant professor at Michigan University School of Medicine, and a tenure track assistant professor and all the way up to tenured full professor at University of South Carolina School of Medicine. His research has focused on exploring novel therapeutic targets for cardiovascular disease. His research has been well funded and currently supported by a R01, a R03, and a VA Merit Award He has near 100 publications; several book chapters; and numerous invited talks and seminars. He served or serves on several grant review study sections including NIH R01 grant reviews and the editorial boards of several peer reviewed journals.

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