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Using induced pluripotent stem cells (iPSCs) derived endothelial cells (ECs) to repair cardiovascular injury

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Interleukin-8 receptors A/B (IL8RA/B) are homing device for neutrophils to target injured tissues. We developed an innovative targeted cell therapy using ECs that overexpress IL8RA/B to repair the cardiovascular injury. We transduced rat aortic ECs (RAECs), induced-pluripotent ECs (rat-iPS-ECs), or porcine coronary artery ECs (PCAECs) with adenoviruses carrying *IL8RA/B* genes. We hypothesize that healthy *IL8RA/B*-ECs can target injured arteries, thus inhibiting infiltration of neutrophils/macrophages and inflammatory responses, and accelerating re-endothelialization and suppressing the injury-induced neointima formation. In rat model, young male SD rats received balloon injury of the carotid artery and were immediately i.v. transfused with: 1) vehicle, 2) 1.5×10^6 control RAECs or rat-iPS-ECs, and 3) 1.5×10^6 *IL8RA/B*-RAECs or rat-iPS-*IL8RA/B*-ECs. One group of rats were sacrificed 24 hr post injury to measure infiltration of neutrophils/macrophages and pro-inflammatory cytokines expression. Another group was sacrificed 2 weeks post injury to measure neointima formation. In pig model, young Yorkshire pigs received stent implantation in the LAD and circumflex coronary arteries and were immediately i.v. transfused with 15×10^6 *IL8RA/B*-PCAECs or vehicle. Pigs were sacrificed 4 weeks after stenting to measure restenosis. Rats transfused with *IL8RA/B*-RAECs or rat-iPS-*IL8RA/B*-ECs had significantly decreased neutrophils/macrophages infiltration, inflammatory cytokines expression, and neointima formation in injured arteries. Pigs transduced with *IL8RA/B*-PCAECs had reduced injury-induced arterial restenosis. Results indicated that transfused adult ECs or iPS-ECs with overexpression of *IL8RA/B* mimic the behavior of neutrophils that target to injured vessels, preventing inflammation and restenosis. Targeted delivery of ECs to arteries with endoluminal injury provides a novel strategy for the treatment of cardiovascular diseases.

Biography

Yiu-Fai Chen has completed his PhD in 1982 from the Department of Physiology and Biophysics, University of Illinois (Urbana-Champaign) and Post-doctoral Training at the University of Alabama at Birmingham (UAB) School of Medicine. He is currently a Professor of Vascular Biology and Hypertension Program, Division of Cardiovascular Disease, Department of Medicine at UAB. He has been actively involved in Cardiovascular Research for more than 30 years and has been continuously funded by NIH, AHA, Pharmaceutical and Biotechnology companies since 1985, upon completion of his postdoctoral training. He has published 176 peer-reviewed articles in high impact journals.

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