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Author(s)	**Zhang, Y; Tse, HF; Lau, CP; Li, GR**
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Impact of glycaemic control on circulating endothelial progenitor cells and arterial stiffness in patients with type 2 diabetes mellitus

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WS Yue, KK Lau, CW Siu, M Wang, GH Yan, KH Yiu, HF Tse
Department of Medicine, Queen Mary Hospital, Hong Kong

Introduction: Patients with type 2 diabetes mellitus (DM) have increased risk of endothelial dysfunction and arterial stiffness. Levels of circulating endothelial progenitor cells (EPCs) are also reduced in hyperglycaemic states. However, the relationships between glycaemic control, levels of EPCs and arterial stiffness are unknown.

Methods: We measured circulating EPCs and brachial-ankle pulse wave velocity (baPWV) in 234 patients with type 2 DM and compared with 121 age- and sex-matched controls.

Results: Patients with DM had significantly lower circulating $LogCD34^+/KDR^+$ and $LogCD133/KDR^+$ EPC counts, and higher LogbaPWV compared with controls (all P<0.05). Among those 120/234 (51%) of DM patients with satisfactory glycaemic control (defined by haemoglobin A1c, HbA1c ≤6.5%), they had significantly higher circulating $LogCD34/KDR^+$ and $LogCD133/KDR^+$ EPC counts, and lower LogbaPWV compared with patients with poor glycaemic control (all P<0.05). The circulating levels of Log $CD34/KDR^+$ EPC (*r*= –0.46, P<0.001) and $LogCD133/KDR^+$ EPC counts (*r*= –0.45, P<0.001) were negatively correlated with LogbaPWV. While the level of HbA1c positively correlated with LogbaPWV (*r*=0.20, P<0.05) and negatively correlated with circulating levels of $LogCD34/KDR^+$ EPC (*r*= –0.40, P<0.001) and $LogCD133/KDR^+$ EPC (*r*= –0.41, P<0.001). Multivariate analysis revealed that HbA1c, $LogCD34/KDR^+$ and $LogCD133/KDR^+$ EPC counts were independent predictors of LogbaPWV (P<0.05).

Conclusion: In patients with type 2 DM, the level of circulating EPCs and arterial stiffness were closely related to their glycaemic control. DM patients with satisfactory glyacemic control had higher levels of circulating EPCs and were associated with lower arterial stiffness.

BK_{Ca} and hEAG channels modulate proliferation and differentiation of human bone marrow–derived mesenchymal stem cells

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YY Zhang, HF Tse, CP Lau, GR Li
Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Bone marrow–derived mesenchymal stem cells (MSCs) are a promising cell source for regenerative medicine. However, cellular physiology is not fully understood in human MSCs. The present study was to determine the potential role of the dominant functional ion channels, large-conductance Ca^{2+}-activated potassium (BK_{Ca}) channel, ether-à-go-go potassium (hEAG1) channel in regulating cell functions, including proliferation and differentiation, in human MSCs.

Methods: Ionic currents were recorded using a whole cell patch-clamp technique. Cell proliferation assay was made with MTT and ^{3}H-thymidine incorporation approaches. Cell cycle distribution was determined by flowcytometry. Lentivirus-based shRNA was used to knock down ion channels specifically. RT-PCR and Western blot analysis were applied. Adipogenic differentiation was visualised by Oil red O staining. Osteogenic differentiation was determined by alizarin red S staining.

Results: We found that paxilline and astemizole respectively reduced BK_{Ca} and hEAG1 current in human MSCs. The cell proliferation assay with MTT and ^{3}H-thymidine incorporation methods revealed that the inhibition of BK_{Ca} with paxilline and hEAG1 with astemizole decreased cell proliferation and reduced DNA synthesis rate in a dose-dependent manner. Flowcytometry analysis displayed that paxilline and astemizole accumulated human MSCs at G0/G1 phase, and decreased cell population of S phase. Moreover, lentivirus-based shRNAs targeted to BKCa or hEAG1 channel remarkably reduced both mRNA and protein expression of BK_{Ca} or hEAG1 channel; and proliferation of human MSCs was reduced by BK_{Ca}-shRNAs or hEAG1-shRNAs. We also found these effects were accompanied by a decreased expression of cyclin D1 and cyclin E. In addition, we found that knock-down of BK_{Ca} or hEAG1 channels reduced differentiation ability of hMSCs. The expression level of PPARγ or osteocalcin was decreased after the knock-down of KCNH1 or KCNMA1 respectively when hMSCs were induced to adipogenic or osteogenic differentiation.

Conclusion: Our results demonstrate that BK_{Ca} and hEAG1 channels participate in the regulation of cell proliferation by promoting G0/G1 cells into cell cycling progression, and are also closely involved in cell differentiation in human MSCs.