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Therapeutic integrin-mediated ECM remodeling pathway by transplantation of vascular angiogenic progenitor cells derived from hESCs on vascular ischemic disease

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Integrin mediated-ECM (extracellular matrix) remodeling is one of the critical steps on vascular re-construction in specific pathological condition including ischemic vascular disease, because ECM provides a stable environment for cell growth, differentiation and migration. After massive ischemic injury on blood vessels, cell transplantation using stem cell source into injured ischemic region can improve vascular function through cell engraftment and forming neo-vessels on injured site.

In this study, we derived vascular angiogenic progenitor cell population from hESC (hESC-VAPCs) and investigate their therapeutic effect and unique therapeutic mechanism on hindlimb ischemia disease model.

As the result, hESC-VAPCs were retaining representative vascular characteristics in vitro and therapeutic effect on hindlimb ischemic model mouse. Blood perfusion rate on hESC-VAPCs transplanted group was significantly improved than cord bold derived EPCs (CB-EPCs) and vehicle medium injection transplantation group. Furthermore, to fine out the therapeutic mechanism of hESC-VAPCs, we applied proteomic analysis tool between hESC-VAPCs and EPCs. Interestingly for this study, we could confirm that main therapeutic behavior was caused by up-regulated participation of several ECM and integrin mediated signaling pathway in hESC-VAPCs.

Together, these data suggest hESC-VAPCs could be a valuable novel cellular source for therapeutic treatment of vascular ischemic disease due to their participation of up-regulated several ECM molecules and integrin mediated pathway.