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# High fidelity episomal cb-ipsc generate vascular progenitors with reduced somatic memory and augmented capacity for regenerating the ischemic retina

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Although human embryonic stem cells (hESC), and human induced pluripotent stem cells (hiPSCs) share high molecular similarity, hiPSCs possess consistently more variable directed differentiation potencies than hESC. Incomplete reprogramming and retention of donor-specific epigenetic memory have been proposed as etiologies for poor or variable hiPSC potency to multiple lineages. We demonstrate that human cord blood (CB)-myeloid progenitors reprogrammed with an efficient episomal method and exhibit augmented hemato-vascular potency. Myeloid-hiPSCs expressed high-fidelity pluripotency circuit signatures, harbored few reprogramming errors, and lacked cancer-associated epigenetic signatures characteristic of standard hiPSCs. In contrast to hESC and hiPSC derived via standard methods, myeloid-hiPSC lacked lineage skewing and displayed unrestricted differentiation propensities to multiple non-hematopoietic lineages.

To evaluate the functional performance of high-fidelity myeloid-iPSC, we differentiated vascular progenitors (VP) from these hiPSC and compared them to a large repertoire of viral-integrated and non-integrated hiPSC lines. We identified a putative $CD31^{+}CD146^{+}$ VP population with high *in vitro* vascular potency. CB-iPSC generated VP with higher efficiencies than fibroblast-iPSC. Moreover, in contrast to fibroblast-iPSC-VP, CB-myeloid-iPSC-VP expressed higher levels of immature vascular markers, and demonstrated less culture senescence and DNA damage sensitivity. Luciferase transgene-marked VP from hESC, CB-iPSC, and fibroblast-iPSC were injected systemically or directly into the vitreous of retinal I/R-injured adult NOD-SCID mice. Only hESC- and CB-iPSC-derived VP reliably homed and engrafted into injured retinal capillaries, with incorporation into damaged vessels for up to 45 days. These findings demonstrate that derivation methods with more effective reprogramming capacities greatly improve the final functional pluripotency of hiPSC.

## Biography

Tea Soon Park has completed her Ph.D. in Dept. of Bioengineering at University of Pittsburgh in 2008 and postdoctoral studies in Institute of Cell Engineering at Johns Hopkins University School of Medicine. She is currently a Research associate at the same institute. Her research interest focuses on generation of clinically relevant induced pluripotent stem cells and generation of functional hematopoietic/vascular progenitors from iPSC.