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Mesoderm subset derived from human pluripotent stem cells from diabetic and nondiabetics improve retinal pathology in a model of type 2 diabetes.

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Human induced pluripotent stem cells (hiPSCs) isolated from diabetics and controls were differentiated into a specific mesoderm subset characterized by KDR$^+$CD56$^+$APLNR$^+$ (KNA$^+$) expression. These cells have robust proliferative potential and ability to differentiate into vascular wall derived reparative cells, called endothelial colony-forming cell (ECFCs). These cells incorporate into blood vessels when implanted subcutaneously into the flank of non-obese diabetic/severe combined immunodeficient mice. KNA cells$^+$ of diabetic or nondiabetic origin when injected into the vitreous of diabetic mice with retinopathy incorporated into blood vessels and increased the number of perfused

capillaries in the damaged retina. Transcriptomic analysis demonstrated that differentiation of hiPSCs derived from diabetics into KNA$^+$ cells reprogram diabetic cells to a pattern like KNA$^+$ cells derived from nondiabetic hiPSCs. Proteomic studies performed on retinas of diabetic mice injected with either control or diabetic donor-derived KNA$^+$ cells showed correction of aberrant signaling in diabetic retinas toward normal healthy retina. These studies support that KNA$^+$ cells and ECFCs can correct vascular dysfunction in diabetic mice.