Human pluripotent stem cell-derived erythropoietin-producing cells improve renal anemia in mice

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The production of erythropoietin (EPO), a principal hormone for the hematopoietic system, by the kidneys is reduced in patients with chronic kidney disease (CKD), eventually resulting in severe anemia. Although recombinant human EPO treatment improves anemia in patients with CKD, returning to full red blood cell production without fluctuations does not always occur. In this study, we established a method to generate EPO-producing cells from human induced pluripotent stem cells (hiPSCs) by modifying previously reported hepatic differentiation protocols. These cells showed increased EPO expression and secretion in response to low oxygen conditions, prolyl hydroxylase domain-containing enzymes inhibitors and insulin-like growth factor-1. The EPO protein secreted from hiPSC-derived EPO-producing (hiPSC-EPO) cells induced the erythropoietic differentiation of human umbilical cord blood progenitor cells in vitro. Furthermore, transplantation of hiPSC-EPO cells into mice with CKD induced by adenine treatment improved renal anemia. Thus, hiPSC-EPO cells may be a useful tool for clarifying the mechanisms of EPO production and may be useful as a therapeutic strategy for treating renal anemia.