



This report... demonstrates the feasibility of cell therapy in renal anaemia



RENAL ANAEMIA

iPSC-derived EPO-producing cells rescue anaemia

Production of erythropoietin (EPO) — the principal regulator of erythropoiesis — is reduced in patients with chronic kidney disease (CKD), leading to renal anaemia. Although recombinant human EPO (rhEPO) and erythropoiesis-stimulating agents can be used to treat anaemia, limitations of these approaches, including the need for frequent administration, have stimulated interest in alternative therapies. In a new study, researchers demonstrate that induced pluripotent stem cells (iPSCs) can be induced to secrete functional EPO and that transplantation of these EPO-producing cells into mice rescues renal anaemia. “This report is the first describing the generation of EPO-producing cells from iPSCs and demonstrates the feasibility of cell therapy in renal anaemia,” says Kenji Osafune.

EPO is predominantly produced in the kidney, but during development and in states of severe anaemia it is produced in the liver.

To generate EPO-producing cells from human iPSCs, Osafune and colleagues developed a modified protocol for differentiating iPSCs into hepatic lineages. “The process by which renal EPO cells are produced has not yet been fully elucidated, making it difficult to generate these cells from iPSCs,” explains Osafune. “We therefore used a hepatic differentiation strategy to generate our EPO-producing cells.”

Cultured cells generated using this protocol were able to secrete EPO, and increased the production of EPO in response to low oxygen and PHD inhibition, indicating that the iPSCs produce EPO through the oxygen-sensitive hypoxia-inducible factor (HIF)–PHD pathway. EPO produced by these cells induced the *in vitro* differentiation of human umbilical cord blood progenitor cells with similar efficacy to rhEPO. Moreover, transplantation of the iPSC-derived EPO-producing cells significantly improved the renal anaemia of mice with adenine-induced CKD. “Only one transplantation procedure was able to cure the renal anaemia of these mice for 7 months, which is impressive given the lifespan of mice,” says Osafune.

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ORIGINAL ARTICLE Hitomi, H. et al. Human pluripotent stem cell-derived erythropoietin-producing cells ameliorate renal anemia in mice. *Sci. Transl. Med.* **9**, eaaj2300 (2017).