

Technology Opportunity, Ref. No. UZ-17/487

***In vitro* hematopoietic stem cell expansion for safety/quality control and improved transplantation**

This invention permits the preparation of high amounts of proliferating homeopathic stem cells directly from routine blood donations without pre-treating donors

Keywords Homeopathic stem cells (HPCs), expansion, quiescence, proliferation, fatty acid metabolism, malonyl-CoA.

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Reference Knobloch et al. (2017), *Cell Rep* **9**: 2144-2155
Giger et al., (2019) *submitted*

Background Hematopoietic stem cell (HSC) transplantation is used in the therapy of many conditions including hematological malignancies, solid tumors, immune-deficiencies and hematologic diseases like anemias. HSCs can be extracted from bone marrow, peripheral blood, amniotic fluid or umbilical cord blood. However, HSCs need to be recruited from the donor's bone marrow into the peripheral circulation through treatment with granulocyte-colony stimulation factor (G-CSF). This treatment is expensive and has potential side effects. In vitro expansion of HSCs would make treatment with G-CSF less necessary and would thus lower the threshold to recruit healthy volunteers for HSC donations. Moreover, expansion of HSCs in vitro for several days would allow for safety and quality control checks of genetically modified HSCs – to correct genetic alterations – that may enter clinical use in the near future. A safe and reliable method for in vitro expansion of HSCs will be highly desirable.

Invention The inventors found that quiescent HSCs show high levels of carnitine palmitoyltransferase 1a (Cpt1a)-dependent fatty acid oxidase (FAO), which is downregulated in proliferating stem cells. Further experiments showed that malonyl-CoA, the metabolite that regulates FAO, can be applied to induce HSC proliferation in a controlled manner (Giger et al., *submitted*). Cells thus treated showed an increased potency to reconstitute the previously ablated bone marrow stem cell population upon serial transplantation in a mouse model. The effect of Malonyl-CoA on in vitro stem cell expansion was confirmed in vitro in human stem cells.

Fields of Use Kit for expansion of HSCs (allowing for either quality and safety checks upon genome modification or to expand HSCs prior to transplantation of HSCs obtained from routine blood-donations).

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