

## Developing hematopoietic stem cell cultivation in a bioreactor

<b>PhD candidate</b>	Brenda Juarez Garza Email: <a href="mailto:B.E.JuarezGarza@tudelft.nl">B.E.JuarezGarza@tudelft.nl</a>
<b>Promotor</b>	Prof. Marcel Ottens
<b>Co-promotor/Supervisor</b>	Dr. Marieke Klijin
<b>Institute</b>	Delft University of Technology Department of Biotechnology Bioprocess Engineering section
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### Project description

Blood transfusion is currently the most common cell therapy applied worldwide. According to the World Health Organization (WHO), around 118.5 million units of donated blood are collected globally every year (WHO, 2022). Severe anemias can only be treated with blood transfusions and stem cell transplantations. However, a lack of immune-matched cells often affects the use of these therapies. Furthermore, adverse risks involved in donor-derived transfusion products include immune reactions and the transfer of blood-borne diseases (Hansen et al., 2019). Employing *in vitro*-produced red blood cells represents an attractive therapy that could overcome these risks.

Embryonic stem (ES) cells can differentiate into all the cells in the body. Even though ES cells have the potential to treat various diseases, these are restricted due to ethical controversies and associated immune reactions (Li et al., 2017). Therefore, the development of induced pluripotent stem cells (iPSCs) started a new era in regenerative medicine. iPSCs are artificial cells that were created by reprogramming human somatic cells and have the potential to produce patient-specific progenitor or functional cells (Martins Fernandes Paes et al., 2017). Hematopoietic cell lineages can be generated *in vitro* from iPSCs. The *in vitro* production of hematopoietic stem cells (HSC) and red blood cells (RBC) from iPSCs opens the possibility of curing anemias through transplantation and transfusion, respectively (Wilkinson et al., 2019). Furthermore, the availability of patient-derived HSCs allows the study of erythropoiesis at the molecular and cellular level to develop new therapies to treat a broad range of hereditary anemias.

This project is part of the TRACER consortium (**T**reating hereditary anemias through stem cell research) and aims to develop a bioreactor process design to produce hematopoietic stem/progenitor cells (HSPC) and RBC from iPSCs. The protocol consists of several major experimental phases: i) iPSC maintenance, ii) embryoid body (EB) formation, iii) EB hematopoietic specification iv) expansion of HSPCs, v) expansion of erythroblasts and vi) terminal differentiation to RBCs. The main goal is to standardize the expansion and differentiation of iPSCs to control the reproducible culture of (HSPCs) in bioreactors. In order to achieve this goal, a strong collaboration has been set up with Sanquin and Getinge-Applikon.

### References

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