Computational Analysis of Stem Cell Production in Bioreactors

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Project Description

Rare monogenic anemias, such as sickle cell anemia (SCA) or Diamond Blackfan anemia (DBA), compromise erythropoiesis, the process in the body which produces red blood cells. For severe anemias, the treatment involves either regular red blood cell transfusions or a curative stem cell transplantation. However, both treatments are donor dependent and therefore availability of suited donor material is not guaranteed. Furthermore, alloimmunization, the body's immune response to foreign antigens of another human, further complicates these types of treatments.

The prospect of using iPCSs for the *in vitro* regeneration of the erythroid system opens new strategies for therapies. *In vitro* generation of functional hematopoietic stem cells (HSCs) and Red Blood cells (RBCs) would allow for gene correction of the patient's own cells, which would both alleviate the availability and the alloimmunization problem of donor material. Furthermore, in vitro generated HSCs/RBCs have great potential to be used as an efficient drug-delivery system.

This project is part of the TRACER consortium (**Tr**eating hereditary **a**nemias through stem **ce**ll **r**esearch) and is focused on using computational modelling to gain a better understanding of the limitations of HSC/RBC production in bioreactors. To this end, a combination of computational fluid dynamic (CFD) simulations and structured kinetic models will be employed to investigate the effect of the bioreactor cultivation conditions (hydrodynamics, mass transfer, mixing etc.) on the cellular response of iPSCs (growth, uptake kinetics, differentiation etc.). Ultimately, these insights can be used to optimize the bioreactor design and operating conditions for reliable high-density, low-cost stem cell production. In order to achieve this goal, a strong collaboration has been set up with Sanquin and Getinge-Applikon.

TRACER TREATING HEREDITARY ANEMIAS THROUGH STEM CELL RESEARCH Sanquin GETINGE TU Delft