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Stem Cells as a source to produce Red Blood Cells in vitro for Transfusion

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Blood transfusions have become indispensable to treat the anemia associated with a variety of medical conditions ranging from genetic disorders and cancer to extensive surgical procedures. In developed countries, the blood supply is generally adequate. However, the projected decline in blood donor availability due to population ageing and the difficulty in finding rare blood types for alloimmunized patients indicate a need for alternative red blood cell (RBC) transfusion products.

Increasing knowledge of processes that govern erythropoiesis has been translated into efficient procedures to produce cultured RBC (cRBC) using primary hematopoietic stem cells, embryonic stem cells, or induced pluripotent stem cells. In addition, proof-of-principle studies in lethally bled animal models suggest that these cRBC may represent alternative transfusion products. Compared to other cell therapies, however, transfusion poses the unique challenge of requiring great cell doses (2.5×10^{12} vs 10^{7} cells). Although production of such cell numbers is theoretically possible, current technologies generate cRBC in numbers sufficient only for quality control and safety studies. Since cRBCs have entered clinical evaluation, several issues related to their production are under intense scrutiny. Examples of issues that will be addressed in the future are the identification of stem cell sources more suitable for cRBC generation, the translation of cRBC culture methods into clinical grade production processes, and the development of protocols to achieve optimal cRBC quality, quantity, and maturation. We will discuss data on size, hemoglobin, blood group antigen expression and phosphoproteomic profiling obtained on cRBCs expanded ex vivo from a limited number of regular blood donors, including a donor with a rare blood phenotype, as examples of the type of measurements that are being generated as part of the quality control assessment of the suitability of cRBCs for transfusion. It is conceived that by the time all these quality studies will be completed, technical barriers to mass cell production will have been eliminated making transfusion with cRBCs a reality.