ABSTRACT

Blood supply shortage is emerging as an issue worldwide, partially due to an aging and shrinking population which diminishes the healthy blood donor pool available to national blood programmes. This pool has been predicted to be greatly reduced by the year 2050. To secure a safe and consistent supply of blood, various strategies have been explored, including the extension of the storage life of RBCs and the use of artificial oxygen carriers as red blood cell substitutes. But neither method has shown to be a permanent solution to the donor shortage problem. With development of various molecular tools, ex vivo generation of RBCs is also emerging as a promising technology to alleviate the blood supply shortage issue. While progress has been made in the production of enucleated RBCs from stem cells, much research is required to optimize the scalability of enucleated RBC production in a culture system, with emphasis on advanced studies into proliferation and maturation stimuli for erythropoetic progenitors.

Meanwhile, the contrasting stories of erythroid hyperplasic anemia and aplastic anemia presents an interesting topic to investigate the underlying mechanisms behind erythroid cell proliferation and maturation. Beta thalassemia is caused by a defective Beta globin gene that destabilizes alpha-tetrameric formation in erythroid cells and causes premature cell death. The continued stimulation of ineffective erythropoiesis leads to erythroid hyperplasic anemia. Conversely, aplastic anemia is a condition characterized by massive erythroid cell depletion in the marrow. While both conditions present anemia clinically, the cascade of events leading up to anemia is different for each case, resulting in two dissimilar marrow microenvironments. Thus, we hypothesized that through studying the differential expressional patterns of progenitors from each condition, we can determine the important mechanistic pathways underlying erythropoiesis and erythroid cell maturation.

In our study, we sought to discover the differential gene expression between Beta Thalassemia and Aplastic Anemia. To that end, we obtained the transcriptomic data of erythroid progenitor cells of beta thalassemia and erythoid anemia, from publicly available databases. We performed exploratory gene expressional analysis to identify differentially expressed genes in each condition. Pathway analysis was then conducted on each set of differentially expressed genes to identify significantly perturbed signalling nodes. These genes and pathways were compared against known literature on erythroid cell proliferation and maturation, to identify novel genes and pathways in our analysis. Future work will test the application of these genes in ex vivo RBC production.

(2359 characters) <2500