Novel derivation and gene editing of human haematopoietic stem cells and differentiation to immune cell types

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Summary:
Human hematopoietic stem cells (HSCs) will be isolated from umbilical cord blood and expanded in large numbers for clinical therapies. This project will use novel cutting edge technology to edit the genetic profile of HSCs to enable their universal transplantation across histocompatibility barriers and their differentiation into strategically sculptured cancer fighting immune cells.

Minimally manipulated and expanded cord blood derived HSCs will be obtained, through the Monash Department of Obstetrics and Gynaecology, for these PhD studies

Multiple samples of human umbilical cord blood are being banked by large private and public banks but are only being used sparingly for treatment of patients receiving chemotherapy for restoration of their bone marrow blood cell populations in a number of cancers. The more widespread use of banked cord blood samples is hampered by the need to partially match the HLA type to the transplant recipient. This project will involve testing the concept of gene editing the major histocompatibility antigens (type I HLA-A, HLA-B and type II HLA-DR). This would essentially create universal compatibility at the major HLA loci. HLA-C, which exists as two types HLA-C1 and C2, is more easily matched to recipients and the presence of HLA-C prevents destruction of HLA-A and HLA–B null (KO) cell types by Natural Killer (NK) cells, so would not need to be edited out for such cells to act as universal donor cells.

In addition, cord blood HSCs can be differentiated into T cells, NK cells, macrophages and other cells of the immune system. The PhD would involve the gene editing of cord blood HSCs and their differentiation, via their transformation into iPSCs, into functional immune cells for assessment of their ability to kill target cancer cells. Their immune compatibility will be tested in vitro and in in vivo models.

The studies will be undertaken in Labs at the Monash Health Translation Precinct.

References:

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