

Prerequisites for establishing a public human UCB SCB; assessment of public acceptance and resistance of UCB to HIV

By

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Psalm 33

- ¹ Sing joyfully to the LORD, you righteous; it is fitting for the upright to praise him.
- ² Praise the LORD with the harp; make music to him on the ten-stringed lyre.
- ³ Sing to him a new song; play skilfully, and shout for joy.
- ⁴ For the word of the LORD is right and true;
he is faithful in all he does.
- ⁵ The LORD loves righteousness and justice;
the earth is full of his unfailing love.
- ⁶ By the word of the LORD the heavens were made,
their starry host by the breath of his mouth.
- ⁷ He gathers the waters of the sea into jars^[a];
he puts the deep into storehouses.
- ⁸ Let all the earth fear the LORD;
let all the people of the world revere him.
- ⁹ For he spoke, and it came to be;
he commanded, and it stood firm.
- ¹⁰ The LORD foils the plans of the nations;
he thwarts the purposes of the peoples.
- ¹¹ But the plans of the LORD stand firm forever,
the purposes of his heart through all generations.
- ¹² Blessed is the nation whose God is the LORD,
the people he chose for his inheritance.
- ¹³ From heaven the LORD looks down
and sees all mankind;
- ¹⁴ from his dwelling place he watches
all who live on earth—
- ¹⁵ he who forms the hearts of all,
who considers everything they do.
- ¹⁶ No king is saved by the size of his army;
no warrior escapes by his great strength.
- ¹⁷ A horse is a vain hope for deliverance;
despite all its great strength it cannot save.
- ¹⁸ But the eyes of the LORD are on those who fear him,
on those whose hope is in his unfailing love,
- ¹⁹ to deliver them from death
and keep them alive in famine.
- ²⁰ We wait in hope for the LORD;
he is our help and our shield.
- ²¹ In him our hearts rejoice,
for we trust in his holy name.
- ²² May your unfailing love be with us, LORD,
even as we put our hope in you.

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I thank my heavenly Father for the gifts that He has given me, enabling me to do every work He has called me to. All the glory and honour be to the Lord from everlasting to everlasting, Amen!

Summary

South Africa is in dire need of a public umbilical cord blood stem cell bank (UCB SCB). A severe shortage of genetically compatible samples for BM transplantation precludes the majority of South Africans from receiving the relevant medical care. UCB is a viable alternative to BM but is currently disposed of post-delivery. UCB could furthermore serve as a resource of genetically compatible haematopoietic progenitor cells (HPCs) that could be used in gene therapy approaches directed towards a cure for HIV-1. Knowing whether HIV-1 affects or infects primitive HPCs is vital to determine the course of action for transplantation of UCB-derived genetically resistant HPCs. Collecting and storing UCB in a public UCB bank could thus serve as a vital resource of genetically compatible samples for BM transplantation.

It was thought that the high incidence of HIV-1 in South African patients and the persistent stigma surrounding HIV-1 would be problematic for collecting sustainable numbers of UCB units and subjecting units to compulsory screening for infectious diseases. This was however, not the case. In the South African context, we are faced with unique and rich challenges relating to cultural and religious differences that are further augmented by linguistic constraints and educational insufficiencies. Nevertheless, the majority of patients within the interviewed patient cohort were supportive of the idea of establishing a public UCB SCB in SA and were willing to undergo additional HIV-1 screening. The Ultrio-Plus[®] assay was verified in this study for screening UCB units for HIV-1 and could be used in routine analyses of UCB units prior to banking.

Conflicting results in the literature exist with regard to HIV-1's ability to infect or affect haematopoietic progenitor cells. Results from this study revealed that HIV-1 was not only able to affect HPCs' ability to form colonies *in vitro*, but was also capable of infecting CD34+ HPCs in some individuals. These results substantiate the theory that some CD34+ HPCs serve as viral reservoirs which could account for residual viraemia in patients on antiretroviral therapy. Results suggest that allogeneic transplantation of HIV-1 infected individuals with UCB-derived, genetically modified HPCs, should be pursued.

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List of abbreviations

AIDS	Acquired Immunodeficiency Syndrome
ASC	Adult stem cell
BFU-E	Burst-forming-unit erythrocyte
BM	Bone marrow
CFU-GEMM	Colony-forming-unit granulocyte, erythrocyte, monocyte, megakaryocyte
CFU-GM	Colony-forming-unit granulocyte-macrophage
CFU-MK	Colony-forming-unit megakaryocyte
CI	Confidence interval
ESC	Embryonic stem cell
FDA	Food and Drug Administration
G-CSF	Granulocyte-colony-stimulating-factor
GvHD	Graft versus host disease
GvL	Graft versus Leukaemia
HBV	Hepatitis B-Virus
HCV	Hepatitis C-Virus
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HPCs	Haematopoietic progenitor cells
HSCs	Haematopoietic stem cells
iPS	Induced pluripotent stem cells
ISSCR	International Society for Stem Cell Research
MTCT	Mother to child transfer
NAT	Nucleic acid testing
PBSC	Peripheral blood stem cells
SABMR	South African Bone Marrow Registry
SANBS	South African National Blood Services
SC	Stem cells
SCB	Stem cell bank
SCT	Stem cell tourism
TMA	Transcription mediated amplification
TNC	Total nucleated count
UCB	Umbilical cord blood
WMDA	World Marrow Donors Association
FBS	Foetal Bovine Serum
DMSO	Demethylsulphoxate