

Cord blood hematopoietic stem cell transplantation - Cures for thalassemia major and HIV infection

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Abstract: Like other forms of hematopoietic stem cell transplantation (HCT), unrelated donor umbilical cord blood hematopoietic stem cell transplantation (CBT) is a lifesaving therapy capable of curing many diseases, including ~80 standard indications, thalassemia major (Thal) and HIV infection.

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Unlike other HCT which require $\geq 10/12$ high resolution HLA A/B/C/DP/DQ/DR matches, CBT has been performed safely with $\geq 4/12$ HLA A/B/DR matches. As such, it lends itself to populations without large bone marrow registries and indications that may not have many donors, such as HIV patients and populations with high prevalence for Thal.

The first proven cured HIV patient is the “Berlin Patient”, who received a graft from an adult donor homozygous for the CCR5-Δ32 mutation [1,2], a technology first disclosed by Chow et al. in their 2001 U.S. patent application #09/998,832. Requiring far less rigorous HLA match than adult donors, CBT is the preferred HCT for this technology as the probability of finding an adult donor is exceedingly small with such rigorous matching and homozygous CCR5-Δ32 donor requirements. However, with only a few hundred CB donor units confirmed homozygous for CCR5-Δ32 mutations in the world’s inventory [3], one cannot opt for the best matched or highest Nucleated Cell Dose (NC) unit or use double CBT. Moreover, instead of the traditional method of a patient searching for a matched donor, our strategy uses the limited inventory to find and match the HIV patient who has a concomitant transplant indication.

Due to frequent transfusion and iron chelation requirements of Thal medical management; compliance, financial and quality of life issues are frequent for

patients. Hematopoietic cell transplantation (HCT) is the only cure for Thal, and is often performed with sibling grafts; however, only ~25-30% of the patients can find a suitable related donor. With relaxed HLA matching requirements, unrelated donor CBT has the potential to expand the use of HCT for Thal; however, transplant related mortality (TRM) of CBT for Thal has been high in previous series. As the critical determinant with CBT is NC, we have developed strategies to maximize NC and other critical cell doses and optimize clinical outcome. When certain strategies are combined, superior long-term survival of ~80-90% and low TRM of ~10% have been reported in the largest series of CBT for Thal [4,5]. Using matched pair analysis and multivariate analysis [6-8], the Chow group found MaxCell cord blood processing technologies [9], NC and CD34+ cell dose, post-thaw wash avoidance, HLA match, Pesaro class and center experience to be important in optimizing CBT for thalassemia [10].

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Biography

Robert Chow, M.D., A.M. is the Founder/Chairman/CEO of CyteTherapeutics. As the Principal Founder, former Chairman, President and CEO of StemCyte, a leading multi-national stem cell therapeutics company, Dr. Chow was instrumental in its rise among the Deloitte & Touche North America Fast 500 companies. Dr. Chow pioneered the concept of using homozygous CCR5- Δ 32 stem cells for HCT of HIV patients (Chow et al. US, PCT, EPO, Japan, etc... patent applications) - acknowledged by the physician of the Berlin Patient [2]. Inventor of the MaxCell Gen 2 Plasma Depletion/Reduction and Gen 3 Max cord blood technologies, Dr. Chow also developed combination strategies to maximize cell dose and improve patient survival and transplant-related mortality, and led the largest Multi-Center Clinical CBT Study for Thalassemia. As one of the first Cord Blood Bank Directors for the U.S. Federal Government National Cord Blood Inventory (NCBI), Dr. Chow's proprietary MaxCell cord blood products have been transplanted to thousands of patients (more than any other cord blood company), and used and trusted by around 300 world class transplant/medical centers in over 38 countries on all 6 continents. Having completed his internship, residency and fellowships at UCLA Medical Center, Dr. Chow holds a Doctor of Medicine from Harvard Medical School, and a Master degree in Cell and Developmental Biology from Harvard University Graduate School of Arts and Sciences.

Conference information

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