Terapia i Recerca amb Sang de Cordó Umbilical

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Background

- The principal limitations of allogenic Bone Marrow (BM) transplantation are the lack of HLA-matched donors and complications due to GVHD that are more severe with increasing HLA disparities

- Cord blood (CB) represents an alternative source of HPCs to BM for allogenic transplantation

History CB

The recipient of the first CB transplant was a young boy with Fanconi Anemia who received HLA-matched CB from his sister. He is currently healthy and cured of the hematological manifestations of Fanconi Anemia (1989)

CB has been used in HLA-matched and partially HLA matched siblings, as well as in related and unrelated HLA-matched and partially HLA-matched allogenic settings

State of art

To date, over 20.000 CB transplants have been performed to treat the same variety of malignant and non-malignant disorders treated by BM transplantation

There are more than 450.000 HLA-defined CB collections stored frozen in cryopreserved form in more than 50 CB banks world-wide

Advantages

- CB represents an **alternative source of HPCs** to BM for allogenic transplantation

- CB can be collected, **non-invasively**, at birth without any harm to the new born infant

- CB is **enriched in primitive stem/progenitor cells** able to produce in vivo long-term repopulating stem cells.

Advantages

- UCBT reduced incidence and severity of GVHD after HLA-matched or HLA-mismatched transplantation, because contains a lower number of activated T-cells in comparison with BM

- CB lymphocytes are more **naïve and immature**

- Extension of the donor pool due to tolerance of **1-2 HLA mismatches out of 6**

- **Higher frequency of rare haplotypes** compared to BM registries, because it is easier to target ethnic minorities

Disadvantages

Limitations of CB transplantation

- low number of cells collected in a single donor unit
- slower speed to engraftment of neutrophils and platelets.

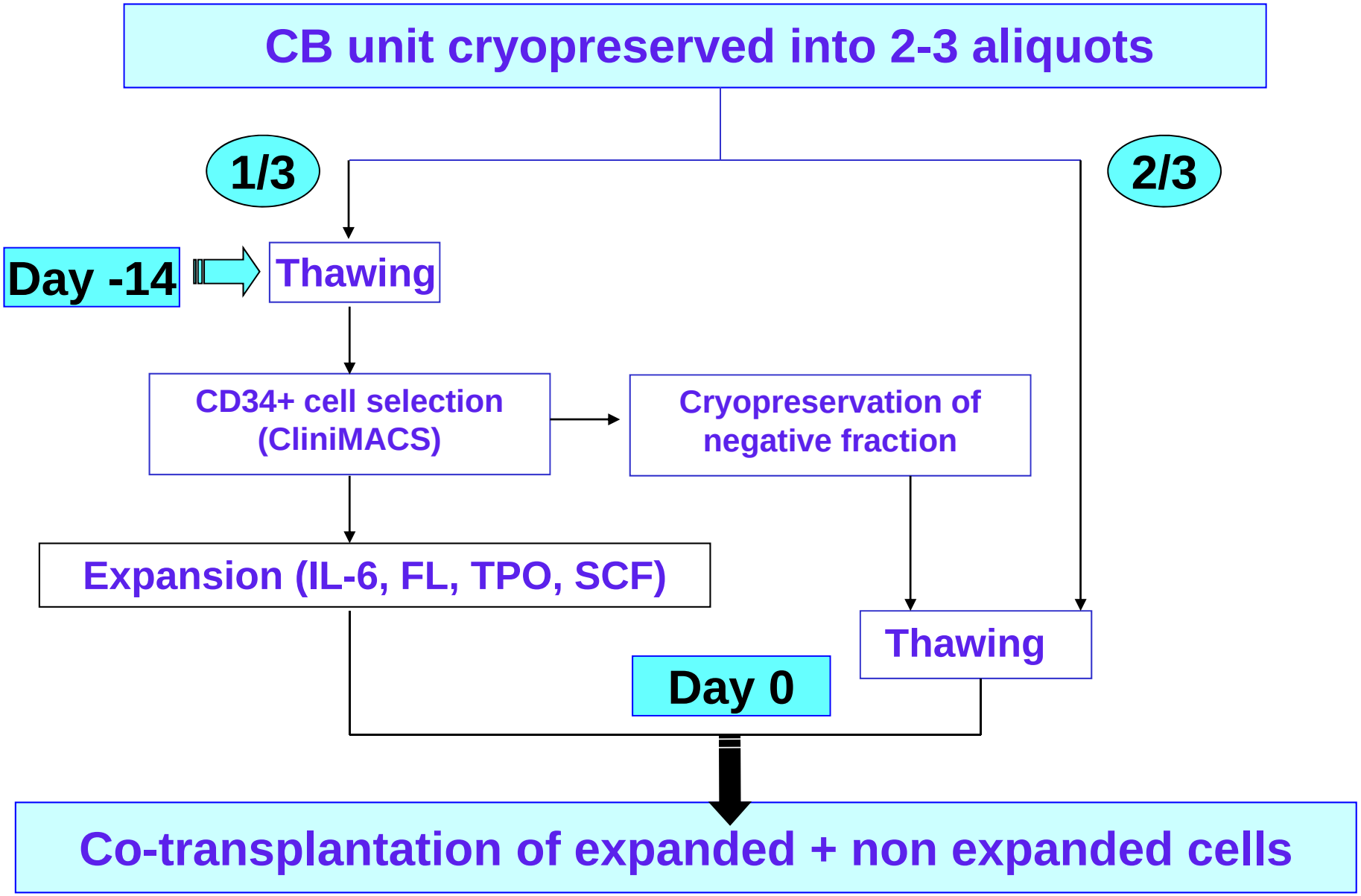
- Several studies have clearly documented that the higher the number of cells infused, the faster the rate of engraftment and the lower the risk of transplant-related mortality

How to improve the effectiveness of CB transplantation

1. Use of more than one CB unit (usually 2 CBs)
   -after one/two months of transplantation only one unit is present in the patient
   -increase of GVHD incidence
   -no improvement of time of engraftment

2. ex-vivo expansion of HSCs and HPCs compartment
   -this approach includes combination of cytokines such as SCF, TPO; Flt3

Clinical protocol: study design



Alternative potential uses of CB cells

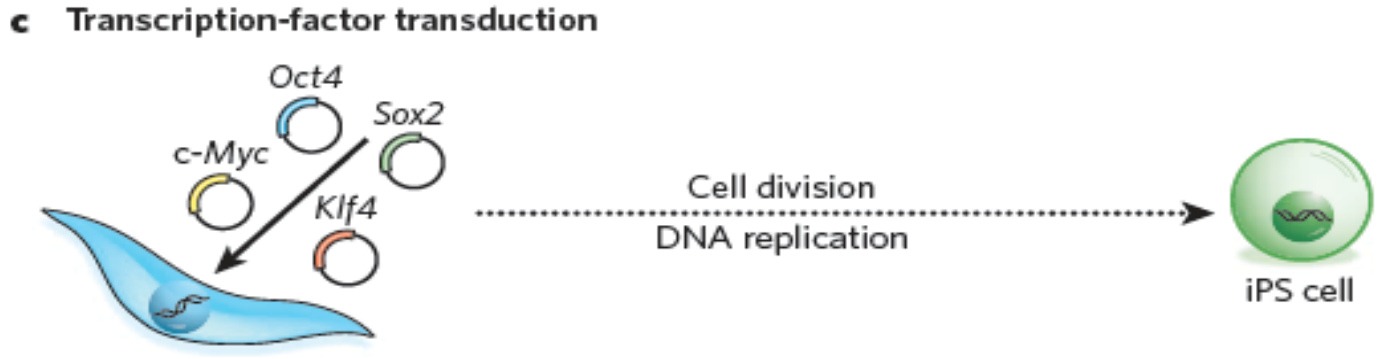
1. Stem/progenitor cells in CB that are not HSCs or HPC such as MSC and EPCs

   -CB derived MSC can generate *in vitro* bone, fat and cartilage. CB-MSC are still not well defined and the frequency is lower in comparison with BM

   -EPCs are derived from CB CD34+ cells but there are still controversies as the role of these cells in neoangiogenesis

Alternative potential uses of CB cells

2. Induced pluripotent stem cells (iPSC) derived from CB cells



Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,[1] Koji Tanabe,[1] Mari Ohnuki,[1] Megumi Narita,[1,2] Tomoko Ichisaka,[1,2] Kiichiro Tomoda,[3] and Shinya Yamanaka[1,2,3,4,*]

Cell, 2007