

# Cord blood banking: justified or not justified?

## Introduction

There is a strong push to bank cord blood. Young couples who will soon be parents are counseled to bank cord blood as a possible health insurance for their baby. Promises are made that the preserved cord blood could be used to treat all sorts of diseases in adult life. However, emerging studies suggest that this may not necessarily be true.

A careful review of literature shows that various clinical trials using autologous bone marrow stem cells for various indications have failed to provide expected results. A recent publication by USFDA suggested that we need to do more basic research before moving to the clinics.<sup>1</sup> In fact few patients have become blind on transplanting adipose tissue derived mesenchymal cells.<sup>2</sup> The underlying reason why bone marrow cells have failed in various trials is because the hematopoietic stem cells (HSCs) are committed progenitors and are not stem cells in the true sense. Thus, although they have been extremely successful to recolonize the bone marrow and are a method of standard care—they do not have the ability to differentiate into other cell types and thus cannot regenerate other organs.

Bone marrow transplantation (BMT) was renamed as ‘stem cell therapy’ and it was postulated that besides treating blood disorders, BM stem cells could cure variety kinds of age-related non-hematopoietic diseases due to the inherent plasticity of HSCs to transdifferentiate into multiple cell types. It was reported that BM stem cells differentiate into all mature blood cells, marrow stromal cells and also into non-hematopoietic cells of ectodermal, mesodermal, and endodermal tissues including liver, pancreas, kidney, lung, skin, gastrointestinal tract, heart, skeletal muscles, and neural tissues.<sup>3</sup>

Various mechanisms were proposed to explain the plasticity including:

- a. Existence of pluripotent stem cell population in bone marrow.
- b. Committed HSCs can Trans-differentiate implying they can change gene expression pattern to a completely different cell type either directly (direct transition into different cell types) or indirectly (first dedifferentiate and then mature along a differentiation path).
- c. Fusion of bone marrow cells with a non-hematopoietic cell to form a heterokaryon and thus the gene expression pattern of original BM cell gets converted to the fusion partner.<sup>4,5</sup>

Armed with this understanding and since BMT is safe, several autologous bone marrow/ cord blood nucleated cells trials were undertaken and the cells were transplanted in patients with varied clinical conditions like for cardiac regeneration, spine injury, neuronal etc. However, various reports suggest that such studies have failed to deliver the desired results.<sup>6,7</sup> and BMT can only treat hematological disorders. This conclusion was not surprising and is in agreement with recent review discussing that HSCs are committed progenitors.<sup>8</sup> and thus are not expected to exhibit any ‘plasticity’ to transdifferentiate into cells of other lineages.

Besides using BM, a huge spurt in banking cord blood in public and private banks has also been observed. Compared to BM/PB which requires a high degree of HLA match, umbilical cord blood (UCB) requires only 4 of 6 HLA class I and II molecules to be matched

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because it has lower number of T cells and relatively naïve status of lymphocytes. There exists a competition between public and private cord blood banks. Aggressive marketing, misinformation and making tall claims motivate individuals to bank in private cord blood banks for self-use later on. Whereas the truth is that self-use is highly unlikely and samples will potentially be wasted. Also when the baby grows old, a single unit of cord blood does not suffice. Rao et al.<sup>9</sup> at National Center for Regenerative Medicine (NCRM), NIH USA proposed to generate iPSCs from cord blood cells to meet the huge unmet demand of hematopoietic cells for blood disorders however NCRM with 400 iPSC cell lines closed down in 2014.<sup>10</sup> Ivan rich at Hemogenix, USA has a very different view on UCB banking. He recently concluded that the UCB used for stem cell transplant is neither tested for stem cell content nor its quality/ potency. Only cord blood samples with high total nucleated cells (TNC) fraction/count get preserved in Public banks. Clinicians also prefer a unit with high TNC for transplantation. However, one needs to understand that TNC does not help to engraft – it is only a small sub-population of stem cells that will ultimately get engrafted. These stem cells need to be evaluated carefully in the samples being banked. However, at present main focus is to enrich CD34+ hematopoietic stem cells,<sup>11,12</sup> study their viability and a CFU assay to routinely characterize samples prior to banking and almost 24% of UCB transplantation cases succumb to graft failure.<sup>13</sup> Private cord blood banking is banned in Italy and France and these banks cannot inform couples that it will provide ‘life insurance’ in USA and UK. Solves et al.<sup>14</sup> associated with a cord blood bank in Spain mentions that initial depletion of RBCs for volume reduction is advantageous.

The ability to regenerate various tissues lies with a sub-population of very small sized, pluripotent stem cells termed VSELs.<sup>15</sup> VSELs express pluripotency markers and also differentiate into 3 germ layers in mouse as well as humans. However, these stem cells are invariably discarded while processing samples.<sup>16,17</sup> Thus similar to the outcome of autologous bone marrow cell trials, cord blood hematopoietic stem cells will have no regenerative potential other than to restore hematopoiesis. Methods need to evolve to bank VSELs which are currently being discarded while banking cord blood for future use.

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## Conflict of interest

Author declares there is no conflict of interest.

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