Stem Cells – What, Why, Whereabouts and When? – Part III

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Ethical and Safety issues

I will not be discussing the ethical issues with embryonic stem cells and personhood in detail here. However other ethical issues relating to stem cell therapy should be noted.

A possible cause for concern with stem cell therapy involves the risk of cancer.[1] Whilst this was hardly considered till a few years ago, nowadays, the literature teems with papers about tumour stem cells.

Mouse experiments involving the injection of stem cells or their progenitors clearly show the link with teratomas.[2]

In the case of embryonic stem cells, prolonged *in vitro* culture can be associated with genetic changes making embryonal stem cells similar to embryonal carcinomas.[3] This raises important questions about safely using embryonic stem cell lines propagated for a long time in vitro as a source of donor stem cells.

Although the amount of therapeutic studies using embryonic stem cells is presently very small, and no such statistics can be calculated, there is theoretically an increased risk of cancer developing from stem cells.

The increased plasticity of adult stem cells and the possibility of creating patient-specific stem cells through processes similar to therapeutic cloning may make this a mute point in the near future.

Regarding tumour stem cells, the author's personal opinion is that tumour cells, upon becoming immortal obtain much of the properties of stem-ness. However, many papers now specifically describe a specific sub-population of tumour stem cells.[4,5] Whichever of these positions is the more accurate, there is little doubt that the more primitive a cell, the more propensity it has for malignant transformation. Due to this, detailed and extensive studies following transplantation of early stem cells (autologous or heterologous) will be required before the procedure will be accepted as one with minimal associated risk.

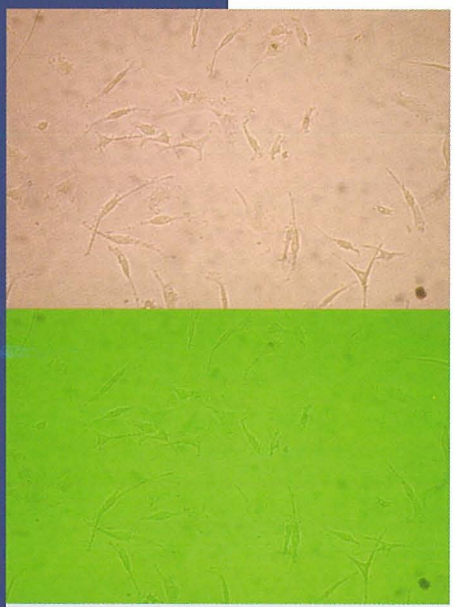

Figure 1: *Cord blood mesenchymal cells cultured in University of Malta Laboratories*

Stem cell collection and banking

With all this stem cell-related research ongoing throughout the world, are there any measures worth taking up locally?

In the author's opinion, the obvious and relatively easy option is to start up public cord blood banking. In fact a proposal document had been submitted to the health authorities by the author on behalf of a private charity a number of years ago.

Cord blood banking has been developed over the last decade or so in a number of countries around the world, including Italy, the Netherlands and the UK. Recognition of the usefulness of this resource were heralded by titles such as 'turning garbage into clinical gold' in some of the world's most prestigious scientific journals.[6]

Cord blood banking can be separated into private and public banking. Private/individual banking normally involves the preservation of the cord blood from a child's placenta at birth and keeping those blood cells for the child in question. This involves an initial payment and sometimes a recurrent payment to cover cryopreservation. Since the blood is only tested for infective organisms and does not need to be cross-matched against other individuals, it is relatively cheap to bank such blood.

In 1999, the American pediatric association issued a recommendation stating 'Families may be vulnerable to emotional marketing at the time of birth of a child and may look to their physicians for advice. No accurate estimates exist of the likelihood of children to need their own stored cells. The range of available estimates is from 1:1000 to 1:200 000. Empirical evidence that children will need their own cord blood for future use is lacking. There also is no evidence of the safety or effectiveness of autologous cord blood transplantation for the treatment of malignant neoplasms. For these reasons, it is difficult to recommend that parents store their children's cord blood for future use'.[7]

recognition of the different types of stem cells found in cord blood and their much greater plasticity potential. However even much more recently, the Canadian Society of Obstetricians and Gynaecologists issued the following amongst a long list of recommendations'.[5] Altruistic donation of cord blood for public banking and subsequent allogeneic transplantation should be encouraged when umbilical cord blood banking is being considered by childbearing women, prenatal care providers, and(or) obstetric facilities.[6] Collection and long-term storage of umbilical cord blood for autologous donation is not recommended because of the limited indications and lack of scientific evidence to support the practice'.[8]

Public banking is much more expensive on a per unit basis but provides a resource for the whole health service. Due to the relative immunological naivety of cord blood, a perfect 6/6 major HLA match is not required for successful transplantation. 4/6 matches are often successful.

Studies by the Turin cord blood bank have in fact found that with just 500 units (1/10th of the amount of cord units which could be collected in a year in Malta) one would be able to successfully cross match about 90% of the Italian population, ie more than 50 million people.[9]

Until recently, cord blood was only found adequate for transplant into children and small adults of less than 50kg body mass, due to a need for more stem cells to adequately replace bone marrow in a larger individual.[10]

Recent studies however are suggesting a wider range of potential recipients due to a number of modifications including the simultaneous transfusion of more than one cord blood unit into the same patient[11] as well as ex-vivo expansion of the stem cell population.[12,13]

Mesenchymal stem cells (MSCs), presently being used in numerous clinical trials (in heart, bone and cartilage regeneration amongst others) are also found in cord blood. These cells, require culturing in the lab however before cord blood freezing, something already being done on a research basis on donated cord blood samples at the University of Malta (Figure 1).

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At the recent meeting in Rotterdam of the Tissue Engineering and Regenerative Medicine International Society, F. P Barry from Galway's National Centre for Biomedical Engineering Science, showed very interesting (presently unpublished) data which indicates that in rat experiments, MSCs transplanted 10 minutes post myocardial infarction engrafted strongly into the heart whilst those given 2 weeks post-MI were much less actively taken up.

This may possibly explain why so many of the present clinical trials on humans with MSCs have been so disappointing so far. What I take this to mean is that, in future, having donor stem cells readily available on your doorstep might well be the most important therapeutic option. Growing your own bone marrow stem cells, or bringing your own stem cells over from abroad may not be much of an option.

So cord blood banking might just be the most useful stem cell-related health investment for the local health authorities. Private public partnerships may also provide a useful option, especially to allay costs. Here, public health authorities could take over cord blood units banked privately for individuals after a fixed time period or after private individuals decide to stop paying cryopreservation costs, thus forfeiting ownership. By performing HLA typing and by recording these units in a database, they will slowly build a local stem cell therapeutic resource, with the private sector having initially footed the start-up cost.

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