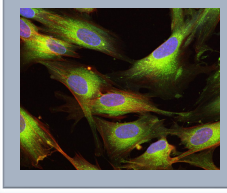
Stem cells technology for treatment neurodegenerative diseases



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Introduction

Stem cells field has their origin in the 60s when they was discover. But it was not until 90s when a revolution occur: isolation of stem cells and a cultivation of them was achieve. From this moment, the progenitor cell have been as the great hope of the new century therapeutics. Studies report some extraordinary information and the idea of treat neurological diseases with stem cells appear. Due to the burden of some neurological diseases, such as Parkinson, Multiple Sclerosis or Amyotrophic lateral Sclerosis diseases, the necessity of new therapies have increased. Nevertheless, the issue that hinder some therapies, like stem cell therapy is the lack of agreement about how is the most suitable way to proceed in the extraction, culture, way of administration and type of stem cell that is suitable to use. Here it is shown one process of this therapy and also, some recent progress.

Neurodegenerative diseases

- Parkinson disease
- Multiple sclerosis disease
- Huntington disease
- Amyotrophic lateral sclerosis

There is no effective treatment! Alternatives needed.

Types of stem cells

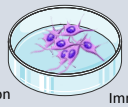
- Embryonic stem cells: pluripotent, inner mass cells (blastocyst)
- Adult Stem cells→ multipotent, different tissues:
  - Neural stem cells
  - Hematopoietic stem cells
  - **Mesenchymal stem cells (MSC)**

Characteristics of MSC

Low probability of tumour

Avoid ethical problems

Anti-inflammatory



Plasticity

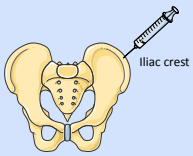
Genetic modification

Immunomodulation

Migration to sites of injury

Methodology

1-ASPIRATION



Aspiration of 10-200ml/patient

2-ISOLATION

Layering onto a limphoprep density gradient

Density gradient centrifugation in Ficoll-Plaque

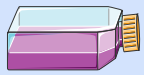
1 Remove anticoagulant medium 900g, 15 min

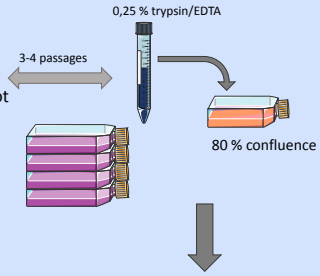
2 Percoll gradient :1100g, 30 min. Collect interphase and wash with *PBS

3- CULTURE and EXPANSION

*DMEM medium:

- 10 % fetal bovine serum or not
- 1 % penicillin/streptomycin





4-HARVEST

Cryopreservation in:

- 4,5% human albumin solution
- 10% dimethyl sulfoxide

Quantity:

- 1-2x10^6 cells/kg or
- 3-5x10^7cells/patient

Resuspended and washed in *DPBS → Remove *FBS

5-CHARACTERISATION

Flow cytometry:

- Presence of Surface markers: CD73,CD90,CD105,CD29,CD44,CD66
- Absence of: CD34,CD45,CD14,CD31

Viability:

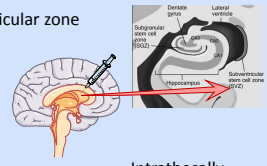
- Tripan blue
- Propidium iodide

Karyotyping

Endotoxin levels

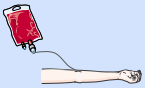
6-ADMINISTRATION

Subventricular zone



3h with basal medium without serum → washed with PBS→ Resuspended in autologous cerebrospinal fluid

Intravenously



Intrathecally

*DMEM: Dulbecco's Modified Eagle Medium; FBS: Fetal Bovine Serum; DPBS: Dulbecco's Phosphate Buffered Saline; EDTA: Ethylenediaminetetraacetric acid; PBS: Phosphate Buffered Saline

Discussion

Safety and feasibility have been reported in the vast majority of the studies. The engraftment of these cells in the injured tissue are not significant. However, the way that they act is via stimulate the endogenous cells, and contribute to neuroprotection. There are numerous reasons for optimism concerning the use of MSC for neural repair. The next step in this therapies is to verify if they can revert the diseases.

Conclusion

According to the studies, there is a lack of common protocols of doing this kind of therapy. In fact, in the summary of the method described above, it can be seen different kinds of protocols with the same objective. Nevertheless, results are positive and the best choice of stem cells to use seem to be the MSC. However, more preclinical studies should done in order to resolve some issues about MSC such as the effect of released factors or the plasticity of the cells. By the other hand, it is not yet completely known the way by MSC can integrate into the damaged central nervous system.

Relevant bibliography

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