Stem Cell Application for Spinal Cord Injury Treatment

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INTRODUCTION

Spinal Cord Injury is one of the main pathologies that affect the central nervous system. It can be produced due to a traumatic experience, and generally disrupts the flow of the nerve impulse through the organism, resulting in a lack of nervous functions such as the motor function or sensitivity. Currently there is no available therapy that reverts the severe symptoms of the injury, so medical efforts are focused on searching a cure for the disease.

Stem Cells are a population of undifferentiated cells capable to differentiate into several different kinds of cells and proliferate, so their regenerative capacity to restore anatomic structures damaged has opened a new way to treat these injuries.

This assay is a review of the current state of the research using all kind of stem cells in order to improve life quality of patient suffering from SCI.

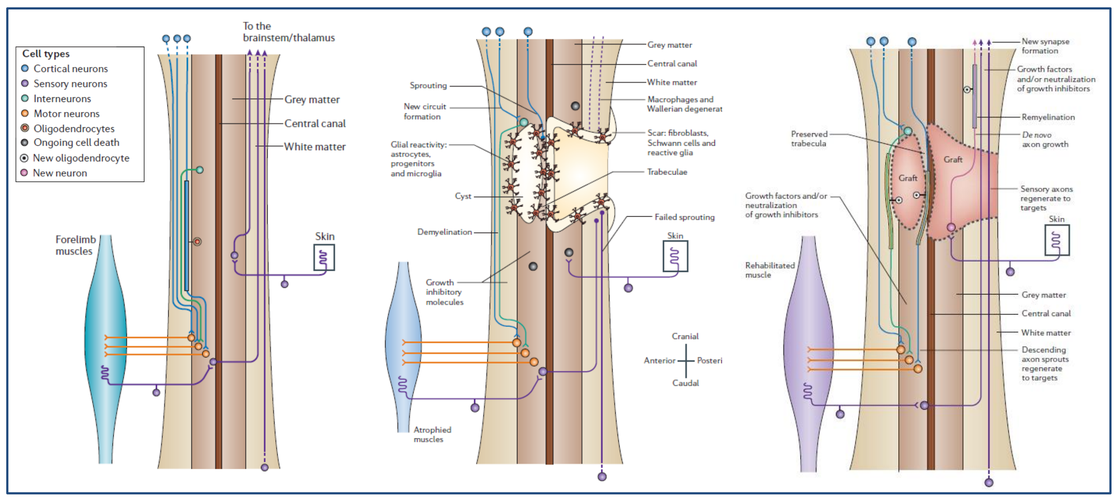

Fig 1. Healthy, Injured and Recovered after Cell Treatment Spinal Cord [1]

MATERIAL AND METHODS

For the realization of this study it has been made an intense research in the database clinicaltrials.gov, run by the National Institute of Health, that includes the main clinical trials that are being performed, as well as in the main electronic tools that store scientific articles. In addition, an expert has been interviewed, doctor Joan Vidal Samsó, Head of Spinal Cord Injury Unit in Guttman Institute, to a better understanding of future perspectives.

RESULTS

In Vitro Studies

In Vitro research with stem cells is focusing on organogenesis, in this case in developing complete spinal cord structures using stem cells. For the moment, just small goals have been achieved and the development of complete cords seems quite far. Embryonic stem cells have been differentiated into neuromesodermal progenitors and previous forms of spinal cord development as neural cyst or spinal cavities.

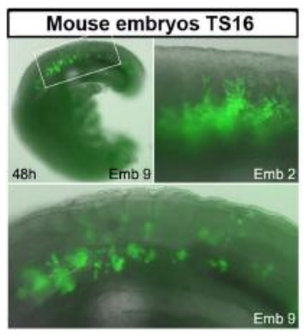

Fig 2. Neuromesodermal progenitors incorporation on mouse embryos [2]

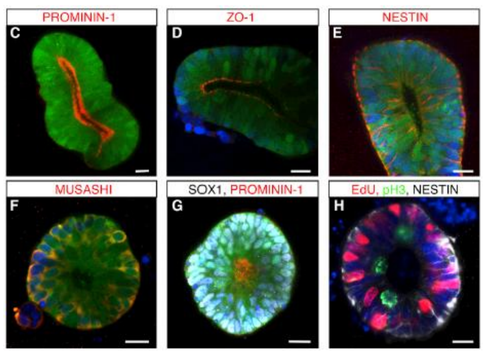

Fig3. Cyst formation from ESCs. It's shown the expressions of some markers of stem cells and neural identity [3]

iPSCs Studies

Just preclinical studies with iPSCs transplants to animals have been performed. iPSCs- derived cells show better results than adult stem cells on motor function recovery.

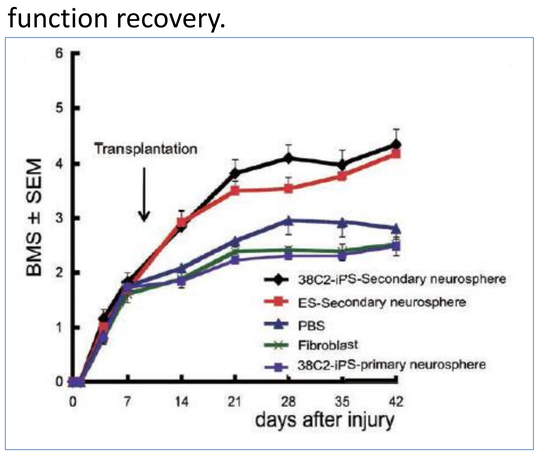

Fig 4. Functional recovery after iPSCs-derived neurospheres transplant gets similar values compared to ES-derived neurospheres [4]

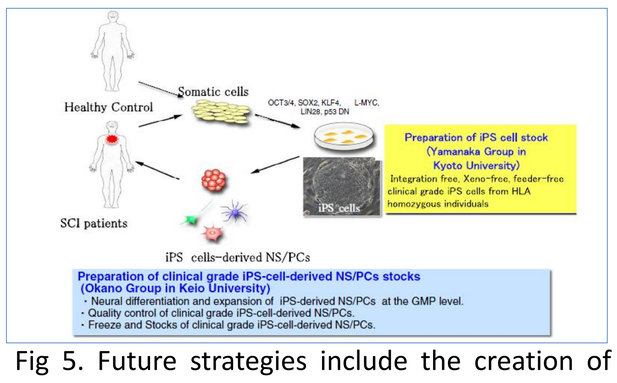

Fig 5. Future strategies include the creation of iPSC stocks from healthy donors for spinal cord transplant in humans [5]

Clinical Trials

A lot of Clinical Trials are been carried out nowadays. The most part of them involve transplant of adult stem cells (specially mesenchymal and neural) to injured patients, and have just achieved phases I/II. They seem to be a secure procedure but with very small improvements on motor and sensory function.

Stem Cell Kind	Injury Level	Time After Injury
Bone Marrow Stem Cells (16)	Cervical (5)	Acute (1)
	Thoracic (3)	Chronic (5)
	Unknown (8)	Unknown (10)
Neural Stem Cells (5)	Cervical (1)	Acute (1)
	Thoracic (2)	Chronic (2)
	Indifferent (1)	Indifferent (1)
	Unknown (1)	Unknown (1)
Adipose Tissue Stem Cells (4)	Unknown (4)	Acute (1)
		Chronic (2)
		Unknown (1)
Oligodendrocyte Precursors (ESCs derived) (1)	Thoracic (1)	Unknown (1)

Table 1. Main clinical trials using stem cells for SCI treatment. Amount of trials is shown in brackets. Data collected from *clinicaltrials.gov*

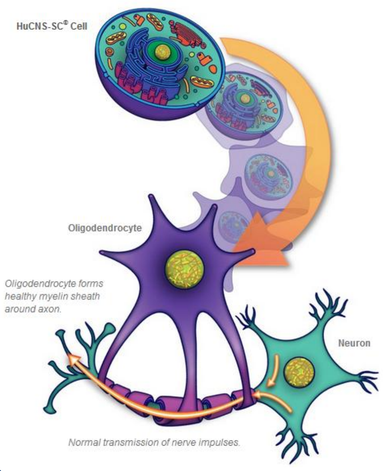

Fig 6.Stem Cells differentiate into oligodendrocytes and promote remyelination of damaged axons. Image extracted from *stemcellsinc.com*

CONCLUSIONS

Until now, just adult stem cells (saving a few lines of embryonic stem cells well differentiated and characterized) seem to be close to medical application on spinal cord recovery. These trials are on initial phases and in spite of been safe therapies, in any case they reach a complete cure. In experts opinion, stem cells may promote new strategies to fight against motor and sensitive dysfunction, but they won't get full recovery of the injury by their own: it will be necessary an integration of regenerative medicine, rehabilitation programs and pharmacological therapies to improve patients' life quality.

Future Perspectives

Adult stem cells' reduced regeneration capability is one of the major barriers on developing a good regenerative medicine strategy. On the other hand, iPSCs are as safe as adult stem cells, but in addition they include a great differentiation and proliferative profile. Due to this, iPSCs seem to be the technique that will reach a better spinal cord regeneration.

REFERENCES

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[2] Gouti M *et al*. In Vitro Generation of Neuromesodermal Progenitors Reveals Distinct Roles for Wnt Signalling in the Specification of Spinal Cord and Paraxial Mesoderm Identity. PLOS Biology. 2014; 12(8)

[3] Meinhardt A *et al.*3D Reconstruction of the Patterned Neural Tube from Embryonic Stem Cells. Stem Cell Reports. 2014; 3: 987–999.

[4] Nakamura M, Okano H. Cell transplantation therapies for spinal cord injury focusing on induced pluripotent stem cells. Cell Research. 2013; 23: 70-80

[5] Okano H, Yamanaka S. iPS cell technologies: significance and applications to CNS regeneration and disease. Molecular Brain. 2014, 7: 22