SHORT-TERM IMPROVEMENT IN SOMATOSENSORY SENSITIVITY IN PATIENTS WITH SPINAL CORD INJURY AFTER TREATMENT WITH WHARTON'S JELLY MESENCHYMAL STEM CELLS

Vanesa Sánchez[1,2], Santiago Saldarriaga[1,2], Julián España[1,2], Jonathan Polo[1,2], Alejandro Ramirez[1,2], July Muñoz[1,2], Yesenia Valencia[1,2], Milena Gómez[1,2], Diana Betancur[1,2], Hector Ortega[1,2], Karolynn Halpert[1,2], **Carolina Quintero-Gil[1,2].**

[1] Grupo de investigación en Terapia Celular y Medicina Traslacional, TeCeMeT, Medellín, Colombia. [2] Bioxcellerator S.A.S.

Poster ID: 183

Author Email:
carolina.quintero@bioxcellerator.com

Introduction

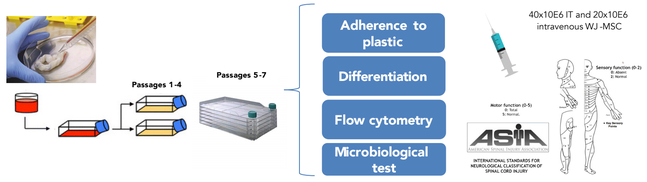
Spinal cord injury (SCI) affects more than one million patients worldwide, all of them suffering from SCI-related paralysis. To date, many pharmacological treatments have been evaluated, but without significative improvements, probably due to the multiple types of cellular damage involved in SCI. Mesenchymal stem cells (MSC) have emerged as a promising therapy for various conditions including neurologic, cardiovascular, autoimmune, and musculoskeletal diseases due to their regenerative effects, and among the MSC sources, umbilical cord Wharton´s jelly MSC (WJ-MSC) represents one of the best sources.

Objective

The aim of this study was to determine the regenerative capacity of the treatment with WJ-MSC in patients with SCI.

Methods

WJ-MSC primary cultures were obtained using a new methodology based on cell migration developed by us (free tissue). WJ-MSC were expanded in culture medium supplemented with 10% human Platelet Lysate (hPL) until passage 7. Positive and negative cell marker expression, in vitro differentiation to mesodermal linage and microbiological tests were conducted. In vitro, expanded WJ-MSC were cultured in cerebrospinal fluid (CSF) and β-III tubulin and Sox2 markers expression was evaluated. In vivo, a treatment protocol with WJ-MSC was designed for patients with a diagnosis of spinal cord trauma. The treatment protocol consisted of two different intrathecal applications of 40x10E6 WJ-MSC and 20x10E6 intravenous WJ-MSC that were repeated two to four times in eighteen months. Patient improvement was evaluated using the ASIA clinical scale.



Results

In vitro, WJ-MSC expressed MSC markers CD105, CD73 and CD90 greater than 89% and hematopoietic markers CD45, CD34, CD11b, CD19 and HLA-DR less than 2.5% (Figure 1A). Trilineage differentiation capability was observed to be present in harvested cells. (Figure 1B). Sox2 expression in cells growth with CSF was 70% compared to 23% in cells growth with medium containing 10 % of hPL (Figure 2B). Three patients were treated with this protocol. Two of them had C5 injury level and one had T1 injury level. After the first application, two patients improved in Pin Prick score, and the other one showed improvement after the second dose.

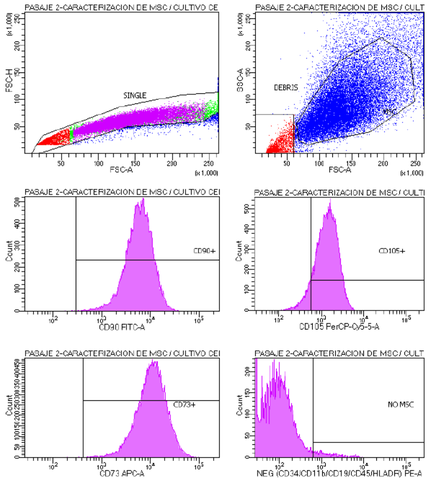


Figure 1A. WJ-MSC characterization by flow cytometry. Expression of CD105, CD73 and CD90 was over 89% and negative markers CD45, CD34, CD11b, CD19 and HLA-DR expression was less than 2.5%

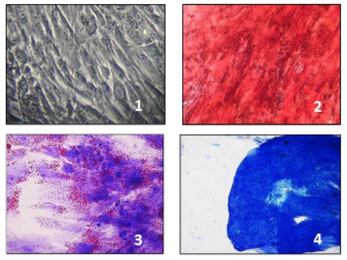


Figure 1B. WJ-MSC in vitro differentiation capability. Fibroblastoid morphology with strong adherence to the culture plates (1). Trilineage ability to differentiate into mesodermal lineage tissues: osteoblasts (2), adipocytes (3) and chondrocytes (4).

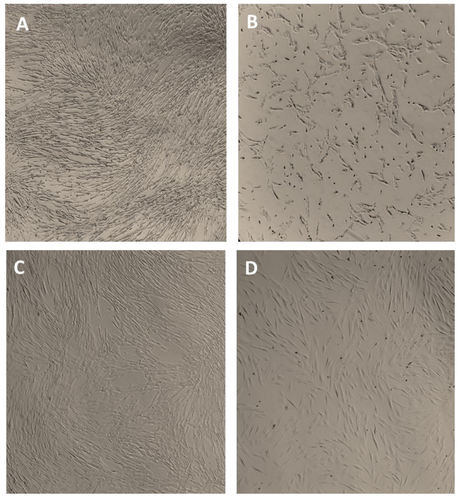


Figure 2A. WJ-MSC plastic adherence and expansion in cerebrospinal fluid. WJ-MSC were cultured during 48 hours in DMEM + 10 % hPL (Control A) or DMEM + 10 % hPL with 25 (B) or 50 % (C) cerebrospinal fluid (CSF). Cells in figure 2D were cultured in 100% CSF.

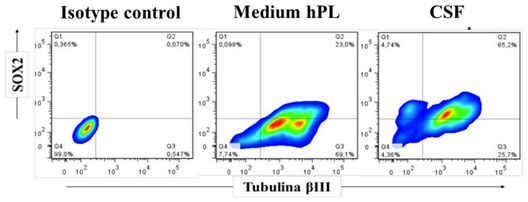


Figure 2B. Expression of neuronal-like markers in WJ-MSC cultured in CFS. WJ-MSC cultured in 100 % CSF expressed 70% of Sox2 compared to 23% of cells cultured in medium with 10% hPL.

Results

The two patients with cervical injury improved in Light Touch score and one of the patients showed improvement in motor score for upper extremities. All of the patients reported improvements in core strength and two of them reported some sensitivity gaining in vesical area (Table 1).

Table 1. ASIA standard neurological classification of SCI in patients after WJ-MSC treatment.

	Visit 1	Visit 2	Visit 3	Visit 4
ASIA motor score upper extremities				
Patient 1 (cervical)	8	18	18	18
Patient 2 (cervical)	9	9	*	*
Patient 3 (thoracic)	50	50	*	*
ASIA motor score lower extremities				
Patient 1 (cervical)	0	0	0	0
Patient 2 (cervical)	0	0	*	*
Patient 3 (thoracic)	0	0	*	*
ASIA light touch score				
Patient 1 (cervical)	28	28	36	36
Patient 2 (cervical)	28	34	*	*
Patient 3 (thoracic)	43	43	*	*
ASIA pin prick score				
Patient 1 (cervical)	28	28	36	36
Patient 2 (cervical)	28	34	*	*
Patient 3 (thoracic)	40	43	*	*

* Pending visit

Conclusion

The results obtained suggest that in vitro expanded WJ-MSC have regenerative capacity through the improvement in somatosensory sensitivity in a patient with SCI. These cells could represent a therapeutic alternative for this type of lesion.