Background: Spinal Cord Injury

Spinal cord injury (SCI) leads to a loss of productivity and daily functional ability.

The cost of care for patients can range from $1.1-4.6 million US over the course of their lifetime.

At the chronic stage (> 6 months after injury), an inhibitory scar forms from the aggregation of proteins called chondroitin sulfate proteoglycans (CSPGs). This prevents all cells of the central nervous system (CNS) from regenerating, thus preventing recovery.

SMaRT Cells

Spinal Microenvironment Modifying and Regenerative Therapeutic (SMaRT) cells are a genetically-engineered line of hiPS-NSCs that lead to targeted release of CSPG-degrading enzymes to help break down the scar.

Methods

Rat Model

Cervical spine has 7 bones C1-C7

Study Timeline

Immunodeficient rats (N=60) at the chronic stage of SCI were randomized into one of the following conditions:

(1) NSCs
(2) SMaRT enzyme-expressing NSCs
(3) Vehicle control
(4) Sham (uninjured) control

Injury

Week

Transplant

Bivweekly Behavioural Testing

Sacrifice

0 8 40

Experiments

2 forms of the SMaRT cell:
• One involves the EF1a promoter for continuous release of CSPG-degrading enzymes.
• Focus of this paper
• The other involves the TetON promoter, which requires the antibiotic doxycycline to control the release of enzymes.
• Study still in development

Hypothesis

The enzymes released by SMaRT cells will be able to degrade the inhibitory CSPG scar and lead to tissue repair by differentiating into various cell subtypes, thus providing a treatment for chronic SCI.

Data collection and analysis of results from behavioural testing is ongoing to determine the degree of functional recovery resulting from these treatments.

Results

In vitro – Cell Analysis

CSPG spot assay - SMaRT cells are able to break down CSPG and grow within the CSPG region compared to conventional NSC (D)

Immunohistochemistry (IHC) – Tissue Analysis

Mature neuronal markers and growth seen at 40-weeks post-injury (E)

Conclusions and Future Directions

• SMaRT cells show promise as a potential treatment for spinal cord injury based on the in vitro and tissue analysis conducted. However, the current in vivo results have yet to be fully analyzed to determine the degree of axonal growth, functional recovery, and scar degradation.

• IHC analysis shows that neurons differentiated from SMaRT cells show growth even at 40-weeks post-injury, thus demonstrating its potential capacity for cellular regeneration and tissue repair at the chronic SCI stage.

• A new version of the SMaRT cell is currently being assessed in a 22-week study using the TetON human promoter which allows for release of enzymes to be controlled by the intake of the antibiotic doxycycline.

References


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