



[ RICK HANSEN INSTITUTE CURE PROGRAM ]

# SUPPORTING PROMISING RESEARCH

*This document is a roadmap that describes the Rick Hansen Institute's (RHI) Cure Program, its objectives and activities. It was developed based on recommendations provided by the RHI Cure Program Advisory Committee which included a face to face meeting on October 6, 2013.*



## DEFINITION OF CURE

A "cure" in spinal cord injury (SCI) is any intervention to return a person to greater functionality after a SCI, whether by protecting the injured spinal cord tissue from secondary degeneration (e.g. through the use of neuroprotective drugs), by promoting neuroplasticity and/or regeneration (e.g. through the use of stem cells), by rehabilitation strategies that could enhance these regenerative efforts (e.g. through the use of locomotor body-weight supported training or epidural stimulation), and by extrinsically activating host neuronal circuitry (e.g. through the use of brain-computer interface). Cure applies to the acutely (newly) as well as the chronically injured. We recognize that a "cure" for paralysis after spinal cord injury may in fact lie in several, incremental cures. A guiding principle for the inclusion of interventions within this definition of 'cure' is that they directly interact with, and positively influence, the injured central nervous system.

Successful efforts towards the cure must be built upon two key pillars that include:

- robust preclinical data in relevant models of SCI; and
- an effective clinical research strategy.

## RHI'S VISION

A world without paralysis after spinal cord injury.

## RHI'S MISSION

To lead collaboration across the global SCI community, by providing resources, infrastructure and knowledge; and to identify, develop, validate and accelerate the translation of evidence and best practices to reduce the incidence and severity of paralysis after SCI, improve health care outcomes, reduce long-term costs, and improve the quality of life for those living with SCI.



## CURRENT STATUS OF CURE-RELATED RESEARCH

Currently, there are a number of clinical trials for SCI that are investigating cure-related interventions. Examples of such interventions include neuroprotective strategies, regenerative strategies and plasticity-promoting rehabilitation strategies. It is recognized that such strategies may have more than one potential mechanism of action (e.g. neuroprotective and neuroregenerative), but that they are ultimately seeking to restore neurologic function. The following paragraphs outline the current work that impacts cure-related research.

### Biology and Physiology of SCI

Despite the promise of clinical trials towards the cure, the current understanding of the biology and physiology of SCI in both humans and in animal models is far from complete. This knowledge gap is greatest in the human setting, where complex histologic, biochemical, and molecular analyses of the injured spinal cord are more challenging to conduct than in the animal setting. There is clearly an unmet need for advancing our understanding of the biology of human SCI. While much has been learned about the biology of SCI in animal models, there is a recognized need to characterize the similarities and differences between the human SCI condition and the preclinical models intended to simulate it. Such insights will facilitate the rationale testing and development of treatments that have a greater likelihood of successful translation into human SCI.

### Interventional Therapies

A better understanding of the biology and physiology of SCI will also enable the rational development of therapeutic intervention for SCI. In particular, such an understanding will promote the development of combinatorial strategies that include distinct and yet possibly synergistic therapeutic mechanisms of action. Such combinatorial strategies may conceivably capitalize upon the additive or synergistic benefits of each. Additionally, interventions that are currently in use or in clinical trials for the treatment of non-SCI neurological indications (e.g. in stroke, muscular dystrophy, traumatic brain injuries) may hold some potential in SCI. Understanding the biology of injury would help to identify those interventions that function through mechanisms of action that are relevant to SCI. Analysis of these interventions in relevant pre-clinical models and then translation to clinical studies if shown to be promising is a reasonable approach towards the development of novel therapies for SCI. For interventions that are already in use for non-SCI indications, their regulatory pathways may be easier to navigate as their safety in humans will have been previously established.

### Functional Measures

There is also a great need to facilitate the conduct of the clinical trials required to evaluate and validate those therapies that are translated to clinical trials. Currently (and historically) the dependence upon functional measures of neurologic impairment is a major impediment to the completion of clinical trials. Although widely used, the International Standards for the Neurological Classification of Spinal Cord Injury (ISNCSCI) assessment and ASIA Impairment Scale (AIS) grading does not capture the complexity of the human injury, and its imprecision at predicting neurologic outcome (particularly when performed in the acute post-injury setting) requires large numbers of patients to be enrolled in trials. Furthermore, the ISNCSCI assessment is impossible to perform in many acutely injured individuals.

## Engaging Individuals with SCI

An important component of any cure-related strategy is the engagement of people with SCI. Early engagement aids in study recruitment, retention and overall experience as well as to ensure the end result or outcome is important to the individual.

## Providing Equitable Care

RHI recognizes that the success of future interventions and the translation of research findings around future cures will be limited if care provided to people with SCI is not standardized. Our ability to better understand, measure and standardize the clinical environment will enable us to provide cures to patients sustaining a SCI and measure the effects in clinical trials.

Objective and quantifiable measures of neurologic injury and function would therefore be extremely valuable for facilitating clinical trials. Such measures could include imaging biomarkers, neurochemical biomarkers, and electrophysiologic assessments. These could provide objective information about the biological extent and severity of the injury and better predictors of neurologic recovery. They could also be utilized to monitor the biological and/or physiological effects of therapeutic interventions. In addition to these practical translational considerations, the study of such aspects of human SCI will further our understanding of its biology and facilitate scientific discovery research.

### Cellular Therapies

The use of transplantation cellular therapies (such as stem cells and Schwann cells) has generated tremendous interest and excitement for their potential to promote neuro-regeneration and restoration of function in both chronic and acute SCI. Extensive pre-clinical research has been published on cell transplantation and this continues to be one of the most active areas of scientific research in SCI. However, cost and regulatory hurdles make the clinical translation of this technology extremely challenging. Current clinical trials in this area are largely focused on determining safety and feasibility, with the hope of detecting some signal of efficacy. The completion of large scale definitive clinical trials to establish efficacy are still many years away, even for therapies that are in early safety studies now.

RHI acknowledges the promising potential of cellular therapies within the context of a broader neuro-regenerative strategy for SCI. However, RHI also recognizes the challenges associated with conducting clinical trials on such cellular therapies, including the stringent regulatory requirements, the high cost of conducting the trials, and potential ethical issues related to the source of cells and/or the recruitment of human subjects. RHI therefore considers clinical trials for stem cell therapies as high risk endeavours that require significant and long term resource commitment. These financial requirements are prohibitive for not-for-profit organizations such as RHI, which depend on limited-term government funding, to actively participate in cellular clinical trials.



### THE CURE PROGRAM AT RHI

The Cure Program at RHI is focused on leveraging RHI's strengths and resources to participate in international collaborative efforts towards curing spinal cord injury. The Program's Advisory Committee is chaired by surgeon-scientist Dr. Brian Kwon and was created to provide RHI with guidance for cure-related activities and recommendations for future activities. The committee is comprised of national and international SCI experts selected to provide strategic representation in clinical and preclinical research (*see sidebar for list of committee members*).

#### Objectives of the RHI Cure Program:

1. To further our understanding of the biology and physiology of SCI.
2. To develop promising therapies for neuro-restoration in acute and chronic SCI.



## AREAS OF FOCUS

RHI acknowledges that there is a vast spectrum of research that is related to curing SCI – the definition itself is intentionally broad. However, based on RHI's Cure Program objectives, RHI will focus its support on the following activities:

- Pre-clinical and clinical studies that increase the understanding of the biology and physiology of acute and chronic SCI. Pre-clinical studies investigating single and/or multiple therapeutic interventions for neuroprotection and cellular therapies for neuroregeneration in acute and chronic SCI.
- Late stage pre-clinical studies evaluating the efficacy of therapeutic agents that have already shown promise in proof-of-concept SCI studies.
- Late-stage pre-clinical studies investigating the use of cellular therapies in treating acute and chronic SCI.
- Late pre-clinical and clinical studies utilizing standardized rehabilitation and activity-based plasticity strategies.
- Clinical studies in the management of acute SCI to reduce long term paralysis and maximize recovery.
- New outcome measures to supplement the ISNCSCI as a measure of neurological impairment as well as further work to improve or develop new measures of neurorecovery.
- Promote, development and adoption of international standards in clinical research in SCI to include standardized datasets.
- Development of a biobank as a repository of biological samples (e.g. CSF, blood, cord tissue) for future investigative purposes and international collaborations on biomarker analysis.



## RHI'S ROLE IN SUPPORTING CURE-RELATED RESEARCH

To support the above areas of focus, RHI plans to carry out the following activities:

- Fund or co-fund research projects.
- Sponsor projects where RHI plays an active operational role.
- Provide informatics platforms for data collection (e.g. RHI Global Research Platform), neurological assessments, patient recruitment and multi-site collaborations.
- Support clinical studies through data analysis and data management services using RHSCIR and other databases.
- Support recruitment of promising researchers in cure-related areas.
- Undertake clinical epidemiology and health economics research to support cure-related research.
- Organize and support national and international conferences that bring together consumers, researchers and clinicians.

## LOOKING AHEAD

# RHI'S PROJECTED TIMELINE OVER THE NEXT 25 YEARS

2013

Renewed funding from the Government of Canada and the Rick Hansen Foundation

2014

RHI international SCI cure strategy

2018

International collaboration on two promising neurorestorative novel therapies  
*Facilitated by: 50% of newly-injured Canadians receive standardized care*

2023

International collaboration on five promising neurorestorative novel therapies  
*Facilitated by: 75% of newly-injured Canadians receive standardized care*

2038

All Canadians have access to SCI-specific novel therapies  
*Facilitated by: All newly-injured Canadians receive standardized care*

## RHI's Role in Cellular Therapies

Based on the extensive and complex regulatory requirements, cost, recruitment challenges and the general uncertainty of the potential efficacy of cellular therapies, RHI will not participate actively in the funding of human trials of these therapies at this time. Instead, RHI will focus on supporting pre-clinical studies that permit a better understanding of the biology of cellular mediated repair of neural tissue, axonal growth and restoration of electrophysiological properties in the damaged spinal cord with the aim of filling the knowledge gaps in understanding cellular repair. RHI's support of pre-clinical studies that provide a better understanding of cellular repair process will help identify candidate therapies that have a greater chance of success in human trials and are a more effective use of its limited resources. While not actively funding clinical trials of cell therapies, RHI will consider opportunities to leverage existing RHI resources (e.g. informatics and/or knowledge translation) to facilitate the efforts of researchers who are engaged in such studies.



## INTERNATIONAL STRATEGIC PARTNERSHIPS

RHI recognizes that the path to the cure involves collaborations across nations, disciplines and organizations. RHI will continue to nurture existing and develop new relationships with the following entities towards building an international collaborative partnership:

- National and international SCI-related foundations
- Consumer groups (national and provincial)
- Other national or regional SCI research institutions and networks
- Canadian and international universities and hospitals
- Accreditation organizations
- Professional and work safety organizations
- Corporations
- Non-SCI entities that have synergy with RHI's objectives



## MOVING FORWARD

Currently, RHI sponsors two clinical studies – CAMPER and minocycline (visit [www.rickhanseninstitute.org/sci-resource/publications-60/sci-research](http://www.rickhanseninstitute.org/sci-resource/publications-60/sci-research) for more information on these projects) that support RHI's Cure Program. In addition, RHI will support two additional clinical studies and at least two pre-clinical studies that meet its cure-related objectives. New pre-clinical and clinical studies for support will be identified through open and/or targeted Request for Proposals (RFP). RFPs will be evaluated through external peer-review as per RHI's review policies.

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*The Rick Hansen Institute is a Canadian-based not-for-profit organization with the goal of creating a world without paralysis after spinal cord injury. It works towards this goal by accelerating research and translating clinical findings into practical solutions to develop new treatments, improve health care outcomes, reduce long-term costs and improve the quality of life for those living with spinal cord injury. [www.rickhanseninstitute.org](http://www.rickhanseninstitute.org).*

## About RHI's Programs

The Rick Hansen Institute's Cure Program is one of four key programs under RHI's new strategic direction for 2013-2018. The key program areas are Cure, Care, Consumer Engagement and Commercialization and are supported by six strategies (translational research, best practices implementation, informatics, network development, consumer engagement and supporting the next generation of the "Best & Brightest" researchers). Together, these programs and strategies will help support RHI's vision of a world without paralysis after spinal cord injury.

Learn more about RHI's strategic direction for 2013-2018 at [www.rickhanseninstitute.org/about-us/who-we-are/strategic-direction](http://www.rickhanseninstitute.org/about-us/who-we-are/strategic-direction).

## CURE PROGRAM

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