



PRAXIS SPINAL CORD INSTITUTE CURE PROGRAM

# SUPPORTING PROMISING RESEARCH

This document is a roadmap that describes the Praxis Spinal Cord Institute's Cure Program, its objectives and activities. It was developed based on recommendations provided by the Praxis Cure Program Advisory Committee in 2013 and subsequent strategic planning meetings in 2018.

## 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;
- an effective clinical research strategy.

## 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.

## OUR VISION & MISSION

VISION: A world without paralysis after spinal cord injury.

MISSION: To lead collaboration across the global spinal cord injury 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.

## 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.

## PRAXIS ADVISORY COMMITTEE (PAC)

The Committee advises Praxis on our strategic direction, including the integration of the activities of the Cure, Care, Consumer and Commercialization programs, to achieve our vision, mission and operational and fundraising goals.

### PAC MEMBERS

\*Member of the Praxis Board of Directors

#### Michael Beattie (Chair)\*

Professor of Neurological Surgery & Co-Director,  
Brain and Spinal Injury Center, University of California

#### Kristine Cowley\*

Assistant Professor, Physiology & Pathophysiology,  
University of Manitoba

#### Graham Creasey

Paralyzed Veterans of America Professor of Spinal Cord Injury  
Medicine Emeritus, Stanford University

#### Richdeep Gill\*

Minimally Invasive Upper Gastrointestinal & Bariatric  
Surgeon, Assistant Professor of Surgery, University of Calgary,  
Peter Lougheed Hospital

#### Hans Keirstead

Chairman & CEO, AIVITA Biomedical Inc.

#### Katie Lafferty

CEO, Heart & Stroke Foundation Canadian Partnerships  
for Stroke Recovery

#### Ian Rigby\*

Emergency Room Physician, Foothills Medical Centre  
Chair, Praxis Board of Directors

#### Christine Sang\*

Director, Translational Pain Research, Brigham and  
Women's Hospital

#### Simon Sutcliffe

Former President, BC Cancer Agency  
Vice Chairman, Omnitura Therapeutics

#### Rob Wudlick

Treasurer & Co-Founder, Get Up Stand Up  
Associate Professor, Harvard Medical School

## 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.

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 transplantation of 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.

Praxis acknowledges the promising potential of cellular therapies within the context of a broader neuro-regenerative strategy for SCI. However, Praxis 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. Praxis 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 Praxis, which depend on limited-term government funding, to actively participate in cellular clinical trials.

## THE CURE PROGRAM AT PRAXIS

The Cure Program at Praxis is focused on leveraging Praxis' strengths and resources to participate in international collaborative efforts towards curing spinal cord injury. The Cure Program Advisory Committee was created to provide ongoing advice on cure-related activities and recommendations on future activities supported by Praxis. The objectives and areas of focus were selected from a planning meeting in 2013 and then updated at a subsequent strategic planning meeting in 2018. In 2020, the Cure Program Advisory Committee transitioned to the Praxis Advisory Committee (PAC). The purpose of the PAC is to provide strategic direction to the Board on the integration of its programmatic activities. Please see box on previous page for more details on the PAC.

### Objectives of the Praxis 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

Praxis' Cure Program supports work leading to better diagnosis of, and promising treatments for SCI. Areas of Focus for Praxis' Cure Program for 2018 to 2022 include the following:

- Biomarkers to Assess Impairment
  - » Developing, applying and validating SCI biomarkers (including neurochemical biomarkers in the cerebrospinal fluid and blood, the microbiome and imaging).
- Neuro-Protective and Neuro-Restorative Therapies
  - » Developing hemodynamic management protocols for acute SCI management;
  - » Developing and evaluating rehabilitation strategies (e.g. high intensity therapy or activity-based therapy) and neuro-restorative technologies (e.g. spinal stimulation, functional electrical stimulation) as well as relevant outcome measures/data sets;
  - » Developing evidence-informed resources to implement activity-based therapy and existing neuro-restorative technologies.

## PRAXIS' ROLE IN SUPPORTING CURE-RELATED RESEARCH

To support the above areas of focus, Praxis will carry out the following activities:

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

## PRAXIS' 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, Praxis will not participate actively in the funding of human trials of these therapies at this time. Instead, Praxis 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. Praxis' 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 cellular therapies, Praxis will consider opportunities to leverage existing Praxis resources (e.g. informatics and/or knowledge translation) to facilitate the efforts of researchers who are engaged in such studies.

## INTERNATIONAL STRATEGIC PARTNERSHIPS

Praxis recognizes that the path to the cure involves collaborations across nations, disciplines and organizations. Praxis 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 international)
- 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 Praxis' objectives

## MOVING FORWARD

Please refer to the [Praxis website](#) for more information.

## CURE PROGRAM PRAXIS CONTACT

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Praxis Spinal Cord Institute  
is proudly accredited by  
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