Spinal Cord Regeneration: Injury Modulation, Repair Strategies, and Clinical Trials: The Howard H. Steel Conference Precourse

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Spinal cord injuries (SCIs) are devastating, life-altering events. Although 20% of SCIs occur in children and adolescents, the vast majority of SCI research, including animal models and therapeutics, focuses on adults. To address this inequity, the *Howard H. Steel Conference: Injuries and Dysfunction of the Spinal Cord in Children*, began with a precourse entitled, “Spinal Cord Regeneration: Injury Modulation, Repair Strategies, and Clinical Trials.” This precourse sought to unite experts in basic science research with ongoing human clinical trials in the hopes of enhancing current research endeavors and cultivating future initiatives. The stated goals of the precourse included (a) obtaining an overview of current strategies of preclinical studies to evaluate the mechanism and the treatment of SCI, (b) obtaining knowledge of the burden of proof required prior to a clinical trial, and (c) obtaining knowledge of available clinical trials worldwide.

The precourse was divided into 4 sessions: (a) preclinical studies, (b) translational research, (c) clinical trials, and (d) panel discussion, perhaps the most engaging as judged by the question-and-answer session. The preclinical studies session included a description by Dr Kirk Dabney of an animal model utilizing computer-generated distraction to induce SCI. In their rat model, they are able to induce mild, moderate, or severe injury dependent on extent of distraction. They use somatosensory evoked potentials to confirm the injury, and described the cellular events that occur at various time points post injury. This should serve as an excellent model for pediatric injury, in which a significant number of injuries are secondary to a distracting mechanism.

Dr Dalton Dietrich provided a thorough overview of hypothermia and its potential applications in SCI. Dr Dietrich’s laboratory has published many of the seminal papers on hypothermia for neurological injury. He described the multifaceted mechanisms of action of hypothermia including decreased excitotoxicity and inflammatory response. The Miami Project to Cure Paralysis has initiated protocols for the application of

modest degrees of hypothermia in patients with acute SCI and those undergoing spinal cord surgery for tumor resection. The future applications for hypothermia should only increase as ongoing research optimizes patient selection, level and duration of hypothermia, and the method employed.

The Spinal Cord Research Center at Drexel University Medical School presented their ongoing research with cellular therapies for SCI. Their data provided encouraging results from bone marrow stromal cells, neural progenitor cells, and cells genetically modified to deliver neurotrophic factors. A key advance has been their ability to demonstrate the feasibility and efficacy of utilizing lumbar puncture for delivery of stem cells. This safe, technically feasible mode of delivery allows for repeated injections of therapeutic agents. Continued research will continue to refine this delivery method with various stem cells.

Session 2 focused on translational research. Pediatric SCI differs mechanistically and physiologically from that in the adult. However, there is no widely accepted model of pediatric SCI. Dr Manuel Gonzalez-Brito provided initial results for a pediatric SCI model in infant piglets. This is a contusion model that is characterized histopathologically, clinically, and with magnetic resonance imaging. Although the results appear promising, as this model may potentially fill a large void in pediatric SCI research, work remains to obtain consistent results. Dr Barth Green provided a general overview of current SCI trials, which served as a prelude to session 3.

Dr Daniel Lammertse provided a summary of the guidelines of the International Campaign for Cures for Spinal Cord Paralysis (ICCP) for SCI clinical trials. The need for such published guidelines is apparent, as the field is relatively new, with numerous case series being reported worldwide. These guidelines provide standards for all aspects of SCI research—from the basic science laboratory to eventual human clinical trials. As more and more potentially promising therapies are discovered, these guidelines will provide a framework for safe, efficient testing in human subjects. Dr Carlos Lima presented his team’s work with olfactory mucosa autografts in human SCI. At the outset, Dr Lima acknowledged that his study was not a clinical trial, but

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rather a case series. He provided some preclinical animal data and then described his series of 7 subjects, all initially classified as ASIA A and between 6 months and 6.5 years post injury. Two subjects converted from ASIA A to C, with some reporting improvement in bowel and bladder function. No adverse events were reported. Although encouraging, these early results with only 7 subjects will need to be substantiated with increased numbers and rigorous clinical assessment prior to generating widespread optimism in the scientific community. Similarly, Dr Hongyun Huang presented a myriad of results from 498 patients who underwent olfactory ensheathing cell transplants for chronic SCI; 55 of these patients have had long-term follow up. Although some clinical improve-

ments are documented, further long-term analysis of both benefits and complications is needed.

The area of SCI research is undergoing a rapid explosion of knowledge. Pediatric SCI comprises a significant portion of all SCIs, although dedicated animal models and clinical trials are still lacking. The precourse presentations stimulated a wide variety of questions and ideas, all of which will hopefully prove fruitful for future research endeavors.

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