Proceedings of the 2nd Translational Preconditioning Meeting Miami

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This issue of *Translational Stroke Research* reports on the proceedings of the 2nd Translational Preconditioning Meeting, held at the University of Miami in December 2011. The main agenda of the meeting was published previously, soon after its conclusion [1]. This special edition serves to further introduce the purpose of the Translational Preconditioning Meetings to the scientific community and to report in greater detail on the discussions and ideas that recently emerged among the attendees in Miami. The current edition also serves to lay the groundwork for upcoming meetings in the future.

Preconditioning is growing as a novel and innovative strategy for the treatment of cerebral ischemia and may evolve into the next frontier of neurotherapeutics. Promising protection is readily achieved in small and large animal models of global and focal cerebral and spinal cord ischemia. Perhaps in attestation to the generalizability of the preconditioning response, similar protection is seen across diverse organ systems in both large and small animal models of hepatic, renal, and myocardial ischemia. Yet, many questions remain on how to optimally translate the promising preclinical results to clinical medicine and potentially avoid the failures of the field of human neuroprotection. As a result, a loose network of scientists and clinicians interested in advancing the translational science of preconditioning met in 2010 at the University of Michigan, Ann Arbor, in the First Translational Preconditioning Meeting hosted by Guohua Xi and Richard Keep. Building on the success of the first meeting, the second meeting of this kind was organized by Miguel Perez-Pinzon and co-chaired by Sebastian Koch at the University of Miami. The number of attendees had increased and included a mixed group of national leaders in the field.

The meeting was planned for a single day and divided into a clinical and basic science session of discussion and brainstorming with few didactic presentations.

The morning session was dedicated to the translational clinical aspects and had its focus on the when, where, and how preconditioning should be applied to clinical medicine. The discussions were led by Michael Wang on whether the Stroke Therapy Academic Industry Roundtable working group criteria are suitable for preconditioning and Sebastian Koch on the readiness of proceeding to clinical preconditioning trials in neurology. These questions led to active discussions by the attendees, which are summarized in the articles by Wang et al. and Koch, respectively. Given the limited clinical experience of preconditioning, Nestor Gonzalez and Sebastian Koch presented preliminary trial experience in remote ischemic limb preconditioning for delayed cerebral ischemia following subarachnoid hemorrhage, which the investigators had independently conceived and led at UCLA and the University of Miami, respectively. This experience has been submitted successfully for peer review and published and is not reported in this particular issue [2, 3]. The relatively more recent strategy of postconditioning and potential clinical application, particularly for treatment of cardiac arrest, is discussed by Dezfulian et al. Suitable clinical settings for preconditioning have included performing the intervention prior to surgeries that carry an inherent risk of cerebral ischemia such as carotid surgery, coronary artery bypass, and for delayed cerebral ischemia following subarachnoid hemorrhage. The alternate setting of preconditioning for traumatic brain injury, a leading cause of morbidity and mortality, including diverse mechanisms of traumatic injury, is explored by Yokobori et al. in a comprehensive review.

The afternoon session was focused on the translation from bench work and on potential mechanisms of conditioning. This section of the proceeding starts with an in-depth review of genetic and epigenetic mechanisms of conditioning.

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The review by Meller and Simon was aimed at identifying and discussing the main genomics studies of ischemic preconditioning. This comprehensive review revealed the immense complexity of the ischemic tolerance network. The next review was that of Azad and Haddad, which provided an overview of genetic studies in *drosophila* and hypoxia tolerance. The fruit fly remains one of the best genetic models to study disease; therefore, this comprehensive review brought to bear how this powerful model can be used to study hypoxia tolerance. Finally, this section was followed by an excellent review by Brand and Ratan on the potential mechanisms of epigenetics and ischemic tolerance. They elaborated on the concept of the tolerasome, which is a multi-protein complex recruited to enhance specific genes following preconditioning.

This section of reviews is followed by three reviews that specifically study three different potential clinical scenarios in which “conditioning” could be efficacious: postconditioning, intracerebral hemorrhage, and the potential value of conditioning on stem cell therapy.

Dr. Zhao provided a review on the more recent conditioning model of postconditioning, which has been established to be protective against stroke in animal models. Dr. Zhao concludes in this review that ischemic postconditioning requires a more detailed assessment prior to any potential future clinical application. This review was followed by Zhao and Aronowski who provided an extensive review of the potential applicability of preconditioning against brain damage caused by intracerebral hemorrhage. They suggested from his own ongoing research that the transcription factor Nrf2 could play key role in a pleiotropic fashion to protect against the deleterious effects of blood lysis products that occur following intracerebral hemorrhage. This section ends with a review by Drs. Yu and Wei who reviews the applicability of preconditioning in stem cell transplantation therapy. They suggested that preconditioning and stem cells may be beneficial when the cells are transplanted into the pathological environment that ensues following cerebral ischemia.

The last three reviews of this special issue examined in depth the steps to translate conditioning from the bench into the clinic. The first of these reviews is by Bahjat et al., who

discussed in depth the steps required to translate preconditioning from basic research or bench work to the clinic. This excellent review explores several key steps required for pre-clinical validation of preconditioning agents prior to clinical trials in patients. This review was followed by one by Drs. McLaughlin and Gidday, who present an overview of the discussion on how to translate the different modalities of conditioning in stroke models. They present a summary of questions, ideas, concerns, and recommendations expressed by speakers and discussants during the meeting in Miami. In this review, they attempted to synthesize the discussions that occurred during the meeting. Furthermore, they proceeded to add their recommendations from these discussions. The final review of these proceedings is by Drs. Anrather and Hallenbeck. These authors first presented an overview of the biological networks in ischemic tolerance and finalized this review with a full section on rethinking the approach of clinical conditioning, with the main goal of avoiding the “trail of tears” that has occurred over the years in the field of all of neuroprotection against stroke.

The strength of the meeting was in the diverse backgrounds of the participants and the close integration of the basic and clinical sciences, along with a vibrant exchange of ideas. No specific guidelines or recommendations emerged in this meeting and perhaps such formulations are the objective of a future meeting. The reviews in these proceedings may lay out the groundwork for the next in the series of Translational Precondition Meetings, which is the planned workshop in Los Angeles in 2013 organized by Dr. John Zhang.

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