



PROGRESS IN NEUROSCIENCE PINS



Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&
The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 2/6/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Development of PSD95 Inhibitors for the Treatment of Stroke: From Bench to Phase 3 Clinical Trials

Michael Tymianski, MD, PhD
Head, Division of Neurosurgery, University Health Network
Professor, Dept of Surgery (Neurosurgery), University of Toronto
Senior Scientist, Toronto Western Hospital Research Institute
Canada Research Chair in Translational Stroke Research

Abstract:



Stroke afflicts 16 million people worldwide, is the second most common cause of death (WHO statistics), and the commonest cause of disability. Yet, there are few approved acute treatments that can minimize stroke damage. Cerebral ischemia and hemorrhage are among the most common conditions cared for by cerebrovascular neurosurgeons, and are also the most common complications of cranial neurosurgery.

This lecture will describe the development of PSD95 inhibitors from the stage of molecular discovery in the basic research lab, through animal experiments including non-human primates, and then through to successful clinical trials. PSD95 inhibitors are molecules that inhibit pro-death signaling in neurons that are exposed to ischemia, and are among the few neuroprotectants that meet the STAIR criteria. However, the major challenges facing the development of neuroprotectants remain the complexity and heterogeneity of human stroke syndromes, the rapidity with which ischemic brain damage develops, and the variability in stroke care systems within and between countries. This lecture will also describe the challenges associated with designing a clinical trial that can demonstrate efficacy of an acute stroke neuroprotectant.

Recent relevant publications:

1. Aarts M, Liu Y, Liu L, Besshoh S, Arundine M, Gurd JW, et al. Treatment of ischemic brain damage by perturbing NMDA receptor- PSD-95 protein interactions. *Science*. 2002;298:846-850
2. Cook DJ, Teves L, Tymianski M. Treatment of stroke with a PSD-95 inhibitor in the gyrencephalic primate brain. *Nature*. 2012;483:213-217
3. Hill MD, Martin RH, Mikulis D, Wong JH, Silver FL, Terbrugge KG, et al. Safety and efficacy of NA-1 in patients with iatrogenic stroke after endovascular aneurysm repair (enact): A phase 2, randomised, double-blind, placebo-controlled trial. *Lancet Neurol*. 2012;11:942-950



Weill Cornell Medical College

