

32nd European Neurology Congress

&

12th International Conference on **Vascular Dementia**

July 22-24, 2019 London, UK

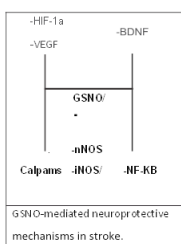


Inderjit Singh

Medical University of South Carolina, USA

Targeting stroke by S-nitrosylation mechanisms: Preclinical studies

Stroke is the leading cause of disability worldwide. It immediately sets into motion various neurodegenerative mechanisms including excitotoxicity and calcium dysregulation leading to inflammatory/nitoxidative-mediated injury mechanisms. Our studies with a rat model of ischemia and reperfusion (I/R) show that an exogenous treatment with S-nitrosoglutathione (GSNO), a multi-targeting naturally-occurring compound provides neuroprotection as well as stimulates neurorepair and aids functional recovery. Stroke was induced by middle cerebral artery occlusion for 60 min followed by reperfusion followed by drug (GSNO) treatment at various time points after reperfusion. The studies show that GSNO-mediated targeting of neuronal nitric oxide synthase/peroxynitrite/calpains and inflammatory NF-KB mechanisms provides protection against neurodegeneration during acute stroke injury. Furthermore, GSNO-mediated mechanisms also stimulated neurorepair process via targeting HIF-1 α /VEGF/PECAM-1 as well as BDNF/CNTF signaling pathways to promote recovery of motor and neurological functions during the chronic disease of stroke. These studies document that targeting of S-nitrosylating mechanisms is potentially attractive therapy for stroke patients. In clinical settings, GSNO is of even greater relevance to stroke therapy because it additionally shows antiplatelet, anti-embolization and vasodilatory properties in humans. Based on the efficacy of GSNO in our preclinical studies using animal models of stroke and absence of toxicity in human uses, we submit that GSNO is a promising drug candidate to be evaluated for human stroke therapy and other neurodegenerative diseases treatment.



Biography

Inderjit Singh is a University Professor at the Medical University of South Carolina, USA. He is investigating the mechanisms of stroke and other neuroinflammatory diseases including vascular dementia associated with Alzheimer's disease. Over the years, he has authored more than 300 high quality peer reviewed original articles and book chapters. He is continuously funded by the NIH for his studies on the disease mechanisms of neurodegeneration. Based on his credentials in neurodegenerative studies; he was awarded Jacob Javits Award for meritorious research in neurological sciences by NINDS/NIH (2002-2009). One of the

32nd European Neurology Congress

&

12th International Conference on **Vascular Dementia**

July 22-24, 2019 London, UK

goals is to evaluate a stroke drug therapy using clinically relevant stroke mouse models of cerebral ischemia and reperfusion (IR) and permanent ischemia (IS). The focus of the present study is on functional recovery and the mechanisms regulated by S-nitrosylation of HIF-1 α using an efficient S-nitrosylating agent S-nitrosoglutathione (GSNO). GSNO is a natural component of the human body and its exogenous administration in human studies is not associated with adverse effects. In neuroinflammatory diseases, the levels of S-nitrosylation are decreased due to increased formation of peroxynitrite from NO and superoxide thus S-nitrosylation-mediated cellular functions are dysregulated. Presently, we are investigating neuroprotection/neuro-recovery therapy using GSNO in stroke, TBI and SCI.

singhi@muscc.edu

Notes: