

Harnessing Adaptive Antiviral Transcription to Prevent Stroke and COVID 19: Implications and Opportunities for Therapeutic Targeting in Acute and Chronic Neurological Diseases

June 30

Tuesday, 12:30 pm

Live Webinar
via Zoom Conference



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Abstract

For almost 30 years, our laboratory has been focused on understanding how extant stresses in the nervous system are converted into adaptive transcriptional responses that can facilitate neuroprotection and possibly repair of the nervous system.

I will discuss how our bodies adapt to viral stress (in the form of accumulations of RNA or DNA in the cytoplasm). These accumulations lead, via distinct routes, to activation of an adaptor protein called STING, recruitment of a kinase called TBK1 and transcriptional activation of the Interferon Response Including the production of Type 1 Interferons. Serendipitously, we have identified an antiviral drug called Tilorone (currently used in humans in Russia and Eastern Europe) that can activate this pathway to robustly protect against permanent or transient stroke in mice or rats and to fortify the blood brain barrier. Parallel studies from our collaborators in North Carolina have shown that tilorone is highly effective in Mice against Ebola and in a dish against COVID-19, likely via its ability to activate this same pathway. These findings lead to the testable hypothesis that driving antiviral responses, specifically type I type Interferons may be therapeutic for Stroke as well as COVID-19.

Of equal interest, there is accumulating data that persistent activation of interferon responses occurs in chronic neurodegenerative conditions such as Parkinson's disease or ALS via sterile accumulation of mt DNA, nuclear DNA, or RNA in the cytoplasm of vulnerable neurons to trigger inappropriate, persistent activation of IFN pathways leading to chronic inflammation. I will try to put these various findings in context and suggest a new model for acute protection and chronic neurological dysfunction that may be relevant to our interest in treating disability in the chronic phase of injury.



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