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## Casein kinase 2 inhibition protects young and aged white matter against ischemia and improves behavioral functions in a subcortical white matter injury model

Hung Nguyen, Wenbin Zhu, and Selva Baltan
Nguyhung@ohsu.edu; Zhuw@ohsu.edu; Baltan@ohsu.edu
Department of Anesthesiology & Perioperative Medicine, School of Medicine Oregon Health & Science University

## Keywords

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## Abstract

White matter injury (WMI) contributes substantially to neurological impairment after ischemic stroke. However, WMI is often ignored in stroke therapeutic developments leading to unsuccessful translation of stroke research to clinical trials. Furthermore, the mechanism of WM injury changes with age which is one of the risk factors for stroke. There is a need for stroke interventions that protect WM in young and aging populations. Casein kinase 2 (CK2) signaling has been shown to associate with diseases such as cancers and ischemia. Previously, we showed that CX-4945, a CK2 inhibitor, protects axon function in young and aged in *ex vivo* WM stroke model. However, the protective effects of CX-4945 in an animal stroke model remain to be investigated. We established an *in vivo* model of focal subcortical WM injury (sWMI) and behavioral assessments. We hypothesize that administration of CX-4945 protects WM and promotes behavioral improvement.

2-month-old and 15-month-old male C57BL6 mice are anesthetized and placed onto the stereotaxic frame. To induce sWMI, 3 injections each of 200ŋl of $N^5$-(1-Iminoethyl)-L-ornithine dihydrochloride (130μM) were deposited at the designated coordinates in the right hemisphere corpus callosum. Compared to baseline, injured mice showed a biased use of contralateral paw over bilateral paw and longer pasta eating time, and more frequent drops of pasta. To test the effects of CX-4945, young and old mice were administered orally either CX-4945 (75mg/kg) or vehicle twice/day for 5 days before undergoing sWMI. CX-4945 protected WM structure, improved bilateral paw use, and decreased the eating time and the frequency of drop of pasta in behavioral tests.

In this study, we established the *in vivo* focal sWMI model that causes significant damage to the WM function and the resulted behavioral deficits in young and aged animals. CK2 inhibition using CX-4945 protects WM against ischemic injury *in vivo* and *in vitro*.