

The protective effect of TND1128, with self-redox ability, on Ca²⁺ overloaded mouse brain slice and its comparison with β -NMN.

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Abstract

Background and purpose: We have no definitive treatment for dementia characterized by prolonged neuronal death due to cerebrovascular degeneration or the enormous accumulation of foreign matters, such as β -amyloid. Since these diseases develop slowly, we may be able to delay the onset and improve these symptoms by enhancing the energy metabolism of individual neurons to assist their viabilities. We examined the effect of TND1128, a derivative of 5-deazaflavin, proven to have the self-redox ability as a possible candidate for a direct activator for mitochondrial energy synthesis. **Experimental Approach:** We prepared brain slices obtained from mice 22 \pm 2 hours pretreated with TND1128 or β -NMN used as an active control. We measured Ca²⁺ concentrations in the cytoplasm ([Ca²⁺]_{cyt}) and mitochondria ([Ca²⁺]_{mit}) by using fluorescence Ca²⁺ indicators, Fura4F, and X-rhod-1, respectively, and examined the protective effects of TND1128 and β -NMN on overloaded cytosolic and mitochondrial Ca²⁺ by repeating 80K exposure. **Key Results:** TND1128 (0.01, 0.1, and 1 mg/kg s.c.) mitigates the dynamics of both [Ca²⁺]_{cyt} and [Ca²⁺]_{mit} in a dose-dependent manner. β -NMN (10, 30, and 100mg/kg s.c.) showed significant dose-dependent facilitatory effects on the recovery of [Ca²⁺]_{cyt} during washing for 5 minutes. However, there was no significant effect on the [Ca²⁺]_{mit} dynamics. **Conclusion and implications:** TND1128 works as a cofactor for activating cellular energy production machinery. TND1128 would rescue deteriorating neurons in various cerebrovascular disorder-related diseases, including Alzheimer's disease and Parkinson's disease. Furthermore, TND1128 will rescue patients with disorders of respiratory organs, such as pulmonary emphysema and COVID-19, which causes respiratory disability

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Figure 1

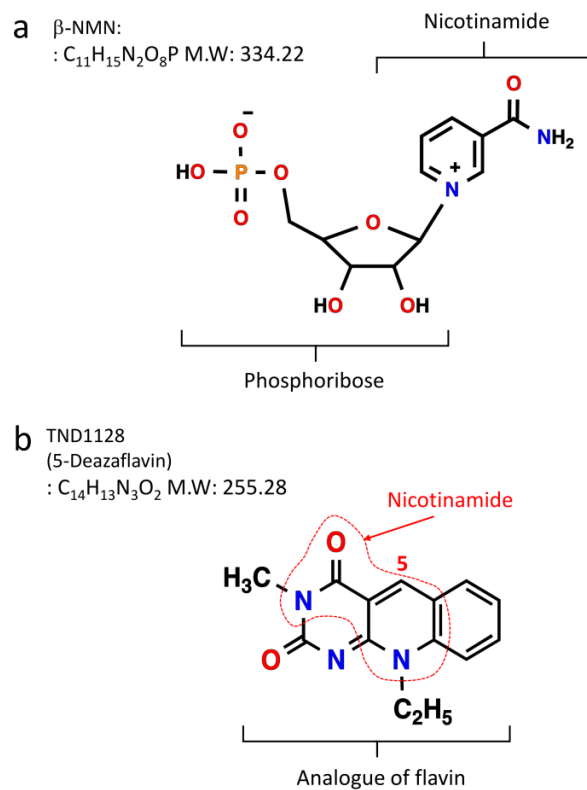
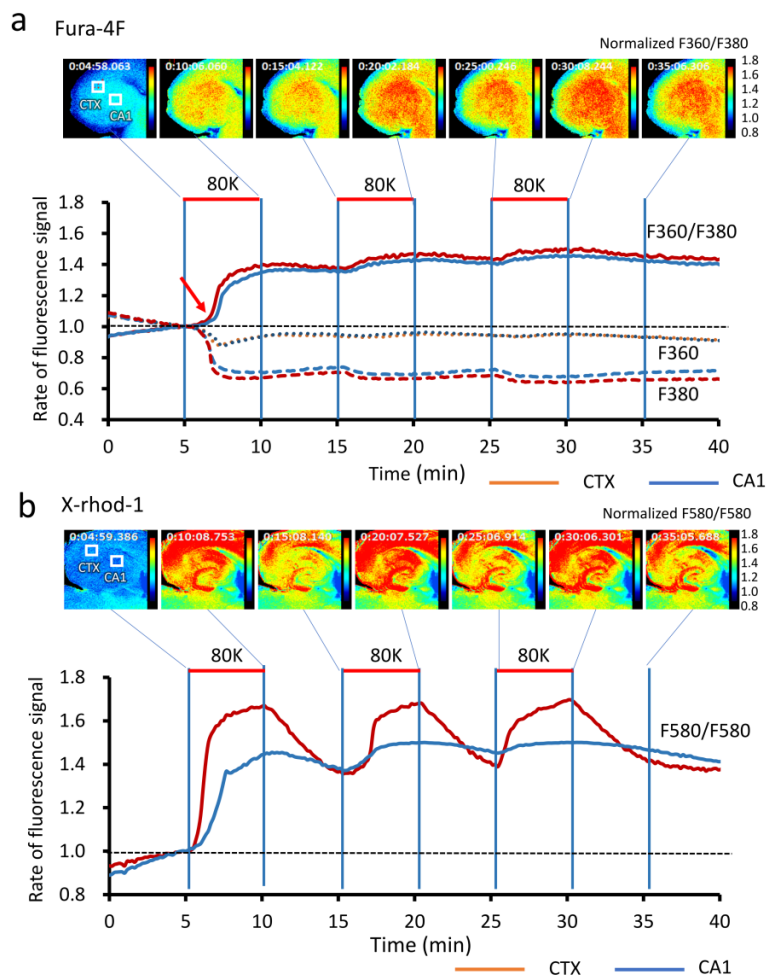


Figure 2



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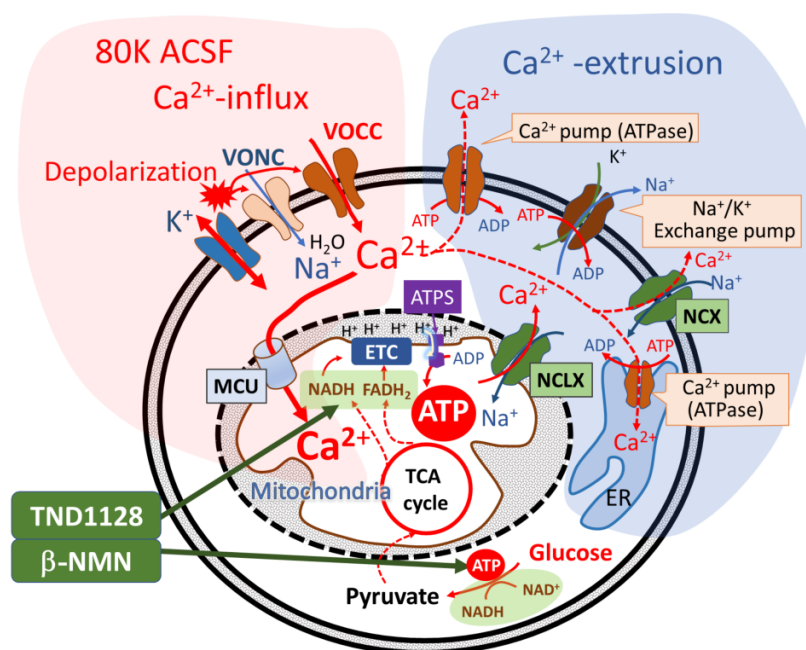
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Figure 7



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Figures for supplemental data.pdf available at <https://authorea.com/users/483408/articles/569542-the-protective-effect-of-tnd1128-with-self-redox-ability-on-ca2-overloaded-mouse-brain-slice-and-its-comparison-with-%CE%B2-nmn>