

BDR SEMINAR via Zoom

Fumito Ichinose

William Thomas Green Morton Professor of Anaesthesia at
Harvard Medical School
Massachusetts General Hospital

Friday, July 9, 2021

10:00-11:00

Meeting URL will be announced on July 8 by e-mail.

※This seminar is open only to BDR members.

Sulfide catabolism ameliorates hypoxic brain injury

This seminar is a part of the QMIN project seminar series.

Summary

The mammalian brain is highly vulnerable to oxygen deprivation, yet the mechanism underlying the brain's sensitivity to hypoxia is incompletely understood. Hypoxia induces accumulation of hydrogen sulfide, a gas that inhibits mitochondrial respiration. Here, we show that, in mice, rats, and naturally hypoxia-tolerant ground squirrels, the sensitivity of the brain to hypoxia is inversely related to the levels of sulfide:quinone oxidoreductase (SQOR) and the capacity to catabolize sulfide. Silencing SQOR increased the sensitivity of the brain to hypoxia, whereas neuron-specific SQOR expression prevented hypoxia-induced sulfide accumulation, bioenergetic failure, and ischemic brain injury. Excluding SQOR from mitochondria increased sensitivity to hypoxia not only in the brain but also in heart and liver. Pharmacological scavenging of sulfide maintained mitochondrial respiration in hypoxic neurons and made mice resistant to hypoxia. These results illuminate the critical role of sulfide catabolism in energy homeostasis during hypoxia and identify a therapeutic target for ischemic brain injury.



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