Energy Matters:
Reprogramming of mitochondrial transport and energy metabolism to power neuron regeneration

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Description:
Mitochondria are cellular power plants that generate energy in the form of ATP. Regeneration requires a high level of energy consumption, which is mainly supplied by local mitochondria within regenerating axons. ATP consumption also supports synapse assembly, drives action potentials, and sustain synaptic transmission. Brain injury triggers acute mitochondrial damage leading to a local energy crisis that contributes to regeneration failure in the central nervous system. To maintain bioenergetics, neurons deploy complex mechanisms transporting and positioning healthy mitochondria into distal axons and synapses and removing and replacing damaged mitochondria from distal areas. Investigations into the mechanisms programming axonal mitochondrial maintenance, repairing energy deficits, and boosting bioenergetic metabolism represent an emerging research frontier (Li & Sheng ***Nature Reviews Neuroscience*** 2022; Cheng, Huang, & Sheng ***Neuron*** 2022). By applying cutting-edge approaches, including live imaging of organelle transport and bioenergetics from diseased mouse and human iPSC models and *in vivo* gene rescue, his laboratory is revealing fundamental cellular pathways and establishing new concepts in the reprogramming of mitochondrial transport and energy metabolism to sustain synaptic transmission and facilitate neural regeneration.

Bio:
Dr. Sheng received Ph.D. in Biochemistry from University of Pennsylvania School of Medicine in 1993. He completed his postdoctoral research with William Catterall from University of Washington in 1996. Dr. Sheng has been an Investigator at NINDS since 1997 and a Senior Investigator and Chief of the Synaptic Function Section since 2007. Over his career at NIH, Dr. Sheng has risen to become a renowned world leader in neuronal transport of mitochondria and lysosomes. Dr. Sheng was elected to AAAS Fellow in 2016 and ASCB fellow in 2017 and received Dr. Francisco S. Sy Award for Excellence in Mentorship at HHS in 2021**.** Dr. Sheng is also the recipient of NIH Director's Award in 2023 for his seminal contributions to the understanding of axonal mitochondrial and lysosomal transport and maintenance of bioenergetics and cellular homeostasis.

Key publications covering the seminar talk:

1. Kang J-S, Tian J-H, Pan P-Y, Zald P, Li C, Deng C, and Sheng Z-H. (2008). Docking of axonal mitochondria by syntaphilin controls their mobility and affects short-term facilitation. ***Cell*** 132, 137-148.
2. Xie Y*, Zhou B*, Lin M-Y, Wang S, Foust KD, and Sheng Z-H. (2015). Endo-lysosome deficits augment mitochondria pathology in spinal motor neurons of asymptomatic fALS-linked mice. ***Neuron*** 87, 355-370.

3. Lin* M-Y, Cheng* X-T, Tammineni P, Xie Y, Zhou B, Cai Q, and Sheng Z-H. (2017). Releasing syntaphilin removes stressed mitochondria from axons independent of mitophagy under pathophysiological conditions. ***Neuron*** 94, 595-610.
4. Zhou B, Yu P, Lin M-Y, Sun T, Chen Y, and Sheng Z-H. (2016). Facilitation of axon regeneration by enhancing mitochondrial transport and rescuing energy deficits. ***Journal of Cell Biology*** 214, 203-119.
5. Li S, Xiong G-J, Huang N, and Sheng Z-H. (2020). Crosstalk of energy sensing and mitochondrial anchoring sustains synaptic efficacy by maintaining presynaptic metabolism. ***Nature Metabolism*** 2, 1077.
6. Huang N, Li S, Xie Y, Han Q, Xu X-M, and Sheng Z-H. (2021). Reprogramming an energetic AKTPAK5 axis boosts axon energy supply and facilitates neuron survival and regeneration after injury and ischemia. ***Current Biology*** 31, 3098-3114.
7. Chamberlain KA*, Huang N*, Xie Y, LiCausi F, Li S, Li Y, and Sheng Z-H. (2021). Oligodendrocytes enhance axonal energy metabolism by deacetylation of mitochondrial proteins through transcellular delivery of SIRT2. ***Neuron*** 109, 3456-3472.
8. Cheng X-T, Huang N, Sheng Z-H. (2022). Programming axonal mitochondrial maintenance and bioenergetics in neurodegeneration and regeneration. ***Neuron*** 110, 1899-1923.