Targeting DHODH to treat epilepsy and MCI (Ramot)

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Our work proposes a specific method to treat epilepsy by reducing activity set-points inhippocampal circuits. In particular, we identified mitochondrial dihydroorotate dehydrogenase (DHODH) enzyme as a central regulator of firing set-points in hippocampal circuits. Inhibition of cerebral DHODH by teriflunomide reduces neuronal firing by inhibiting mitochondrial calcium overload without compromising homeostatic feedback responses and information processing.

This results in suppression of spontaneous and evoked seizures in experimental epilepsymodels. Our work provides the foundation for developing new therapeutic strategies to treat epilepsy by rescuing firing set-point dysregulation.

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