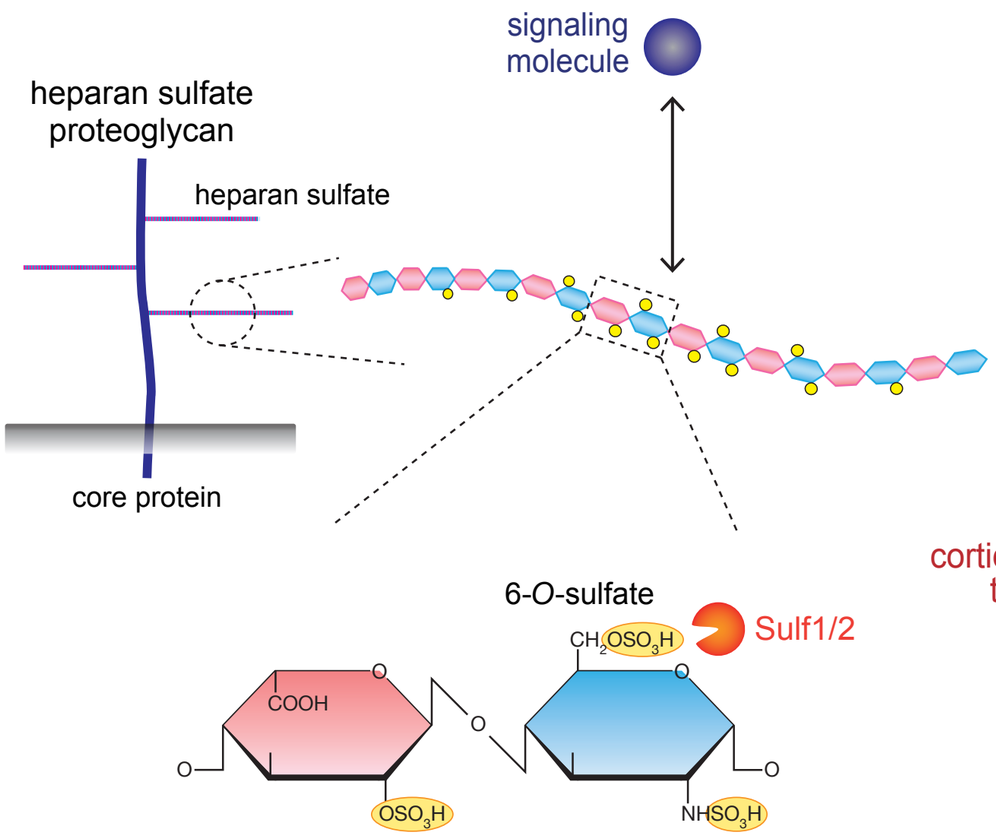
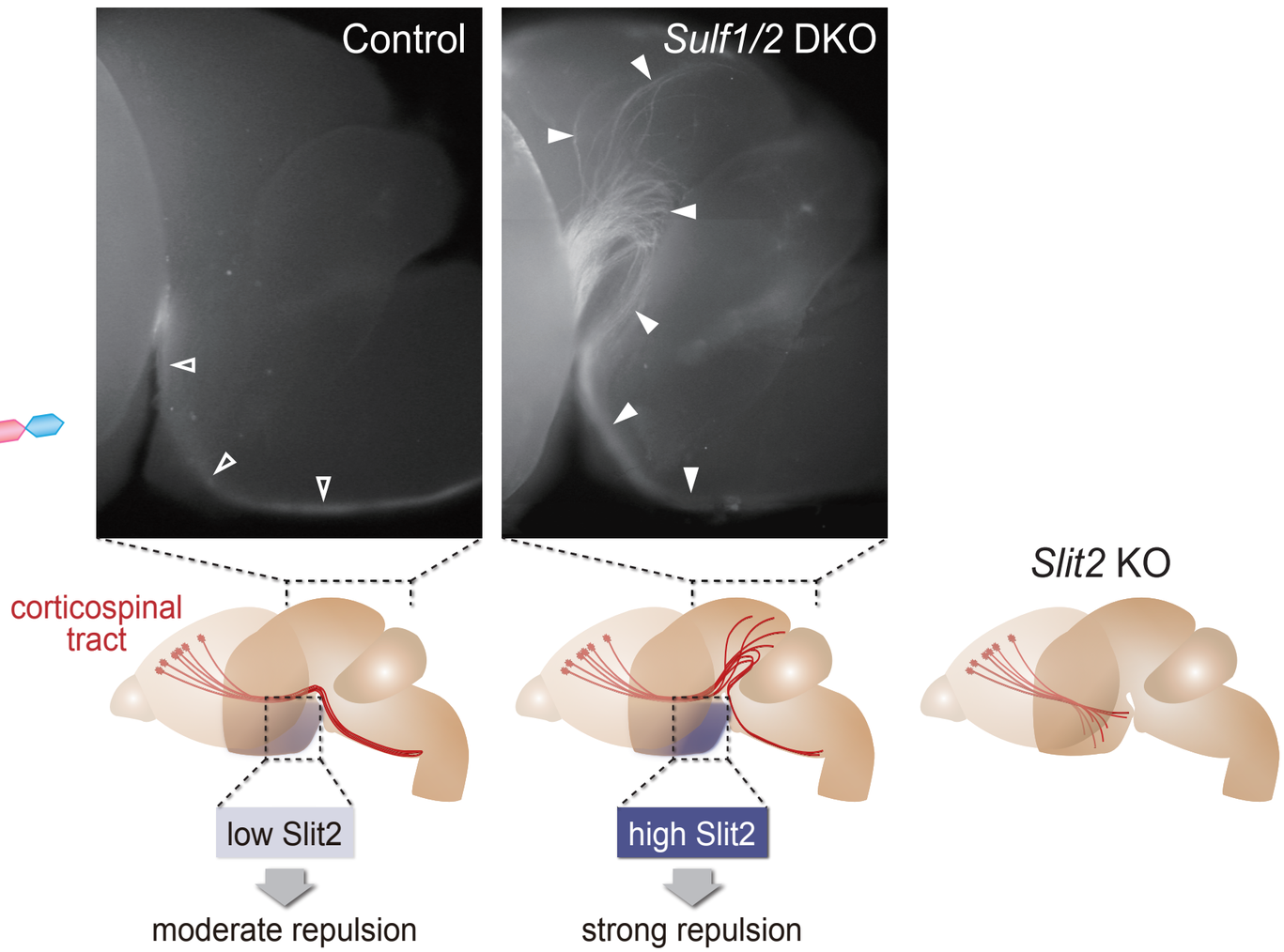
From Department of Molecular Neurobiology

Desulfation of Heparan Sulfate by Sulf1 and Sulf2 Is Required for Corticospinal Tract Formation





Heparan sulfate (HS) has been implicated in a wide range of cell signaling. Here we report a novel mechanism in which extracellular removal of 6-*O*-sulfate groups from HS by the endosulfatases, Sulf1 and Sulf2, is essential for axon guidance during development. In *Sulf1/2* double knockout (DKO) mice, increased 6-*O*-sulfated HS results in excessive accumulation of Slit2 (a repulsive axon guidance molecule) in the hypothalamus, leading to the dorsal displacement of the corticospinal tract. This contrasts sharply with the phenotype of *Slit2* KO mice, in which the axons invade the ventral brain owing to the lack of repulsion. Our fndings demonstrate that Sulf-mediated HS desulfation in the extracellular matrix controls axon guidance of the corticospinal tract through regulating the appropriate Slit2 presentation.

References: T Okada, K Keino-Masu et al., ***Scientific Reports*** 2017; 7: 13847
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