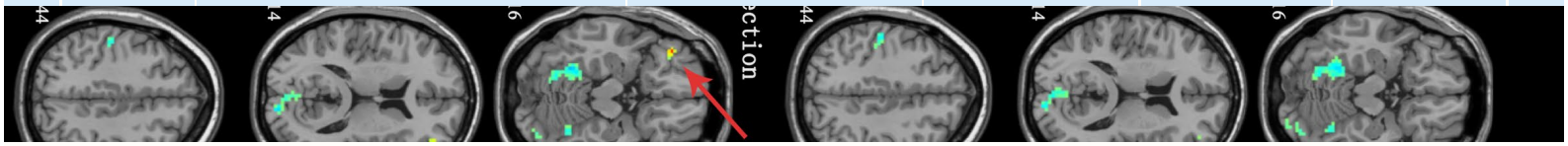

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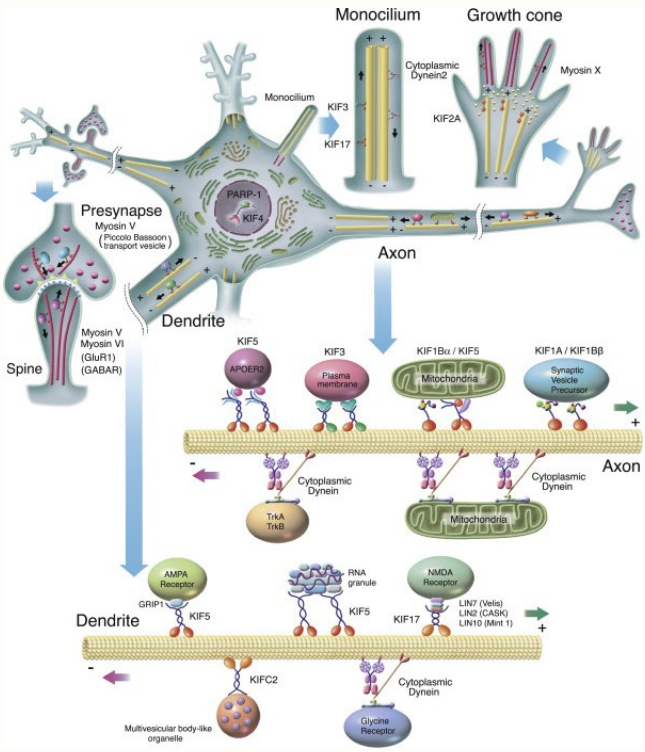
Traffic Tie-up May Lead to ALS, Scientists Say

January 22, 2018 News in Brief Michelle Pflumm

A mitochondrial pileup in motor neurons may contribute to at least one form of ALS according to a new report from the University of Ulm in Germany. The study, led by Jochen Weishaupt, found that mutations in the gene encoding the microtubule motor protein Kif5A is associated with ALS and segregates with the disease.

The intracellular delivery vehicle, according to preclinical studies led by University of Tübingen's Ludger Schöls in Germany, transports mitochondria along axons in motor neurons (Karle et al., 2012). Other cargo includes RNA granules which may contain FUS, hnRNP A/B, hnRNP A1, EWSR1, and SYNCRIP (hnRNP Q) – key RNA-binding proteins also implicated in the disease (see March 2013, January 2017 news; Kanai et al., 2004; Couthouis et al., 2012; Kim et al., 2013; Bakkar et al., 2018).



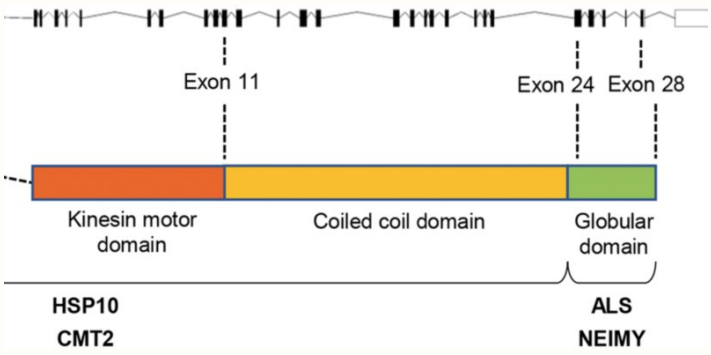
Neuronal gridlock? *Impairment of the intracellular delivery vehicle Kif5A is linked to ALS, suggesting that a traffic-tie up of key cargo including mitochondria may lead to the disease (Brenner et al., 2018). [Image: Axonal Transport. Courtesy of Hirokawa et al., 2010, Neuron.]*

The report builds on a previous genome-wide association (GWAS) analysis, led by University of Massachusetts Medical School's John Landers in Worcester, in partnership with Project MinE, which identified mutations in the same region of the gene in people with ALS but this association did not reach statistical significance (Kenna et al., 2016).

Kif5A is one of a growing number of components of the intracellular transport machinery that, when disrupted, results in ALS suggesting that a traffic tie-up in motor neurons may play a key role in at least some forms of the disease (see October 2017 news; Yang et al., 2001; Münch et al., 2004; Nishimura et al., 2004; Smith et al., 2014; for review, see De Vos et al., 2017).

The study is published on January 12 in *Brain*.

The results appeared just one month after John Landers announced at the 2017 International Symposium on ALS/MND in Boston, Massachusetts that his team, in collaboration with Project MinE, CReATe, GTAC, Answer ALS and the New York Genome Center, confirmed that Kif5A variants were associated with the disease ($P = 6.4 \times 10^{-10}$; OR = 1.38).



A failure to deliver? *Mutations in the C-terminus of Kif5A leads to ALS suggesting that the disease may occur due to its inability to bind, and therefore deliver cargo along axons in motor neurons. [Courtesy of Brenner et al., 2018, Brain].*

The findings add to a growing number of studies, which suggest that the disruption of axonal transport of key cargo including mitochondria and RNA granules in motor neurons may contribute to motor neuron toxicity in ALS (see March 2012, March 2017 news; Magrané et al., 2014; Gopal et al., 2017).

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To learn more about the emerging role of axonal transport in ALS, check out *FUS Jams Mutant Axons, Blocking a Deacetylase Might Help.*

Featured Paper

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