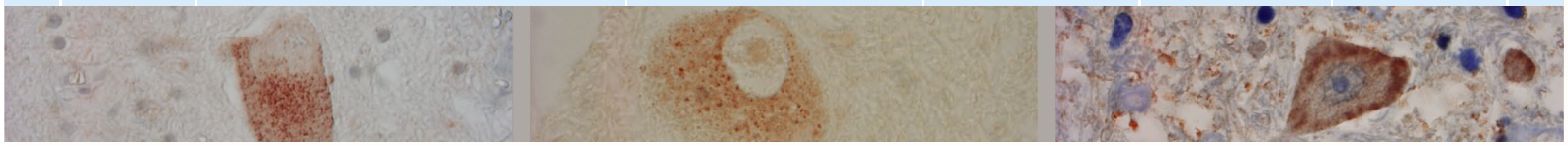

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Sanofi Sets Its Sights on RIPK1 in ALS

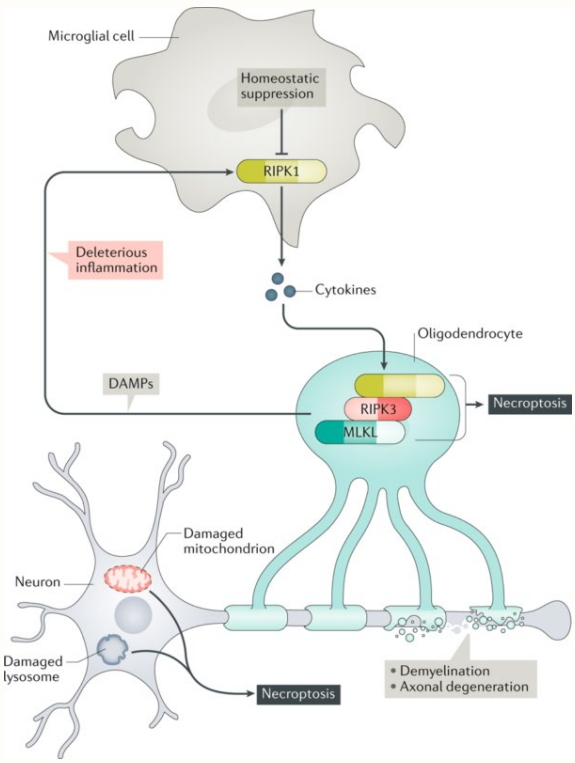
December 1, 2018 News analysis Michelle Pflumm

A new partnership paves the way to evaluate an emerging neuroprotectant in the ALS clinic. The milestone-based deal, which could reach an estimated $1.02 billion USD, will include support from French drug maker Sanofi for the clinical testing of inhibitors of RIPK1 kinase in ALS. The inhibitors are being developed by Denali Therapeutics in San Francisco, California. RIPK1 is increasingly implicated in the destruction of motor neurons in the disease (July 2018 news; for review, see Yuan et al., 2018).

One of these inhibitors, DNL747, is currently being developed as a potential treatment for ALS, Alzheimer's disease and multiple sclerosis. The approach is emerging as a key alternative to GlaxoSmithKline's GSK2982772, due to its ability, according to Denali Therapeutics, to be delivered to the brain (see Harris et al., 2017).

Sanofi announced the partnership with Denali Therapeutics on November 1.

RIPK1 kinase may contribute to ALS by promoting inflammation and axonal loss (see September 2016 news; Ito et al., 2016). The strategy, originally introduced at Harvard Medical School by Junying Yuan and Alexei Degeterev, now at Tufts University School of Medicine, aims in part to block necroptosis, a programmed form of necrosis, which may destroy motor neurons in the disease (see Feb 2014 news; Re et al., 2014; Degterev et al., 2008).



Double Trouble. *Activation of RIPK1 may contribute to inflammation and motor neuron loss in ALS. [Courtesy of Yuan et al., 2018, Nature Reviews Neuroscience.]*

The results of a phase 1 safety study of DNL747 in healthy volunteers will be presented by Denali Therapeutics in New York on December 10, 2018.

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Further Reading

Yuan J, Amin P, Ofengeim D. Necroptosis and RIPK1-mediated neuroinflammation in CNS diseases. Nat Rev Neurosci. 2018 Nov 22. [PubMed].