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Potential new drug target in Lou Gehrig's disease

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Two proteins conspire to promote a lethal neurological disease, according to a study published online this week in the *Journal of Experimental Medicine*.

Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a devastating neurodegenerative disorder that results in progressive loss of motor function and ultimately death. More than 90% of ALS cases have no known genetic cause or family history. However, in some patients, spinal cord cells contain unusual accumulations of a protein called TDP-43.

Jean-Pierre Julien and colleagues at Laval University in Quebec now find that TDP-43 binds to an inflammatory protein called NF-kB p65 in the spinal cords of ALS patients but not of healthy individuals. TDP-43 and p65 were also more abundant in ALS than healthy spinal cords. In spinal cord cells called microglia, TDP-43 and p65 cooperated to ramp up production of factors capable of promoting inflammation and killing nearby neurons. In a mouse model of ALS, treatment with an agent capable of blocking p65 activity minimized neuron loss and eased disease symptoms.

These findings highlight p65 as a potential therapeutic target for this debilitating disorder.

More information: Swarup, V., et al. 2011. J. Exp. Med. doi:10.1084/jem.20111313