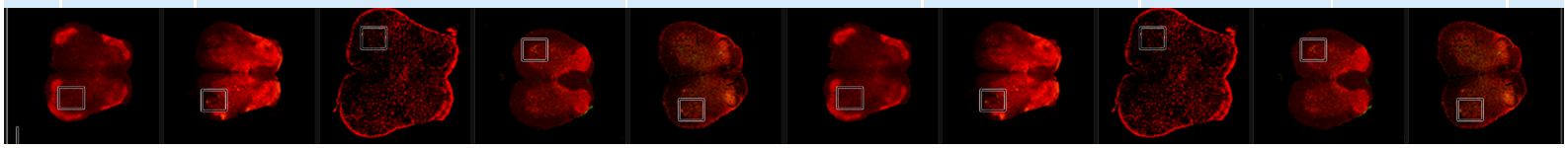

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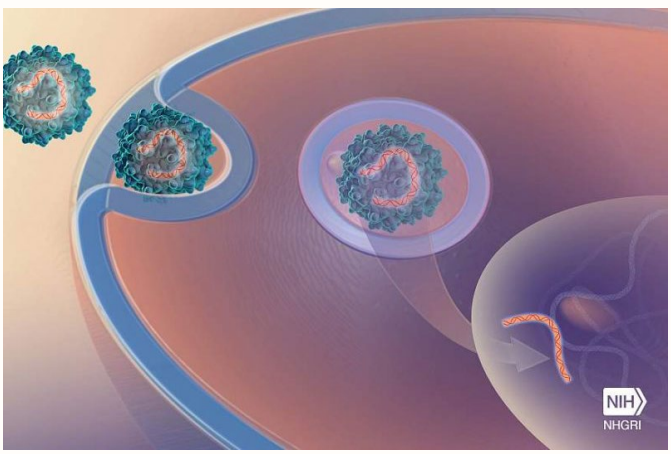
Potential SOD1 ALS Gene Therapy Right on Target, Scientists Say

September 22, 2018 News in Brief Michelle Pflumm

Researchers are one step closer to developing a potential gene therapy for SOD1-ALS. The AAV9-based approach, developed by a research team led by University of Sheffield's Pamela Shaw and Mimoun Azzouz in England, aims to reduce motor neuron toxicity in the disease by lowering levels of SOD1. The misfolded enzyme is thought to contribute to ALS by multiple mechanisms (for review, see Taylor et al., 2016).



Silencing SOD1. *Scientists at the University of Sheffield are developing a potential gene therapy for SOD1 ALS. The strategy, unlike existing approaches, is injected directly into the CNS intrathecally, to lower the dosage (viral load) needed to reduce the risk of unwanted side effects.[Image: National Human Genome Research Institute.]*

The potential gene therapy, according to a new study, reduced neuronal loss in a mouse model of the disease up to 88% and increased its survival by up to 42% depending on treatment timing. No off-target effects could be detected.

The strategy uses a short hairpin RNA (shRNA) to silence the SOD1 gene. The approach is one of a growing number of strategies that aims to lower levels of the misfolded enzyme in motor neurons using RNA interference technologies (December 2017 news; Foust et al., 2013; see also May 2017 news).

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The study appeared on September 7 in *Molecular Therapy Nucleic Acids.*

Meanwhile, a research team led by Timothy Miller at the Washington University-St. Louis in Missouri is using a different strategy to tackle SOD1 ALS. They developed a SOD1 antisense oligonucleotide to lower levels of the misfolded enzyme (see May 2018 news). The approach, according to preclinical studies, may also help reduce motor neuron toxicity mediated by cell non-autonomous mechanisms in the CNS (see August 2017 news; Hoye et al., 2017). The strategy is at the phase 1 stage (see May 2018 news). The approach is being developed in partnership with Biogen in Cambridge, Massachusetts and Ionis Pharmaceuticals in Carlsbad, California.

Featured Papers

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Further Reading

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