This week in therapeutics

Indication	Target/marker/pathway	Summary	Licensing status	Publication and contact information
Neurology				
Amyotrophic lateral sclerosis (ALS)	Chromosome 9 open reading frame 72 (C9orf72)	<p>Studies in patient samples and mice suggest antisense oligonucleotides targeting the hexanucleotide repeat in <i>C9orf72</i> could help treat some patients with ALS. GGGGCC repeats in <i>C9orf72</i> represent the most common genetic cause of ALS. In postmortem brain tissue from patients with ALS or various types of neurons derived from ALS patient fibroblasts carrying the repeats, RNA foci formed and sequestered RNA-binding proteins, including heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1), purine-rich element binding protein A (PURA) and adenosine deaminase RNA-specific B2 (ADARB2). These RNA foci disrupted normal gene splicing and transcription and induced glutamate-mediated excitotoxicity. In the ALS neurons or tissues, antisense oligonucleotides targeting <i>C9orf72</i> or the repeat expansions suppressed RNA foci formation and partially corrected expression of the dysregulated genes. They also decreased glutamate-induced excitotoxicity compared with scrambled antisense oligonucleotides. In normal mice, <i>C9orf72</i> antisense oligonucleotides were well tolerated and did not cause any symptoms of ALS. Next steps include selecting the best antisense oligonucleotide for clinical development. Isis Pharmaceuticals Inc. was involved with each manuscript and has antisense oligonucleotide candidates in preclinical development to treat ALS.</p> <p>SciBX 6(45); doi:10.1038/scibx.2013.1298 Published online Nov. 21, 2013</p>	For all three studies, patent applications filed by Isis Pharmaceuticals covering antisense oligonucleotides; unavailable for licensing	<p>Sareen, D. <i>et al. Sci. Transl. Med.</i>; published online Oct. 23, 2013; doi:10.1126/scitranslmed.3007529 Contact: Robert H. Baloh, Cedars-Sinai Medical Center, Los Angeles, Calif. e-mail: robert.baloh@csmc.edu</p> <p>Donnelly, C.J. <i>et al. Neuron</i>; published online Oct. 16, 2013; doi:10.1016/j.neuron.2013.10.015 Contact: Jeffrey D. Rothstein, The Johns Hopkins University, Baltimore, Md. e-mail: jrothstein@jhmi.edu Contact: Rita Sattler, same affiliation as above e-mail: rsattler1@jhmi.edu</p> <p>Lagier-Tourenne, C. <i>et al. Proc. Natl. Acad. Sci. USA</i>; published online Oct. 29, 2013; doi:10.1073/pnas.1318835110 Contact: John Ravits, University of California, San Diego, La Jolla, Calif. e-mail: jravits@ucsd.edu Contact: Don W. Cleveland, same affiliation as above e-mail: dcleveland@ucsd.edu</p>