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IN BRIEF

ANTIBIOTICS

Antifungal agent blocks MRSA

New agents targeting multidrug resistant *Staphylococcus aureus* (MRSA) are urgently needed. Here, Chen *et al.* screened a collection of commercially available drugs for their ability to inhibit biosynthesis of staphyloxanthin, an important virulence factor that protects *S. aureus* from host oxidant killing. They found that the US Food and Drug Administration (FDA)-approved antifungal agent naftifine is a reversible competitive inhibitor of diapophytoene desaturase (CrtN), an enzyme that is essential for staphyloxanthin biosynthesis. Naftifine attenuated the virulence of MRSA strains in mouse models of infection, revealing CrtN as an attractive and druggable target against *S. aureus* infections.

ORIGINAL ARTICLE Chen, F. *et al.* Small-molecule targeting of a diapophytoene desaturase inhibits *S. aureus* virulence. *Nat. Chem. Biol.* http://dx.doi.org/10.1038/nchembio.2003 (2016)

MUSCULAR DYSTROPHY

Gene editing restores muscle function

Duchenne muscular dystrophy (DMD) is a progressive muscle-wasting disease caused by mutations in the gene encoding dystrophin. Three papers now report the use of adeno-associated viruses to locally or systemically deliver the clustered regularly-interspaced short palindromic repeats (CRISPR)–Cas9 system to the mdx mouse model of DMD, to remove the mutated exon 23 from the dystrophin gene. This gene-editing approach resulted in expression of the modified dystrophin gene and partial restoration of dystrophin protein expression in skeletal and cardiac muscle, as well as in muscle stem cells, leading to improved skeletal muscle function in mdx mice.

ORIGINAL ARTICLES Tabebordbar, M. *et al. In vivo* gene editing in dystrophic mouse muscle and muscle stem cells. *Science* **351**, 407–411 (2016) | Nelson, C. E. *et al. In vivo* genome editing improves muscle function in a mouse model of Duchenne muscular dystrophy. *Science* **351**, 403–407 (2016) | Long, C. *et al.* Postnatal genome editing partially restores dystrophin expression in a mouse model of muscular dystrophy. *Science* **351**, 400–403 (2016)

HUNTINGTON DISEASE

Blocking DREAM delays neurodegeneration

Disrupted Ca^{2+} homeostasis contributes to endoplasmic reticulum stress and has been implicated in Huntington disease (HD) pathogenesis. Here, Naranjo *et al.* report decreased expression of downstream regulatory element antagonist modulator (DREAM) — a member of the potassium channel-interacting protein subfamily of neuronal Ca^{2+} sensors that is important for Ca^{2+} homeostasis — in *in vitro* and *in vivo* mouse HD models, as well as in postmortem brain samples from patients with HD. This reduction in DREAM was found to be a neuroprotective, leading to derepression of activating transcription factor 6 signalling and activation of the prosurvival unfolded protein response. Chronic administration of the DREAM-binding antidiabetic drug repaglinide blocked DREAM activity in a mouse model of HD, delaying onset of motor dysfunction, reducing striatal atrophy and prolonging life span.

ORIGINAL ARTICLE Naranjo, J. *et al.* Activating transcription factor 6 derepression mediates neuroprotection in Huntington disease. *J. Clin. Invest.* **126**, 627–638 (2016)