

IN BRIEF

NEUROLOGICAL DISORDERS**Reversing Rett syndrome**

Rett syndrome (RTT) is an X-linked neurodevelopmental disorder caused by loss-of-function mutations in the gene that encodes methyl-CpG binding protein 2 (MECP2). Here, Gogliotti *et al.* report that expression of metabotropic glutamate receptor 7 (mGlu7) is reduced in motor cortical tissue from patients diagnosed with MECP2 mutation-positive RTT and in MECP2-deficient mouse models. mGlu7-positive allosteric modulators restored deficits in long-term potentiation, improved learning and memory, and corrected apnoeas in RTT model mice.

ORIGINAL ARTICLE Gogliotti, R. *et al.* mGlu7 potentiation rescues cognitive, social, and respiratory phenotypes in a mouse model of Rett syndrome. *Sci. Transl. Med.* **9**, eaai7459 (2017)

RNA-BASED THERAPEUTICS**Increasing efficacy**

Existing antisense oligonucleotide therapeutics (ASO) — such as mipomersen — consist of numerous stereoisomers, which can limit efficacy. Iwamoto *et al.* now report a novel method termed SOSICS (stereocontrolled oligonucleotide synthesis with iterative capping and sulfurization) to produce ASOs with high stereochemical purity. SOSICS was applied to synthesize stereochemically pure components of mipomersen, which revealed that phosphorothioate (PS) stereochemistry affects the physicochemical and pharmacological properties of ASOs. A specific stereochemical code in the DNA core of the PS ASO that is recognized by RNase H1 and that enhanced activity *in vitro* and in mice was identified.

ORIGINAL ARTICLE Iwamoto, N. *et al.* Control of phosphorothioate stereochemistry substantially increases the efficacy of antisense oligonucleotides. *Nat. Biotechnol.* <http://dx.doi.org/10.1038/nbt.3948> (2017)

CNS INJURY**Promoting neural repair**

Disruption of the axons of the corticospinal tract (CST) following traumatic injuries, such as spinal cord injury and stroke, results in motor functional deficits. Here, Liu *et al.* show that adeno-associated virus-assisted co-expression of two soluble proteins — insulin-like growth factor 1 and osteopontin — in cortical neurons stimulated CST regrowth and improved functional recovery in two CST-related injury mouse models. Additional treatment of these mice with 4-aminopyridine-3-methanol (a voltage-gated potassium channel blocker that increases axon conduction) further improved CST-dependent behavioural tasks.

ORIGINAL ARTICLE Liu, Y. *et al.* A sensitized IGF1 treatment restores corticospinal axon-dependent functions. *Neuron* **95**, 817–833 (2017)

INFECTIOUS DISEASE**Blocking malaria transmission**

Inclusion of transmission-blocking agents in combination therapies for malaria could help eliminate the disease. Through a screen of compounds from the Novartis-GNF Malaria Box, Vanaerschot *et al.* identify hexahydroquinolines (HHQs) as potent *Plasmodium falciparum* (Pf) gametocyte (GAM) and asexual blood stage inhibitors. Transmission-blocking activity of HHQs was confirmed in *in vitro* assays using Pf GAMs and gametes. In *Plasmodium berghei*-infected mice, HHQs suppressed blood-stage parasite proliferation. *In vitro* HHQ resistance selection studies identified mutations in Pf multidrug resistance gene-1, which sensitized parasites to first-line antimalarial drugs.

ORIGINAL ARTICLE Vanaerschot, M. *et al.* Hexahydroquinolines are antimalarial candidates with potent blood-stage and transmission-blocking activity. *Nat. Microbiol.* <http://dx.doi.org/10.1038/s41564-017-0007-4> (2017)