IN BRIEF

NEUROMUSCULAR DISEASE

Sarcolemma-localized nNOS is required to maintain activity after mild exercise.

Kobayashi, Y. M. *et al. Nature* **456**, 511–515 (2008).

Many neuromuscular conditions are characterized by an exaggerated exercise-induced fatigue response. Using mouse models, Kobayashi and colleagues show that the exaggerated fatigue response to mild exercise is due to a lack of contraction-induced signalling from sarcolemma-localized neuronal nitric oxide synthase (nNOS), which decreases cyclic GMP-mediated vasomodulation in the vessels that supply active muscle after mild exercise. These results suggest that patients with an exaggerated fatigue response might benefit from treatment strategies — such as PDE5 inhibition — that improve nNOS signalling.

HIV

Human domain antibodies to conserved sterically restricted regions on gp120 as exceptionally potent cross-reactive HIV-1 neutralizers.

Chen, W. *et al. Proc. Natl Acad. Sci. USA* **105**, 17121–17126 (2008)

HIV-1 has acquired the ability to escape neutralization by antibodies generated by the immune system. This paper describes the identification and characterization of a human antibody heavy-chain variable domain that targets highly conserved but sterically restricted CD4-induced structures on the HIV-1 envelope glycoprotein. Such antibodies are potent and broadly cross-reactive HIV-1 inhibitors that could have potential for prevention and therapy of HIV-1 and could help identify conserved structures that are essential for viral replication.

MALARIA

Selection of a trioxaquine as an antimalarial drug candidate.

Coslédan, M. *et al. Proc. Natl Acad. Sci. USA* **105**, 17579–17584 (2008)

Coslédan and colleagues describe the preparation, pharmacological properties and *in vivo* activity of an antimalarial drug candidate. From a selection of 120 trioxaquines and trioxolaquinines that had *in vitro* activity, 72 compounds were tested orally in malaria-infected mice, of which 25 underwent toxicological testing. Finally, one compound with good oral bioavailability was shown to be highly active on multidrug-resistant *Plasmodium falciparum* strains obtained from fresh patient isolates, and completely cured mice infected with chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium*.

PHYSIOLOGY

H_2S as a physiologic vasorelaxant: hypertension in mice with deletion of cystathionine γ-lyase.

Yang, G. *et al. Science* **322**, 587–590 (2008)

Several gaseous signalling molecules have important roles in mammalian physiology. This paper shows that H_2S is physiologically generated by cystathionine γ-lyase (CSE). Mice lacking this enzyme had reduced H_2S levels in serum, heart, aorta and other tissues, and displayed pronounced hypertension and diminished endothelium-dependent vasorelaxation. CSE was activated by calcium–calmodulin, which is a mechanism for H_2S formation in response to vascular activation. So, H_2S is a vasodilator and regulator of blood pressure, which raises the possibility that enhancement of H_2S formation could be an alternative approach for the treatment of hypertension.