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IN BRIEF

AGEING

Improving muscle function

The biological effects of urolithins (metabolites of ellagitannins, which are found in pomegranates, nuts and berries) are poorly characterized. Here, Ryu and colleagues report that urolithin A (UA) extends lifespan and improves fitness of *Caenorhabditis elegans*. These effects were mediated by the induction of mitophagy, which prevented the accumulation of dysfunctional mitochondria, thereby improving respiratory capacity, mobility and pharyngeal pumping. Dietary supplementation of UA similarly stimulated mitophagy in mice, resulting in improved muscle function and increased spontaneous exercise in aged mice and enhanced running endurance in young mice.

ORIGINAL ARTICLE Ryu, D. *et al.* Urolithin A induces mitophagy and prolongs lifespan in *C. elegans* and increases muscle function in rodents. *Nat. Med.* **22**, 879–888 (2016)

INFECTIOUS DISEASE

3D structure of Zika virus protease

The NS2B-NS3 protease of Zika virus (ZIKV) mediates polyprotein processing and therefore represents an attractive drug target. Lei *et al.* now report the 2.7 Å crystal structure of ZIKV protease in complex with a peptidomimetic boronic-acid inhibitor (cn-716). In the structure of the complex, the boronic acid moiety forms a cyclic diester with glycerol through the formation of a six-membered ring that fits neatly into the S1′ pocket of the enzyme. The amino group of the 4-amino-methyl-phenylalanyl residue in the P2 position of the inhibitor forms a salt bridge with Asp83 of the NS2B polypeptide. The presence of this Asp residue enables ion pairing with the P2 residue, which partially explains the enzyme's high catalytic activity. ZIKV NS2B-NS3 forms an unusual dimer with non-crystallographic, quasi-twofold symmetry that has not been seen with other flavivirus proteases.

ORIGINAL ARTICLE Lei, J. *et al.* Crystal structure of Zika virus NS2B-NS3 protease in complex with a boronate inhibitor. *Science* **353**, 503–505 (2016)

FUNGAL INFECTION

Protecting from *Candida albicans*

Candida albicans is the most common cause of human fungal infections; despite the availability of antifungal drugs, invasive candidiasis has a high mortality. Although the mechanisms that protect from fungal infections are not fully understood, recognition of fungal pathogens is known to rely on surface pattern-recognition receptors such as the C-type lectin receptors (dectins 1–3) and their downstream signalling kinase SYK, which initiate the innate immune response. Two papers now report that the E3 ubiquitin ligase casitas B lymphoma-b (CBLB) is a negative regulator of fungal recognition during systemic *C. albicans* infection in mice. CBLB binds to and targets dectin-1, dectin-2 and SYK for polyubiquitination and proteasomal degradation. In mice, CBLB deficiency protected from lethal systemic *C. albicans* infection due to elevated pro-inflammatory responses, enhanced macrophage reactive oxygen species production and increased fungal cell killing. Xiao *et al.* further demonstrate that a systemically delivered *Cblb*-specific small interfering RNA administered after *C. albicans* infection lowered kidney fungal burden and prevented death in mice. Similarly, Wirnsberger *et al.* show that injection of a cell-permeable CBLB inhibitory peptide into mice after lethal *C. albicans* infection blocked weight loss, reduced kidney fungal load and protected from mortality.

ORIGINAL ARTICLE Xiao, Y. *et al.* Targeting CBLB as a potential therapeutic approach for disseminated candidiasis. *Nat. Med.* **22**, 906–914 (2016) | Wirnsberger, G. *et al.* Inhibition of CBLB protects from lethal *Candida albicans* sepsis. *Nat. Med.* **22**, 915–923 (2016)