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IN BRIEF

CARDIOVASCULAR DISEASE

Dietary supplement protects the heart

Ageing is typically associated with cardiac hypertrophy and decline of diastolic function. Eisenberg *et al.* report that dietary supplementation with the natural polyamine spermidine significantly extends the median lifespan of mice. Moreover, in aged mice, spermidine reversed age-associated hypertrophy and improved cardiac diastolic function through modulation of autophagy. Spermidine supplementation also lowered blood pressure and improved cardiac function in a rat model of hypertension-induced congestive heart failure. In human subjects, dietary intake of spermidine was inversely associated with high blood pressure and risk of cardiovascular disease.

ORIGINAL ARTICLE Eisenberg, T. *et al.* Cardioprotection and lifespan extension by the natural polyamine spermidine. *Nat. Med.* **22**, 1428–1438 (2016)

ANTIBACTERIALS

Microcins limit intestinal infection

Small proteins known as microcins that are secreted from commensal intestinal bacteria exhibit antibacterial properties *in vitro*. Sassone-Corsi *et al.* now show in mouse colitis models, that inoculation with a probiotic microcin-secreting *Escherichia coli* strain (EcN) outcompetes and limits gut colonization with commensal *E. coli*, *Salmonella enterica* serovar Typhimurium (STm) and adherent invasive *E. coli* (frequently isolated from patients with Crohn disease), in contrast to a mutant EcN unable to secrete microcins. EcN inoculation also reduced STm colonization, inflammation and weight loss in mice with an active STm infection.

ORIGINAL ARTICLE Sassone-Corsi, M. *et al.* Microcins mediate competition among Enterobacteriaceae in the inflamed gut. *Nature* http://dx.doi.org/10.1038/nature20557 (2016)

ALZHEIMER DISEASE

BACE1 inhibitor reduces β-amyloid production in humans

Inhibition of aspartyl protease β-site amyloid precursor protein cleaving enzyme 1 (BACE1), required for production of β-amyloid (Aβ) peptides, is an attractive approach to lower Aβ levels in AD. Kennedy *et al.* present verubecestat (MK-8931), the first BACE1 inhibitor to reach phase III clinical trials. Orally administered verubecestat safely reduced plasma, cerebrospinal fluid (CSF), and cortical $Aβ_{40}$, $Aβ_{42}$ and soluble amyloid precursor protein-β (sAPPβ) production in rats and monkeys. In both healthy human subjects and patients with AD, verubecestat reduced $Aβ_{40}$, $Aβ_{42}$ and sAPPβ in the CSF and was well-tolerated.

ORIGINAL ARTICLE Kennedy, M. E. *et al.* The BACE1 inhibitor verubecestat (MK-8931) reduces CNS β-amyloid in animal models and in Alzheimer's disease patients. *Sci. Transl Med.* **8**, 363ra150 (2016)

COMPUTATIONAL CHEMISTRY

Novel virtual screening approach

Structure-based drug discovery methods are generally based on predicting the binding affinity of a ligand to a protein. Ruiz-Carmona *et al.* introduce a novel computational procedure termed dynamic undocking (DUck), which evaluates the structural stability of protein–ligand complexes. DUck calculates the work needed to break a key native contact and reach a quasi-bound state. In test systems, active compounds were structurally stable and presented higher quasi-bound values than inactive ones. DUck is orthogonal to existing virtual screening methods: in a fragment screening against HSP70, DUck identified novel chemotypes and had a hit rate of 38%.

ORIGINAL ARTICLE Ruiz-Carmona, S. *et al.* Dynamic undocking and the quasi-bound state as tools for drug discovery. *Nat. Chem.* http://dx.doi.org/10.1038/nchem.2660 (2016)