

IN BRIEF

LIPIDS

Celastrol protects against fatty liver through SIRT1

Celastrol ameliorates the effects of nonalcoholic fatty liver disease (NAFLD) resulting from a high-fat diet (HFD) through NAD-dependent protein deacetylase sirtuin 1 (SIRT1), according to a new study in mice. Administration of celastrol to wild-type mice fed a HFD resulted in a reduction in body weight, fat content and levels of circulating fatty acids and triglycerides compared with untreated mice, and also decreased lipid droplet formation and intracellular levels of triglycerides in the liver. Furthermore, the drug modulated the hepatic expression of crucial genes that are involved in fat metabolism, such as sterol regulatory element-binding protein 1C, and improved glucose tolerance, insulin sensitivity and the anti-inflammatory and antioxidant status of cells in the liver. Importantly, the beneficial effects of celastrol were accompanied by an increase in SIRT1 expression but were eliminated in SIRT1-deficient HFD-fed mice. These results suggest that celastrol reverses metabolic liver damage by decreasing lipid synthesis, inflammation and oxidation, and that SIRT1 has an important role in this process.

ORIGINAL ARTICLE Zhang, Y. et al. Celastrol ameliorates liver metabolic damage caused by a high-fat diet through Sirt1. *Mol. Metab.* <http://dx.doi.org/10.1016/j.molmet.2016.11.002> (2016)

CARDIOVASCULAR ENDOCRINOLOGY

Spermidine enhances cardiovascular health

Ageing is associated with a progressive decline in heart function. New research has now found that spermidine, a dietary polyamine, promotes long life and exerts a cardioprotective effect in mice. Feeding spermidine to old mice (≥ 23 -month-old) delayed age-associated cardiac changes, such as diastolic dysfunction and cardiac hypertrophy, and increased autophagy and mitophagy in the heart, promoting cell repair. The cardioprotective effects of spermidine were abolished in mice lacking autophagy protein 5, supporting a crucial role for autophagy in the effects of spermidine. The team then conducted a food questionnaire in humans and found that dietary levels of spermidine were inversely associated with the risk of cardiovascular disease and high blood pressure, which indicates that spermidine supplementation could provide a new strategy for alleviating age-related cardiovascular disease.

ORIGINAL ARTICLE Eisenberg, T. et al. Cardioprotection and lifespan extension by the natural polyamine spermidine. *Nat. Med.* <http://dx.doi.org/10.1038/nm.4222> (2016)

DIABETES

High diabetes-mellitus-linked mortality in Mexico

A large prospective study examining 146,046 participants in Mexico City found that diabetes mellitus is associated with a far worse prognosis in this population than in populations that were analyzed in previous studies conducted primarily in high-income countries. Around a quarter of participants aged 60–74 years were diagnosed with diabetes mellitus. Individuals with diabetes mellitus had a fourfold higher all-cause mortality than participants without diabetes mellitus, in contrast to patients with diabetes mellitus from high-income countries, who have a less-than-twofold increased mortality. The team suggest that inadequate medical care contributes to this difference; participants with diabetes mellitus had poor glycaemic control, with a baseline HbA_{1c} >10% in 36% of patients, and rates of treatment with antihypertensive and lipid-lowering drugs were low.

ORIGINAL ARTICLE Alegre-Díaz, J. et al. Diabetes and cause-specific mortality in Mexico City. *New Engl. J. Med.* **375**, 1961–1971 (2016)