IN BRIEF

CARDIOVASCULAR DISEASE

Inhalation therapy for heart failure

Drug delivery via inhalation is commonly used for respiratory disorders, but its potential for therapeutically targeting the heart has not been explored. Here, Miragoli *et al.* demonstrate in mice that following inhalation, their previously reported small, biocompatible and biodegradable negatively charged calcium phosphate nanoparticles (CaPs) cross the pulmonary barrier and reach the intracellular compartment within the heart. Inhalation of CaPs loaded with a cell-penetrating peptide that improves myocardial contraction restored cardiac function in a mouse model of diabetic cardiomyopathy. Intramyocardial delivery of a peptide-loaded CaP formulation was also demonstrated in pigs.

ORIGINAL ARTICLE Miragoli, M. *et al.* Inhalation of peptide-loaded nanoparticles improves heart failure. *Sci. Transl Med.* **10**, eaan6205 (2018)

ANTIBACTERIALS

Synthetic peptides eradicate resistant infections

Synthetic peptides based on naturally occurring antimicrobial peptides (AMPs) represent promising antibacterial agents. Now, de Breij and colleagues have synthesized novel peptides with improved antimicrobial and antibiofilm activities (SAAPs), based on a principle human AMP, LL-37. The most potent of these, SAAP-148, was effective against a panel of multidrug-resistant pathogens, including an *Escherichia coli* isolate resistant to colistin. SAAP-148 prevented biofilm formation by *Staphylococcus aureus* and *Acinetobacter baumannii*, and eliminated established biofilms and persister cells. SAAP-148 ointment completely eradicated acute and established methicillin-resistant *S. aureus* and *A. baumannii* infection from mouse skin *in vivo* and wounded human skin *ex vivo*.

ORIGINAL ARTICLE de Breij, A. *et al.* The antimicrobial peptide SAAP-148 combats drug-resistant bacteria and biofilms. *Sci. Transl Med.* **10**, eaan4044 (2018)

ALZHEIMER DISEASE

Identification of blood-based biomarkers

There is a significant need for a minimally invasive, cost-effective and reliable method to diagnose early-stage Alzheimer disease. Building on previous work, Nakamura *et al.* demonstrate the use of immunoprecipitation coupled with mass spectrometry to measure plasma amyloid-β (Aβ) biomarkers. Using two independent data sets, which included cognitively normal individuals and individuals with mild cognitive impairment or Alzheimer disease, they demonstrate that plasma amyloid-β precursor protein (APP)669–711/Aβ_{1-42} and Aβ_{1-40}/Aβ_{1-42} ratios, and their composites, can accurately predict brain Aβ burden.

ORIGINAL ARTICLE Nakamura, A. *et al.* High performance plasma amyloid-β biomarkers for Alzheimer's disease. *Nature* **544**, 249–254 (2018)

CANCER

Targeting the ubiquitin pathway

Aberrations in the ubiquitin–proteasome system — which maintains cellular protein homeostasis — are implicated in tumour development and progression. Here, Hyer *et al.* report the identification of TAK-243, a first-in-class inhibitor of the ubiquitin-activating enzyme. *In vitro*, TAK-243 induced defective protein turnover and proteotoxic stress, impaired cell cycle progression and inhibited DNA repair, leading to cytotoxicity in a panel of human cancer cell lines. In mice bearing subcutaneous xenograft tumours, representing both solid and haematological cancers, intravenous TAK-243 treatment for 3 weeks induced a marked and robust antitumour effect.

ORIGINAL ARTICLE Hyer, M. *et al.* A small-molecule inhibitor of the ubiquitin activating enzyme for cancer treatment. *Nat. Med.* **24**, 186–193 (2018)