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IN BRIEF

CARDIOVASCULAR DISEASE

Improving cardiomyocyte contractility

Post-translational detyrosination of microtubules (dTyr) promotes mechanical resistance to cardiac contraction, but the role of dTyr in heart failure has not previously been investigated. Here, Chen et al. analysed left ventricular tissue of failing and non-failing human hearts, which revealed that upregulation and stabilization of the cytoskeleton is a prominent feature of end-stage heart failure. Moreover, the microtubule network was highly proliferated and detyrosinated in failing versus non-failing myocytes, which increased myocyte stiffness and impeded contractility. Pharmacological suppression of dTyr-microtubules, or adenoviral overexpression of tubulin tyrosine ligase, significantly lowered stiffness and enhanced contractility in failing, human cardiomyocytes.

ORIGINAL ARTICLE Chen, C. et al. Suppression of detyrosinated microtubules improves cardiomyocyte function in human heart failure. *Nat. Med.* https://doi.org/10.1038/s41591-018-0046-2 (2018)

CANCER

Releasing tumour suppressors

Targeting microRNAs (miRs) dysregulated in malignancy, to release the co-silencing of tumour suppressor genes, represents a promising anticancer strategy. Here, Meng et al. report that the co-silencing of expression of the tumour suppressor genes *KLF17*, *CDH1* and *LASS2* in cancer patients is correlated with poor survival. In cancer cells, overexpression of the tumour suppressors reduced malignant progression and promoted apoptosis. Screening of miRNA databases identified miR-9 to contribute to *KLF17*, *CDH1* and *LASS2* co-silencing. Nanoparticle-mediated transfer of an artificial, circular single-stranded DNA (CSSD) molecule containing multiple miR-9 complementary sites into tumour cells reduced miR-9 content and increased tumour suppressor gene expression in tumour cells, reducing tumour progression and lung metastasis in patient-derived xenograft models.

ORIGINAL ARTICLE Meng, J. et al. Derepression of co-silenced tumor suppressor genes by nanoparticle-loaded circular ssDNA reduces tumor malignancy. *Sci. Transl Med.* **10**, eaao6321 (2018)

INFECTIOUS DISEASE

Curbing cholera

Modulation of gut microbiota is emerging as a potential strategy to alleviate various gastrointestinal disorders. Two new papers report bacterial-based interventions that prevent virulent *Vibrio cholerae* infection in animal models. Hubbard et al. engineered a live, orally administered cholera vaccine candidate, HaitiV, by introducing nine genetic modifications into the Haitian outbreak strain of *V. cholerae* to delete known factors associated with virulence, reactogenicity and drug resistance, and to prevent reversion. Administration of HaitiV to an infant rabbit model of cholera protected against lethal doses of virulent *V. cholerae* strains given 24 hours later. Killed HaitiV did not confer such resistance, suggesting that the rapid protection may result from a probiotic effect. Meanwhile, Mao et al. demonstrate that oral administration of *Lactococcus lactis* — which is used as a probiotic to promote general health — to infant mice at the same time or 5 hours before *V. cholerae* exposure reduced *V. cholerae* burden and substantially increased survival through the production of lactic acid. The authors bioengineered *L. lactis* to produce *L. lactis* CSL that detects quorum-sensing signals of *V. cholerae* in the gut and triggers expression of an enzymatic reporter, which could be detected in faecal samples of mice to diagnose cholera.

ORIGINAL ARTICLES Hubbard, T. et al. A live vaccine rapidly protects against cholera in an infant rabbit model. *Sci. Transl Med.* **10**, eaap8423 (2018) | Mao, N. Probiotic strains detect and suppress cholera in mice. *Sci. Transl Med.* **10**, eaao2586 (2018)