IN BRIEF

CHRONIC KIDNEY DISEASE

Targeting dynamin oligomerization

Dysregulation of the actin cytoskeleton in glomerular podocytes plays a key part in the development of proteinuria associated with chronic kidney diseases (CKDs). The GTPase dynamin — which is essential for podocyte structure and function — has been shown to undergo actin-dependent oligomerization, to regulate the actin cytoskeleton of the cell. Here, Schiffer *et al.* report that the small molecule Bis-T-23 promotes dynamin oligomerization in zebrafish and mice, to restore podocyte function and attenuate transient proteinuria. Moreover, Bis-T-23 reversed proteinuria in diverse mouse models of CKD, significantly extending lifespan.

ORIGINAL RESEARCH PAPER Schiffer, M. *et al.* Pharmacological targeting of actin-dependent dynamin oligomerization ameliorates chronic kidney disease in diverse animal models. *Nat. Med.* http://dx.doi.org/10.1038/nm.3843 (2015)

ASTHMA

DNAzyme attenuates allergic asthma

Allergic asthma is characterized by activation of type 2 helper T cells and associated cytokine production, under the control of the transcription factor GATA3. Here, Krug *et al.* report the results of a Phase IIa clinical trial evaluating the safety and efficacy of SB010 — a novel DNA enzyme (DNAzyme) that cleaves and inactivates GATA3 mRNA — in 40 patients with mild allergic asthma. Twenty-eight days of once daily inhalation of SB010 significantly attenuated the early and late asthmatic responses (by 11% and 34%, respectively, compared to a 1% and 10% increase with placebo) following an allergen challenge.

ORIGINAL RESEARCH PAPER Krug, N. *et al.* Allergen-induced asthmatic responses modified by a GATA3-specific DNAzyme. *N. Engl. J. Med.* **372**, 1987–1995 (2015)

INFECTIOUS DISEASE

Fragment screening identifies novel HIV-1 RT inhibitors

HIV-1 reverse transcriptase (RT) — which plays an essential role in the virus life cycle — is the target of two classes of approved anti-HIV drugs. Now, La *et al.* use a combination of saturation-transfer difference (STD) NMR and *in vitro* activity assays to screen a library of fragment-sized compounds with the aim of identifying new drug scaffolds targeting HIV-1 RT. Three compounds were found to potently inhibit HIV-1 RT in cell culture, including RT variants displaying resistance to existing clinical inhibitors. Importantly, two of the compounds have mechanisms distinct from those of existing agents, competitively inhibiting HIV-1 RT with respect to the dNTP substrate or the DNA template or primer.

ORIGINAL RESEARCH PAPER La, J. *et al.* Identification of mechanistically distinct inhibitors of HIV-1 reverse transcriptase through fragment screening. *Proc. Natl Acad. Sci.* **112**, 6979–6984 (2015)

AUTOIMMUNE DISEASE

SIRT1 inhibition suppresses multiple sclerosis

The protein deacetylase SIRT1 has been implicated in the regulation of the immune response and its dysfunction is probably involved in autoimmune diseases. Although previous studies have indicated an anti-inflammatory role of SIRT1, Lim *et al.* now reveal that SIRT1 can promote the generation and function of pro-inflammatory T helper 17 (T_H17) effector cells by interacting with and modulating the activity of the transcription factor RORγt. In a mouse model of multiple sclerosis, T cell specific *Sirt1* deletion or treatment with a SIRT1 inhibitor impaired production of pro-inflammatory T_H17 cells and reduced disease susceptibility.

ORIGINAL RESEARCH PAPER Lim, H. *et al.* SIRT1 deacetylates RORγt and enhances Th17 cell generation. *J. Exp. Med.* **212**, 607–617 (2015)