

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 ROR γ t. 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 ROR γ t and enhances TH17 cell generation. *J. Exp. Med.* **212**, 607–617 (2015)