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plex. They showed that kartogenin disrupts the binding of filamin A to CBF- β , resulting in the translocation of CBF- β to the nucleus, where it can then bind RUNX and regulate the transcription of chondrogenic genes. Silencing of CBF- β or RUNX1 inhibited the ability of kartogenin to differentiate MSCs into chondrocytes.

The RUNX proteins have previously been implicated in chondrocyte proliferation or differentiation, and the identification of kartogenin provides a new tool to regulate their activity by modifying the subcellular localization of their binding partner CBF- β . In addition, the study provides insight into the potential of MSCs to repair damaged joints that may help inform the development of future stem cell therapies for osteoarthritis in humans. —AF

■ IMMUNOLOGY

Targeting IL-17 in psoriasis

Two recent clinical trials provide evidence that interleukin-17 (IL-17) and its receptor are viable targets to treat psoriasis.

In one of these phase 2, randomized, double-blind trials, Kim Papp *et al.* (*N. Engl. J. Med.* **366**, 1181–1189) tested different doses of brodalumab, a monoclonal antibody against the IL-17 receptor A, or placebo in 198 patients with psoriasis. In a separate trial, Craig Leonardi *et al.* (*N. Engl. J. Med.* **366**, 1190–1199) treated 142 people with psoriasis with placebo or different doses of ixekizumab, a monoclonal antibody that directly targets IL-17.

After 12 weeks of treatment, both teams reported that the antibody-treated patients showed statistically significant improvements on the psoriasis area-and-severity index, a scale commonly used to quantify disease progression. Moreover, the safety profile of both antibodies was satisfactory.

Antibodies against other cytokines such as IL-12 and IL-23 are effective against psoriasis, acting at least in part by reducing the production of IL-17 and the generation of T helper type 17 immune responses. The clinical development of IL-17–targeting molecules may nevertheless be advantageous in terms of selectivity, as inhibiting the IL-12/IL-23 axis can also affect T helper type 1 responses, which are important in fighting infection. Phase 3 clinical trials will be necessary to establish the long-term safety and efficacy of brodalumab and ixekizumab. —JCL

Written by Michael Basson, Eva Chmielnicki, Alison Farrell, Juan Carlos López and Meera Swami.

New from NPG

Regulation of circadian behaviour and metabolism by REV-ERB- α and REV-ERB- β

Cho, H. *et al.* *Nature* doi:10.1038/nature11048 (29 March).

Regulation of circadian behaviour and metabolism by synthetic REV-ERB agonists

Solt, L.A. *et al.* *Nature* doi:10.1038/nature11030 (29 March).

These two studies disclose the contribution of the nuclear receptors REV-ERB- α and REV-ERB- β to the regulation of circadian rhythms and metabolic function, and provide evidence that this signaling pathway may be pharmacologically targeted.

Genome-wide meta-analysis identifies 56 bone mineral density loci and reveals 14 loci associated with risk of fracture

Estrada, K. *et al.* *Nat. Genet.* doi:10.1038/ng.2249 (15 April).

The authors carried out a meta-analysis on lumbar spine and femoral neck bone mineral density, identifying 56 loci that showed association, of which 32 loci were new associations. The associated loci had functions that included RANK signaling, mesenchymal stem cell differentiation, endochondral ossification and Wnt signaling.

NLRC4-driven production of IL-1 β discriminates between pathogenic and commensal bacteria and promotes host intestinal defense

Franchi, L. *et al.* *Nat. Immunol.* doi:10.1038/ni.2263 (8 April).

The authors provide new understanding of how the immune system discriminates between commensal and pathogenic bacteria. They show that resident intestinal phagocytes, when infected with pathogenic bacteria, produce the cytokine IL-1 β through activation of the NLRC4 inflammasome. This pathway, which is important in the clearance of the pathogenic bacteria, is not activated when the phagocytic cells are infected by commensal bacteria.

Tanycytes of the hypothalamic median eminence form a diet-responsive neurogenic niche

Lee, D.A. *et al.* *Nat. Neurosci.* doi:10.1038/nn.3079 (25 March).

Adult neurogenesis in the hypothalamus has been reported, and these authors now show that new neurons are formed in a part of the hypothalamus called the median eminence. Notably, median eminence neurogenesis was increased in mice on a high-fat diet, and blocking the formation of these neurons reduced weight gain and increased energy consumption in mice, even in those on a high-fat diet.

of cartilage at bone joints, for which there is no cure. Kristen Johnson *et al.* have now identified a small molecule with effects on mesenchymal stem cells (MSCs) that reduced the severity of disease in two rat models of osteoarthritis. The findings suggest new avenues for the development of drugs or stem cell therapies to combat this disease (*Science* doi:10.1126/science.1215157).

Chondrocytes are cartilage-resident cells that can build and repair cartilage and are generated from MSCs. Thus, directing the differentiation of MSCs into chondrocytes to stimulate joint repair could be a potential therapeutic strategy for osteoarthritis. Using this rationale, Johnson *et al.* screened 22,000 compounds and found that only one, kartogenin, could promote the differentiation of primary human MSCs into chondrocytes. When injected into the joints of rats following surgical or collagenase-induced damage, kartogenin restored cartilage and joint function. By coupling a derivative of kartogenin to biotin and a photoactivatable crosslinker and analyzing the MSC proteins bound to this kartogenin construct after ultraviolet irradiation, the researchers identified filamin A as the target of kartogenin. Filamin A crosslinks actin filaments, but this function was unaffected by kartogenin. Instead, the authors found that the kartogenin-binding region of filamin A also binds core-binding factor- β (CBF- β), the regulatory subunit of the CBF- β -RUNX transcription factor com-