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IN BRIEF

STEM CELLS

PTH regulates bone marrow progenitor fate

New research published in *Cell Metabolism* reveals an important mechanism underlying the anabolic effects of parathyroid hormone (PTH) on bone. Mice with conditional deletion of the gene encoding the PTH 1 receptor (PTH1R) in bone marrow progenitors had increased bone marrow adipose tissue (BMAT), which was accompanied by increased bone resorption and decreased bone mass. Adipocytes purified from the bone marrow of mutant mice strongly expressed adipocytic transcription factors, adipocyte differentiation markers and RANKL. Direct regulation of BMAT by PTH was confirmed by the marked reduction in the volume of BMAT in control mice but not in mutant mice in response to administration of $PTH_{1–34}$. Moreover, analysis of bone biopsy samples from patients with osteoporosis revealed a 27% reduction in the number of bone marrow adipocytes after 18 months of treatment with $PTH_{1–34}$. The findings indicate that PTH reduces marrow adipogenesis by regulating the bone–fat fate of mesenchymal progenitors.

ORIGINAL ARTICLE Fan, Y. *et al.* Parathyroid hormone directs bone marrow mesenchymal cell fate. *Cell Metab.* http://dx.doi.org/10.1016/j.cmet.2017.01.001 (2017)

GENETICS

Unlocking the secrets of adult human height

Although height is a complex, highly hereditable human trait, height variants identified by genome-wide association studies have typically been common, with small effect sizes cumulatively explaining only ~20% of the heritability. Now, in a new study published in *Nature*, rare and low-frequency coding variants with height-increasing or height-decreasing effects of up to 2 cm per allele have been identified. Using a genotyping array approach, the association between 241,453 variants (83% of which were coding variants with a minor allele frequency (MAF) ≤5%) and adult height variation was tested in 711,428 (predominantly European) individuals. 83 height-associated variants (32 rare; 51 low-frequency) were identified (MAF range: 0.1–4.8%), of which rare missense variants in *AR*, *CRISPLD2*, *IHH* and *STC2* had the largest effect sizes. Carriers of the *STC2* variant were ~2.1 cm taller than non-carriers; carriers of any of the other three variants were ~2.0 cm shorter than non-carriers.

ORIGINAL ARTICLE Marouli, E. *et al.* Rare and low-frequency coding variants alter human adult height. *Nature* **542**, 186–190 (2017)

NAFLD

Vitamin D-induced autophagy prevents steatosis

The beneficial effects of 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$) on nonalcoholic fatty liver disease (NAFLD) have been well documented; however, the underlying mechanism was not known. In a new study, $1,25(OH)_2D_3$ is shown to protect against hepatic steatosis by inducing autophagy — a protective pathway that maintains intracellular homeostasis in response to different stressors. Feeding mice a high-fat diet (HFD) for 4 weeks induced hepatic steatosis; however, liver damage was attenuated in HFD-fed mice injected with $1,25(OH)_2D_3$. Autophagic flux and expression of markers of autophagy were increased in HFD-fed mice treated with $1,25(OH)_2D_3$; moreover, inhibition of autophagy by 3-methyladenine abrogated the protective effects of $1,25(OH)_2D_3$ against HFD-induced hepatic steatosis. $1,25(OH)_2D_3$ also reduced inflammation and regulated lipid metabolism in HFD-induced fatty livers. The findings highlight the potential of using $1,25(OH)_2D_3$ and of inducing autophagy to treat NAFLD.

ORIGINAL ARTICLE Li, R. *et al.* $1,25(OH)_2D_3$ attenuates hepatic steatosis by inducing autophagy in mice. *Obesity* http://dx.doi.org/10.1002/oby.21757 (2017)