IN BRIEF

EPIGENETICS

Transgenerational effects of *in utero* malnutrition

In utero malnutrition of male mice (generation F_1) can predispose their own offspring (F_2) to metabolic disorders. Both generations were shown to have low birth weight, although over time the animals developed obesity and glucose intolerance. This metabolic change is linked to a change in DNA methylation — the epigenetic mark is notably present in the sperm of the F_1 mice — and a reduction in expression of the liver X receptor alpha (*Lxra*) gene that is also maintained in the liver cells of the F_2 generation.

ORIGINAL RESEARCH PAPER Martínez, D. *et al.* *In utero* undernutrition in male mice programs liver lipid metabolism in the second-generation offspring involving altered *Lxra* DNA methylation. *Cell Metab.* http://dx.doi.org/10.1016/j.cmet.2014.03.026 (2014)

DISEASE GENETICS

Genome-wide consequences of Down's aneuploidy

Dissecting the precise gene expression consequences of chromosome 21 trisomy is challenging because background genetic variation complicates comparisons between patients and healthy controls. Letourneau *et al.* used high-throughput RNA sequencing to characterize differences in gene expression in fetal skin fibroblasts from a human twin pair that were discordant for chromosome 21 trisomy but that were otherwise isogenic. The extra copy of chromosome 21 led to large domains of altered gene expression genome wide. These regions correlated with known domains that are associated with the nuclear lamina and DNA replication timing, and were characterized by differences in the activating chromatin mark H3K4me3. Thus, the trisomy has widespread consequences on the chromatin environment throughout the genome.

ORIGINAL RESEARCH PAPER Letourneau, A. *et al.* Domains of genome-wide gene expression dysregulation in Down's syndrome. *Nature* **508**, 345–350 (2014)

STEM CELLS

Histone deacetylase inhibitors for stem cell boost

Stem and progenitor cells hold promise as cell-based therapies in regenerative medicine, but optimal *ex vivo* culture conditions are key for maximizing their therapeutic potential. Chaurasia *et al.* studied human umbilical cord blood cells, which are a limited source of haematopoietic stem cells for transplantation into allogeneic recipients that suffer from haematopoietic abnormalities. Testing the effects of various growth factors and small molecules on cord blood cells *ex vivo*, they found that the histone deacetylase inhibitor (HDACi) valproic acid increased the number of stem cells, upregulated the expression of pluripotency genes and enhanced the repopulation of the haematopoietic system when transplanted into immunodeficient mice. In a separate study, Palii *et al.* studied human endothelial progenitor cells (EPCs) derived from cord blood for their ability to repair vascular tissue in a mouse model of ischaemic tissue damage. They identified a key role for the transcription factor TAL1 in the repair, which recruits histone acetyltransferase p300 to effector genes. Treatment of EPCs with the HDACi trichostatin A — to mimic TAL1 function — enhanced vascular repair. Overall, chromatin-modulating small molecules could be valuable for optimizing gene expression programmes in stem-cell-based therapy applications, provided that they are safe.

ORIGINAL RESEARCH PAPERS Chaurasia, P. *et al.* Epigenetic reprogramming induces the expansion of cord blood stem cells. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI70313 (2014) | Palii, C. G. *et al.* Trichostatin A enhances vascular repair by injected human endothelial progenitors through increasing the expression of TAL1-dependent genes. *Cell Stem Cell* **14**, 644–657 (2014)