expression was induced in retinal ganglion cells (RGCs) subjected to a nerve crush injury. Levels of regeneration were significantly higher in OSK mice than in controls, with similar levels observed in 1-month-old, 3-month-old and 12-month-old mice, indicating that the axon-regenerating ability of OSK treatment is not age-dependent.

Post-injury, the DNA methylation age of RGCs increased and their global DNA methylation patterns were altered, but both these effects were reversed by OSK expression, consistent with the ability of OSKM to reset DNA methylation age. Subsequent knockdown analyses confirmed that OSK-mediated regeneration is dependent on TET1- or TET2-catalysed DNA demethylation. Similar effects of OSK expression on axon regeneration and DNA methylation were noted for differentiated human neurons treated with an injury-inducing drug, suggesting that the reprogramming abilities of OSK are conserved across mice and humans.

Next, the authors demonstrated that OSK expression restored axon density and improved visual acuity in a mouse model of glaucoma, a leading cause of age-related blindness. Naturally occurring age-related vision loss in old (12 months) mice was also restored by OSK expression, although there were no changes in axon density. However, gene expression patterns in treated RGCs were similar to those of younger cells, and the improvement in RGC function was associated with TET1- or TET2-dependent reversal of age-related DNA methylation signatures.

The focus of the current study was DNA methylation, but the authors note that other epigenetic marks and transcription factors are likely to be involved in the ageing process. Although many mechanistic details remain unknown, epigenetic age reprogramming could provide a means to reverse age-related degeneration and disease. Dorothy Clyde

modifications that suggest that H1 normally acts to promote the repression methylation mark H3K27me3 and inhibits the permissive H3K36me2; these activities were linked to genome-wide H1 stoichiometry. RNA sequencing revealed mostly increased gene expression upon H1 depletion, in particular of genes regulating T cell activation.

In the second study, Yusufova et al. analysed H1c/H1e double-knockout (H1DKO) mice, showing that loss of these two H1 variants increased fitness of germinal centre B cells by enhancing their capacity for self-renewal. In the H1DKO mice and in patients with mutations in both H1c and H1e, B cells exhibited stem-cell-like gene expression profiles, including upregulation of genes normally marked by H3K27me3. Hi-C analyses in sorted H1DKO germinal centre B cells showed widespread decompaction of chromatin and a B-to-A compartment shift, coincident with gain of H3K36me2 and loss of H3K27me3 marks as detected by chromatin immunoprecipitation followed by sequencing (ChIP-seq), consistent with the findings by Willcockson and colleagues. Analysis of H1 allele mutations and deletions from The Cancer Genome Atlas (TCGA) data found the highest frequency of mutant H1 alleles in B cell lymphomas compared with other cancer types, establishing that variants in H1c and H1e are among the top ten driver mutations in diffuse large B cell lymphomas. Indeed, offspring of H1DKO mice bred with mice overexpressing Bcl2 in haematopoietic lineages developed aggressive lymphomas, indeed, offspring of H1DKO mice bred with mice overexpressing Bcl2 in haematopoietic lineages developed aggressive lymphomas with upregulation of stem cell genes, mirroring transcriptional signatures identified in human disease. Taken together, these studies establish histone H1 as a regulator of the cellular epigenetic landscape through localized chromatin compaction and genome architecture. Linda Koch

RESOURCE Mapping metastasis

The metastatic potential of human cancers is poorly understood and has been difficult to study at scale. Now, a study in Nature reports a metastasis map (MetMap) that reveals organ-specific metastasis patterns for 500 cancer cell lines, representing 21 solid tumour types. The data for MetMap were generated by differentially barcoding the cell lines, which were then pooled and injected into mice; after 5 weeks, organs were harvested from the mice and barcodes quantified by bulk RNA sequencing. As proof of its utility, the authors used MetMap to identify breast cancers that could and could not metastasize to the brain and demonstrated through molecular and perturbation analyses that lipid metabolism is a key determinant of brain metastasis.

ORIGINAL ARTICLE Jin, X. et al. A metastasis map of human cancer cell lines. Nature 588, 331–336 (2020)

IN BRIEF

EPIGENETICS

Uncovering distinct roles for H3K9me3

Feng et al. report the use of EpiGo-KRAB to introduce H3K9me3 at targeted genomic regions and to monitor its effects on nuclear localization, chromatin structure and gene expression. Ectopic H3K9me3 was shown to induce co-localization with HP1α condensates, mediate de novo formation of heterochromatin-like domains and lead to A-to-B switches in genome compartmentalization. However, only genes that gained H3K9me3 and lost H3K4me3 and H3K27ac were transcriptionally repressed, suggesting H3K9me3 has distinct functions in gene expression and genome organization.

ORIGINAL ARTICLE Feng, Y. et al. Simultaneous epigenetic perturbation and genome imaging reveal distinct roles of H3K9me3 in chromatin architecture and transcription. Genome Biol. 21, 296 (2020)

TECHNOLOGY

SARS-CoV-2 detection goes mobile

Fozouni et al. describe a CRISPR–Cas13a-based approach that promises to offer rapid, accurate, portable and low-cost point-of-care detection of SARS-CoV-2 in infected individuals. Unlike other CRISPR diagnostics, the assay is quantitative, directly detecting target RNA without prior amplification of the viral genome. Sensitivity and portability are achieved by the use of a mobile phone camera for signal detection. The test is also fast, accurately identifying SARS-CoV-2-positive clinical samples with a measurement time as low as 5 minutes.

ORIGINAL ARTICLE Fozouni, P. et al. Amplification-free detection of SARS-CoV-2 with CRISPR-Cas13a and mobile phone microscopy. Cell https://doi.org/10.1016/j.cell.2020.12.011 (2020)

GENOMICS

Spaceflight causes mitochondrial stress

In this Cell article, the health risks of spaceflight are investigated by a wide-ranging analysis of transcriptomic, epigenomic, proteomic and metabolomic data from NASA’s GeneLab. GeneLab contains data for 59 astronauts and hundreds of samples that have been flown in space, including mouse strains, human cell models, and mouse and human tissues. Pathway analyses implicated mitochondrial stress and dysregulation as major drivers of health risks, and some key findings were confirmed using data from the NASA Twin study.

ORIGINAL ARTICLE da Silva eir, W. A. et al. Comprehensive multi-omics analysis reveals mitochondrial stress as a central biological hub for spaceflight impact. Cell 183, 1185–1201 (2020)