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IN BRIEF

CHROMOSOME BIOLOGY

Mitotic chromatin condensin'

Kim *et al.* investigated the function of the SMC (structural maintenance of chromosomes) complex condensin in the organization of the fission yeast genome. The yeast condensin protein Cut14 localized to both centromeres and target genes of the transcription factors Ams2 and Ace2. Condensin formed long-range chromatin interactions (condensin domains) between loci that are separated by >100 kb to >1 Mb, notably between the Ams2 and Ace2 target loci and centromeres. Condensin domain formation was most prominent during mitosis, when Ams2 and Ace2 are highly expressed; indeed, condensin was recruited to the Ams2 and Ace2 target genes by the respective transcription factor. During mitosis, condensin was necessary for correct chromatin condensation at Ace2 target loci, and disruption of target loci binding to centromeres resulted in chromosome segregation defects. Thus, mitotic transcription factors recruit condensin to shape mitotic chromosome organization and segregation.

ORIGINAL ARTICLE Kim, K. D. *et al.* Transcription factors mediate condensin recruitment and global chromosomal organization in fission yeast. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3647 (2016)

MECHANISMS OF DISEASE

Metabolic reprogramming cures liver disease

Hereditary tyrosinaemia type I (HT-I) is a lethal liver disease that is caused by mutations in *FAH*, which encodes fumarylacetoacetate hydrolase, the enzyme that catalyses the final step of tyrosine catabolism. FAH deficiency leads to the accumulation of toxic metabolic intermediates that cause hepatocellular carcinoma. Pankowicz *et al.* tested the efficacy of reprogramming tyrosine metabolism by gene disruption, which should be more feasible than *FAH* gene correction. They injected the CRISPR–Cas components to the tail vein of HT-I ($Fah^{-/-}$) mice and inactivated *Hpd*, the gene encoding hydroxyphenylpyruvate dioxygenase, which functions upstream of FAH. Edited ($Fah^{-/-}/Hpd^{-/-}$) hepatocytes had a growth advantage over non-edited ($Fah^{-/-}$) hepatocytes and they replaced the entire liver in a few weeks. $Fah^{-/-}/Hpd^{-/-}$ mice had significantly reduced levels of toxic metabolic intermediates and were cured of HT-I.

ORIGINAL ARTICLE Pankowicz, F. P. *et al.* Reprogramming metabolic pathways *in vivo* with CRISPR/Cas9 genome editing to treat hereditary tyrosinaemia. *Nat. Commun.* **7**, 12642 (2016)

MECHANOTRANSDUCTION

Stretching chromatin promotes transcription

Whether chromatin stretching and decondensing by physiological forces affects gene expression is unclear. Tajik *et al.* used 3D magnetic twisting cytometry to apply force to chromatin in Chinese hamster ovary cells carrying a genomic insertion of an array of *DHFR* genes. Each *DHFR* gene contained *lac*-operator repeats that, when bound by GFP–lac repressors, enabled visualization of chromatin stretching as increased distance between GFP spots. Applying local shear stresses to focal adhesions on the cell surface induced chromatin stretching, depending on the angle (directionality) of the force. Chromatin stretching induced *DHFR* expression within seconds, measured by mRNA FISH, as well as the expression of a tested endogenous gene. Force transmission to chromatin depended on cytoskeletal tension, the LINC (linker of nucleoskeleton and cytoskeleton) complex and the nuclear lamina.

ORIGINAL ARTICLE Tajik, A. *et al.* Transcription upregulation via force-induced direct stretching of chromatin. *Nat. Mater.* http://dx.doi.org/10.1038/nmat4729 (2016)