Nature Reviews Genetics | AOP, published online 16 January 2013

IN BRIEF

SMALL RNA

Long-lived microRNA complexes

This study shows that in quiescent mammalian cells, microRNAs (miRNAs) can remain stable for at least 3 weeks in complexes that contain Argonaute. These complexes are smaller than the RNA-induced silencing complex (RISC) and lack GW182 (a protein that is essential for miRNA-mediated silencing). The authors studied quiescent immune cells, and when these cells were given mitogenic stimulation, the miRNA–Argonaute complexes were recruited into RISCs. The stable miRNA–Argonaute complexes could allow cells to retain long-term information for post-transcriptional regulation.

ORIGINAL RESEARCH PAPER Olejniczak, S. H. *et al.* Long-lived microRNA–Argonaute complexes in quiescent cells can be activated to regulate mitogenic responses. *Proc. Natl Acad. Sci. USA* 17 Dec 2012 (doi:10.1073/pnas.1219958110)

DNA REPLICATION

ChIP–seq for human replication origins

Previously, the identification of replication origins (ORIs) in metazoans has been hampered by the lack of stringent and sensitive genome-wide techniques for identifying these sites. The authors here present a genome-wide map of human ORIs obtained by chromatin immunoprecipitation followed by sequencing (ChIP–seq) against ORC1 (a crucial component of the origin recognition complex). Human ORIs were found to be associated with transcription start sites. The timing of firing of these ORIs was linked to the level of transcription: higher transcription was associated with earlier firing in S phase.

ORIGINAL RESEARCH PAPER Dellino, G. I. *et al.* Genome-wide mapping of human DNA-replication origins: levels of transcription at ORC1 sites regulate origin selection and replication timing. *Genome Res.* 27 Nov 2012 (doi:10.1101/gr.142331.112)

TRANSCRIPTION

A role for DNA topoisomerase in activation

DNA topoisomerases are thought to facilitate transcription by removing excess topological strain induced by the tracking of the polymerase. A study in *Saccharomyces cerevisiae* deficient for topoisomerases I and II has now suggested that *in vivo* these enzymes are also involved in gene activation. Genes particularly affected in topoisomerase mutants have features associated with highly regulated transcription, such as a TATA box, which is indicative of a repressible and/or inducible mode of transcription. For the gene *PHO5*, the authors showed that topoisomerases are required for transcription factor binding.

ORIGINAL RESEARCH PAPER Pedersen, J. M. *et al.* DNA topoisomerases maintain promoters in a state competent for transcriptional activation in *Saccharomyces cerevisiae*. *PLoS Genet.* **8**, e1003128 (2012)

COMPLEX TRAITS

Chromatin marks to aid fine mapping

Some SNPs could influence a phenotype by altering gene regulation in cell types relevant to that phenotype. Starting from this hypothesis, the authors of this study used statistical approaches to show that some cell-type-specific chromatin modifications can be used for mapping phenotype-associated SNPs to regulatory variants. They found that chromatin marks linked to gene activation — particularly histone H3 lysine 4 trimethylation — overlap approximately one-quarter of trait-associated variants in relevant cell types (such as the liver and pancreatic islet cells for type 2 diabetes). This approach could provide leads for functional follow-up.

ORIGINAL RESEARCH PAPER Trynka, G. *et al.* Chromatin marks identify critical cell types for fine mapping complex trait variants. *Nature Genet.* 23 Dec 2012 (doi:10.1038/ng.2504)