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IN BRIEF

RNA

New CLIP pipeline improves interactome discovery

A novel experimental and computational crosslinking and immunoprecipitation (CLIP) workflow called FAST-iCLIP (fully automated and standardized iCLIP), which reduces experimental time by ~50%, promises to improve research into RNA–protein interactions across human and pathogen RNAs. The researchers' aim was to address common limitations of CLIP investigations by improving the efficiency of sample preparation and extending analyses across protein-coding, non-coding and user-definable non-human transcriptomes. In addition, resulting data formats were standardized to facilitate comparisons between RNA-binding proteins. Application of FAST-iCLIP to the human and viral interactomes of poly(C)-binding protein 2 (PCBP2) revealed novel RNA–protein interactions and confirmed known functional protein roles. This pipeline should facilitate functional analyses of protein-coding and non-coding human transcriptomes, as well as the study of pathogen and microbiome interactomes.

ORIGINAL RESEARCH PAPER Flynn, R. A. *et al.* Dissecting noncoding and pathogen RNA–protein interactomes. *RNA* http://dx.doi.org/10.1261/rna.047803.114 (2014)

EPIGENETICS

Dad's diet controls offspring phenotype

Using a fly model of paternally induced obesity, Öst *et al.* show that acute changes in paternal diet — as short as 24 hours — reprogram offspring metabolism without affecting growth and development. Paternal intergenerational metabolic reprogramming altered chromatin states and gene expression in the F_1 generation via mechanisms that are dependent on Polycomb proteins and the core heterochromatin machinery. Specifically, obesity susceptibility resulted from reduced stage-specific epigenetic regulation of histone H3 lysine 27 trimethylation (H3K27me3)- and H3K9me3-defined domains both in mature sperm and in offspring embryos. The authors propose a model whereby phenotype is evolutionarily encoded directly into the chromatin state of specific loci and suggest that this mechanism directionally controls phenotypic variation within a population. Analysing two murine and three human microarray data sets of adipose tissue samples from lean and obese individuals, the team identified conserved gene signatures for epigenetically defined phenotypic variation.

ORIGINAL RESEARCH PAPER Öst, A. *et al.* Paternal diet defines offspring chromatin state and intergenerational obesity. *Cell* http://dx.doi.org/10.1016/j.cell.2014.11.005 (2014)

DISEASE GENETICS

Therapeutic targeting of a long non-coding RNA

Antisense oligonucleotides (ASOs) against the long non-coding RNA UBE3A antisense transcript (*UBE3A-ATS*) could represent a feasible therapy for the monogenic disorder Angelman syndrome, a new study reports. The disease results from loss of expression of the maternal *UBE3A* allele in the presence of the imprinted (that is, silenced) paternal allele. Meng *et al.* were able to activate expression of the paternal *Ube3a* allele in cultured mouse neurons and in live mice by specifically targeting the silencing *Ube3a-ATS* with ASOs. Restoration of UBE3A protein in a mouse model of Angelman syndrome was sufficient to ameliorate cognitive deficits. Given that genomic organization and regulation at the imprinting control centre is highly conserved between mice and humans, the researchers posit that their findings highlight a viable therapeutic strategy in humans.

ORIGINAL RESEARCH PAPER Meng, L. *et al.* Towards a therapy for Angelman syndrome by targeting a long non-coding RNA. *Nature* http://dx.doi.org/10.1038/nature13975 (2014)