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IN BRIEF

DISEASE GENETICS

Interactome remodelling in cystic fibrosis rescue

Most cases of cystic fibrosis are caused by a deletion of phenylalanine 508 in the cystic fibrosis transmembrane conductance regulator (ΔF508 CFTR), which results in defects that can be partly rescued by low temperature or histone deacetylase (HDAC) inhibition. Pankow *et al.* used co-purifying protein identification technology (CoPIT) to analyse the interactomes of wild-type CFTR (WT CFTR) and ΔF508 CFTR, and identified a greater number of proteins as interacting with ΔF508 CFTR than with WT CFTR. Analysis of interactome dynamics following temperature shift or inhibition of HDACs revealed that functional rescue is associated with extensive remodelling of the ΔF508 CFTR-specific interactome. The authors identified key interactors that are lost during rescue or are crucial for CFTR biogenesis, providing valuable insight into the molecular mechanisms that underlie cystic fibrosis.

ORIGINAL ARTICLE Pankow, S. *et al.* ΔF508 CFTR interactome remodelling promotes rescue of cystic fibrosis. *Nature* http://dx.doi.org/10.1038/nature15729 (2015)

POPULATION GENOMICS

Genomic analysis of South American ancestry

A new study sheds light on the genetic events that shaped the population structure of South America. Homburger *et al.* analysed genome-wide single-nucleotide polymorphism (SNP) data to trace the European and Native American ancestral origins of admixed Latino individuals from five South American countries. Principal component analysis identified the Iberian Peninsula as the predominant source of European ancestry. The origins of Native American ancestral components differed between Latino populations, indicating that admixture between European colonists and Native American populations occurred across South America. Modelling based on ancestry tract length indicated that the initial admixture events occurred between 9 and 14 generations ago, and that a later burst of European migration to South America occurred between 3 and 9 generations ago. The heterogeneity revealed by this study demonstrates the importance of including diverse populations in genetic association studies.

ORIGINAL ARTICLE Homburger, J. R. *et al.* Genomic insights into the ancestry and demographic history of South America. *PLoS Genet.* http://dx.doi.org/10.1371/journal.pgen.1005602 (2015)

RNA

Differential regulation of APA isoforms

Alternative cleavage and polyadenylation (APA) allows genes that contain multiple cleavage and polyadenylation signals (CPAs) to encode multiple RNA isoforms and has an important role in the regulation of gene expression. Now, Neve *et al.* report the differential regulation of APA isoforms in cytoplasmic and nuclear RNA fractions of human cell lines. APA isoforms with shorter 3′ untranslated regions (UTRs), owing to cleavage at promoter-proximal **versus** promoter-distal CPAs, were over-represented in the cytoplasm in all non-neuronal cell lines analysed, but not in neuroblastoma-derived cells. Further experiments indicated that the nuclear retention of distal CPA isoforms (with longer 3′ UTRs) can be partly attributed to incomplete splicing, and demonstrated that the nuclear endoribonuclease DICER1 controls subcellular APA profiles by influencing CPA site selection and through microRNA-mediated stabilization.

ORIGINAL ARTICLE Neve, J. *et al.* Subcellular RNA profiling links splicing and nuclear DICER1 to alternative cleavage and polyadenylation. *Genome Res.* http://dx.doi.org/10.1101/gr.193995.115 (2015)

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