*Nature Reviews Genetics* | Published online 21 Mar 2016

# IN BRIEF

## COMPLEX DISEASE

### A global view of regulatory networks

Marbach *et al.* have developed a novel resource of 394 human cell type- and tissue-specific gene regulatory networks, representing 146 different cell types, 111 tissues and 137 cell lines. Transcriptional regulatory circuits were inferred on the basis of expression profiles of enhancers and promoters, their integration with transcription factor sequence motifs, and linking of regulatory elements with target genes on the basis of genomic distance and joint expression in a given tissue. Analysis of data from across 37 genome-wide association studies (GWAS) revealed that disease-related variants often disrupt network modules that are specific for trait-relevant tissues, which suggests that perturbed regulatory modules can help define disease-relevant tissues. All networks and tools are freely available at http://regulatorycircuits.org.

**ORIGINAL ARTICLE** Marbach, D. *et al.* Tissue-specific regulatory circuits reveal variable modular perturbations across complex diseases. *Nat. Methods* http://dx.doi.org/10.1038/nmeth.3799 (2016)

## TECHNIQUE

### Unwanted sequences DASH off

A new method called DASH (Depletion of Abundant Sequences by Hybridization) exploits the unique properties of the endonuclease Cas9 to target and prevent the amplification of unwanted sequences during next-generation sequencing (NGS) protocols, enabling enrichment of rare and less abundant non-targeted sequences in NGS libraries or amplicon pools at no additional cost. Wu *et al.* showcase the utility and efficacy of their technique by targeting abundant mitochondrial rRNAs in sequencing libraries prepared from total RNA extracted from HeLa cells. After DASH, reads mapping to 12S and 16S mitochondrial rRNA genes were reduced from 61% of all uniquely mapped human reads in the untreated samples to 0.055% of reads. Integration of DASH into the analysis of patient samples of cerebrospinal fluid known previously to be infected with pathogens lowered the sequencing depth required to detect pathogen sequences, highlighting the utility of DASH for diagnostic purposes.

**ORIGINAL ARTICLE** Gu, W. *et al.* Depletion of Abundant Sequences by Hybridization (DASH): using Cas9 to remove unwanted high-abundance species in sequencing libraries and molecular counting applications. *Genome Biol.* **17**, 41 (2016)

## GENETIC TESTING

### Whole-exome sequencing for clinical diagnostics

A prospective study has found that singleton whole-exome sequencing (WES) as a first-tier test in infants with suspected monogenic genetic disorders outperforms standard care. The team compared the rate of diagnosis, clinical utility and impact on management of singleton WES with that of standard investigations, such as single- or multigene panel sequencing, which were undertaken in parallel if clinically indicated. Overall, WES led to a diagnosis in 46 out of 80 participants (57.5%), whereas standard genetic tests led to a diagnosis in 13.75% of infants. Clinical management improved as a result of WES, as management was altered for 15 out of 46 participants after WES-based diagnosis. Finally, a greater number of relatives benefited from WES compared with standard care; a genetic diagnosis following additional testing was determined for 12 versus 5 cases, respectively, and 28 versus 13 couples were found to have a high recurrence risk for future pregnancies.

**ORIGINAL ARTICLE** Stark, Z. *et al.* A prospective evaluation of whole-exome sequencing as a first-tier molecular test in infants with suspected monogenic disorders. *Genet. Med.* http://dx.doi.org/10.1038/gim.2016.1 (2016)