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IN BRIEF

TECHNOLOGY

Prediction of reprogramming factors

A computational framework called Mogrify predicts the reprogramming factors required to induce transdifferentiation — the direct conversion from one somatic cell type to another. The system, which is based on gene expression and regulatory network data, predicts the set of transcription factors with optimal influence over genes that are differentially expressed between the target and donor cell types. Mogrify was applied to data sets from ~300 cell types and tissues to generate an atlas of predictions for human cell conversions. The system correctly predicted known human conversion factors that had previously been identified by experimental means. The transduction of cells with viruses encoding transcription factors predicted by Mogrify induced two new human cell conversions (fibroblast to keratinocyte-like cells and keratinocyte to endothelial-like cells), demonstrating the tool's predictive power. The developers suggest that Mogrify will aid in the development of transdifferentiation protocols, paving the way for the routine manipulation of cells.

ORIGINAL ARTICLE Rackham, O. J. L. *et al.* A predictive computational framework for direct reprogramming between human cell types. *Nat. Genet.* http://dx.doi.org/10.1038/ng.3487 (2016)

RNA

Exonic splicing mutation prevalence

A new study reveals that exonic splicing mutations are more common than had been estimated. Soukarieh *et al.* used exon 10 of the *MLH1* gene, which is associated with hereditary cancer, as a model to determine the proportion of single nucleotide variants (SNVs) that affect RNA splicing in a given exon. Minigene assays and patient RNA analysis revealed that an unexpectedly high proportion of SNVs (77% of 22 analysed) represented splicing mutations, most of which affected splicing by altering potential splice regulatory elements (ESRs). As ESRs are considered to be difficult to predict, the authors combined their data with data sets from previous studies of disease-associated genes to assess the capabilities of three bioinformatics tools for the identification of ESR mutations. Two of these approaches performed well in identifying ESR mutations and could predict the severity of the splicing defects. These findings suggest that *in silico* approaches can be used to stratify exonic variants for functional testing, which may facilitate the identification of disease-causing SNVs.

ORIGINAL ARTICLE Soukarieh, O. *et al.* Exonic splicing mutations are more prevalent than currently estimated and can be predicted by using *in silico* tools. *PLoS Genet.* **12**, e1005756 (2016)

TECHNIQUE

Single-cell CNV detection

Knouse *et al.* describe a high-specificity analytical approach for the detection of megabase-scale copy number variants (CNVs) in single somatic cells. Applying their approach to single-cell sequencing data from brain and skin cells, the authors detected CNVs exceeding 5 Mb in 8–9% of somatic cells across tissues. Notably, two recurrent CNVs were identified across individuals. In germline cells, megabase-scale CNVs are present in 1% of individuals and are often associated with disease. By contrast, this study shows that large CNVs are tolerated and relatively prevalent in somatic cells.

ORIGINAL ARTICLE Knouse, K. A., Wu, J. & Amon, A. Assessment of megabase-scale somatic copy number variation using single cell sequencing. *Genome Res.* http://dx.doi.org/10.1101/gr.198937.115 (2016)