IN BRIEF

VIRAL EVOLUTION

Predicting HIV drug response

HIV evades antiretroviral therapy by hyperaccumulating mutations. These authors developed a tool that uses probabilistic models to predict the series of mutations that occur following drug treatment. This approach predicts the success of different therapeutic combinations based on the likelihood of the virus being able to evolve resistance to them. This measure outperformed current approaches to predict viral load when applied to data from a large patient cohort.

ORIGINAL RESEARCH PAPER Beerenwinkel, N. *et al.* The individualized genetic barrier predicts treatment response in a large cohort of HIV-1 infected patients. *PLoS Comput. Biol.* **9**, e1003203 (2013)

EPIGENOMICS

Genome-wide investigation of position effects

Position-effect variegation (PEV) describes the dependency of the expression of a gene on its local chromatin environment. PEV has been difficult to assess on a genome-wide scale, as reporter genes must be individually assessed in clonal cell lines and locating the integration site is difficult. These authors developed a method called thousands of reporters integrated in parallel (TRIP) which enables the parallel assessment of reporter genes using genetic barcodes and sequencing. Using TRIP they assessed 27,000 integration sites in mouse embryonic stem cells.

ORIGINAL RESEARCH PAPER Ahktar, W. *et al.* Chromatin position effects assayed by thousands of reporters integrated in parallel. *Cell* **154**, 914–927 (2013)

FUNCTIONAL GENOMICS

Conserved functions of small open reading frames

Small open reading frames (smORFs) encode peptides of <100 amino acids. They are present in animal and plant genomes but investigation of their functions has been mostly neglected because of technical challenges. These authors identified two *Drosophila melanogaster* smORFs that are translated and function in Ca^{2+} transport in the heart, where they are important for heart muscle function. They found that these smORFs have human homologues and suggest that they have a potentially conserved function in the heart. This evidence highlights the need for the further investigation of smORF functions.

ORIGINAL RESEARCH PAPER Magny, E. G. *et al.* Conserved regulation of cardiac calcium uptake by peptides encoded in small open reading frames. *Science* http://dx.doi.org/10.1126/science.1238802 (2013)

GENETIC SCREENS

Human mutant-gene library

Thousands of genes of unknown function are present in the human genome, creating a need for simple, inexpensive and efficient models to interrogate their function. Human cell line models are particularly useful in this case, as many genes, including many involved in human disease, do not have orthologues in commonly used model organisms. These authors have generated a collection of human cell lines that are genetically identical with the exception that each has a unique insertion in a single gene. This collection was derived from a haploid cell line; thus, even genes which are haplosufficient will have a phenotype. The authors targeted a total of 3,396 genes, which is a third of all the genes that are expressed in humans. In addition, most of the insertions are reversible; thus, the phenotype could be rescued using the same tool.

ORIGINAL RESEARCH PAPER Bürckstümmer, T. *et al.* A reversible gene trap collection empowers haploid genetics in human cells. *Nature Methods* http://dx.doi.org/10.1038/nmeth.2609 (2013)

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