IN BRIEF

GENOMICS

The UK Biobank

Bycroft, C. et al. *Nature* **562**, 203–209 (2018).

How are human genetic variations linked to disease phenotypes? In order for this question to be answered in any detail, large amounts of patient data are needed. The UK Biobank is building such a unique resource: researchers involved in the project collected genotype data on ~500,000 individuals in conjunction with phenotypic data such as measures of physical activity, blood, saliva and urine biomarkers, in addition to MRI images of heart and brain. Bycroft et al. analyzed the quality of the array-derived genotype data, as well as their population structure and relatedness. Imputation allowed them to increase the number of variants to 96 million. In particular, the imputation of variation at human leukocyte antigen (HLA) genes provided the researchers with signal for the association of particular HLA gene alleles and several diseases. *NR*

https://doi.org/10.1038/s41592-018-0245-2

BIOCHEMISTRY

Enhanced antibody validation

Edfors, F. et al. *Nat. Commun.* **9**, 4130 (2018).

The need for better validation of the specificity and reproducibility of antibody reagents for biological research applications has been a recent hot-button topic. To begin to address the many challenges, the International Working Group for Antibody Validation recently proposed five 'pillars' for antibody validation: genetic knockdown, recombinant expression, independent antibodies, capture mass spectrometry analysis, and orthogonal methods. Edfors et al. applied the five pillars, including an original approach for orthogonal validation combining transcriptomics and proteomics analysis across multiple cell lines, to thousands of antibodies in the Human Protein Atlas resource in order to validate their use in western blotting. They report more than 6,000 antibodies with enhanced validation, meaning that their good performance for western blotting was validated by at least one of the pillar approaches; 263 antibodies were validated by three or more pillars. *AD*

https://doi.org/10.1038/s41592-018-0248-z

CHEMICAL BIOLOGY

Split proteins by design

Dagliyan, O. et al. *Nat. Commun.* **9**, 4042 (2018).

Optogenetic and chemogenetic tools represent a powerful suite of technologies for controlling cellular behavior and studying protein function. One approach for generating proteins that can be regulated by a researcher is to make split versions of a protein and then fuse the individual pieces to proteins that dimerize; dimerization can be induced by either light or small-molecule treatment. However, it has been challenging to design constructs that can reassemble efficiently without high levels of spontaneous assembly. Dagliyan and colleagues developed an approach called "split proteins regulated by a ligand or by light" (SPELL) to computationally identify split sites on the basis of the 'split energy' of the protein. They show that their approach works robustly for a range of enzymes including a tyrosine kinase, TEV proteinase, and a guanine exchange factor. *RS*

https://doi.org/10.1038/s41592-018-0246-1

GENOMICS

Cell portrait of a mouse

The *Tabula Muris* Consortium. *Nature* **562**, 367-372 (2018).

Single-cell atlas projects have enormous potential to catalog cell types within tissues and to serve as reference datasets that define baseline gene expression in model organs. The *Tabula Muris* project undertook single-cell RNA sequencing of more than 100,000 cells in 20 different organs from three-month-old mice. For data generation, roughly half of the cells were sequenced via droplet-based 3′ -end sequencing, and the other half were sequenced via plate-based full-length sequencing after cell sorting. Libraries were likely sequenced to saturation and highlighted differences between the technologies: the plate-based method tended to detect many more genes, although this varied by organ. Fine-grained cell clustering allowed the identification of universal and organ-specific gene expression patterns in cell types shared across organs. The authors also were able to extract transcription factor signatures that defined cell types. *TN*

https://doi.org/10.1038/s41592-018-0247-0

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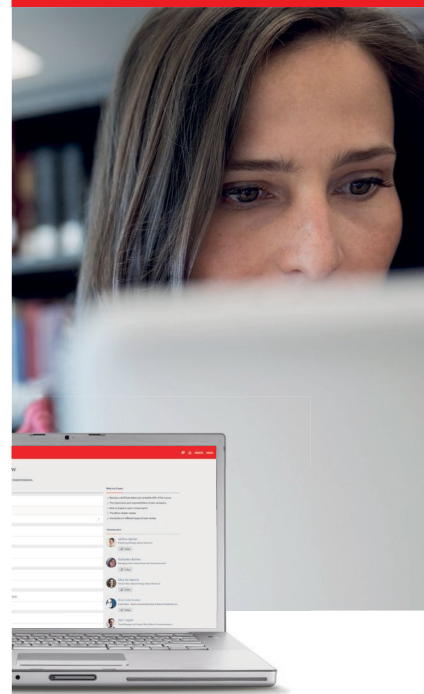

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