TOOLS IN BRIEF

MICROBIOLOGY

Technologies converge on the human gut

The Human Functional Genomics Project, a collaboration between teams in Boston and the Netherlands, aims to combine omics technology with functional tests to characterize how genetic makeup, environment and the microbiome impact immunity and health. In a series of studies, over 500 healthy volunteers were assessed for the effect of intrinsic and environmental factors (ter Horst *et al.*), host genomic variants (Li *et al.*) and intestinal flora (Schirmer *et al.*) on cytokine production and baseline immune parameters. The studies profiled peripheral blood in response to natural conditions or *in vitro* pathological or physiological stimulation; they revealed factors, including novel candidate genetic loci and microbial mediators, that affect individual human immune responses.

Li, Y. *et al. Cell* **167**, 1099–1110 (2016).
ter Horst, R. *et al. Cell* **167**, 1111–1124 (2016).
Schirmer, M. *et al. Cell* **167**, 1125–1136 (2016).

STRUCTURAL BIOLOGY

Faster to a structure with RELION-2

Single-particle cryoelectron microscopy (cryo-EM) is becoming an increasingly popular approach for solving challenging protein and protein complex structures. However, a methodological bottleneck that still limits progress in this field is the need for computationally intensive image classification and structure refinement steps. Kimanius *et al.* present RELION-2, a substantially faster version of the popular RELION tool for cryo-EM-based structure determination. The use of graphics processing unit (GPU) acceleration greatly shortens the time required for image processing and structure determination as compared to the original RELION package. The authors demonstrate that a high-resolution structure can be determined using RELION-2 within days on a desktop computer or within just hours on a GPU cluster. The tool is likely to have significant practical benefits for researchers utilizing cryo-EM.

Kimanius, D. *et al. eLife* http://dx.doi.org/10.7554/eLife.18722 (2016).

GENOMICS

A database for CRISPR screens

CRISPR–Cas9-based genome-wide screens have accumulated a large body of data that shed light on genotype–phenotype relationships. To facilitate access to this information, Rauscher *et al.* present a database that hosts more than half a million data points from over 80 high-throughput perturbation experiments that induced null mutations or used transcriptional activation or repression in human cells. GenomeCRISPR (http://genomecrispr.org) can be mined for single genes or for genomic regions, it can be used to rank single guide RNAs based on their effect, and it facilitates comparative analyses in multiple cell lines using phenotypic and genome tracks. The authors plan to expand the database as more data become available and include organisms other than human for cross-species comparison.

Rauscher, B. *et al. Nucleic Acids Res.* http://dx.doi.org/10.1093/nar/gkw997 (2016).

PROTEOMICS

Reverse-polarity activity-based protein profiling

Activity-based protein profiling (ABPP) is a technique used to profile the binding of small-molecule probes to proteins on a proteomic scale. The approach has been applied to assign functions to understudied enzymes. Typically, ABPP has been used to target reactive, nucleophilic amino acids such as serine and cysteine using electrophilic small-molecule probes. Matthews *et al.* turned this concept around to develop 'reverse-polarity' ABPP. By utilizing nucleophilic probes, they show it is now possible to capture electrophilic protein cofactors and post-translational modifications. Hydrazine-based ABPP probes covalently attach to electrophilic protein cofactors or modifications via click chemistry, enabling their purification and identification by mass-spectrometry-based proteomics. Using this approach, the authors discovered that the enzyme *S*-adenosyl-L-methionine decarboxylase contains a pyruvoyl cofactor that is controlled by intracellular methionine levels.

Matthews, M.L. *et al. Nat. Chem.* http://dx.doi.org/10.1038/nchem.2645 (2016).