METHOD OF THE YEAR 2012
Our choice for Method of the Year 2012—our annual celebration of methods in biological research—is targeted proteomics. With targeted proteomics technologies, specific proteins of interest in biological samples can be measured with high sensitivity, quantitative accuracy and reproducibility. Historically, antibody reagents have been widely used for targeted protein detection in biological samples, but mass spectrometry technology has been undergoing rapid evolution in the past several years, opening up new applications in systems biology and in translational research. In our special feature, a News Feature, Primer, Commentary and Perspective discuss how the mass spectrometry technology for targeted proteome analysis was developed, how it works, how it is being applied for both basic and translational research, what the current limitations are and how future technology development could address these limitations. In the Methods to Watch section, we feature key areas of future methods development.

Resource p47

High-quality short microbial markers
To assess the diversity in microbial samples, many researchers sequence marker genes such as the 16S rRNA gene that encodes part of the prokaryotic ribosome. Until recently, long amplicons were sequenced with the Roche 454 pyrosequencer and filtered for quality with software specifically designed for this platform. The good news for scientists is that short amplicon sequencing on Illumina instruments is now an alternative that provides much higher throughput; the bad news is that 454-based quality filtering cannot be applied to the new data. Caporaso and colleagues therefore carefully tested the parameters that indicate high quality of Illumina platform–derived amplicon sequences and provide guidelines for how to best interpret short amplicon data.

Brief Communication p57

An indirect reprogramming strategy
There is huge interest in using cellular reprogramming to generate individualized human cell types for research and therapy. In one approach, a somatic cell is reprogrammed to pluripotency and then differentiated into the cell type of interest. In a second approach, a somatic cell is directly converted to the cell type of interest using lineage-specific transcription factors. Two papers in this issue demonstrate a third strategy: human somatic cells are transiently exposed to pluripotency factors to induce a plastic state and are then differentiated into the desired cell type. Izpisua Belmonte and colleagues use this strategy to reprogram human fibroblasts, including adult cells, to bipotent angioblast-like progenitors that can yield functional vascular endothelial cells. Pei, Pan and colleagues start with easily accessible cells from adult human urine and reprogram them to expandable neural progenitor cells that yield functional neurons.

Articles p77, p84

Real-time fragment assignment
Almost every genomic analysis begins by mapping short sequencing reads to a reference sequence. The bottleneck in mapping comes with assigning ambiguously mapping reads—sequence fragments that could belong to more than one site in the genome. Roberts and Pachter introduce an innovative solution with eXpress, software that can assign ambiguous fragments directly as they stream from mapping software. eXpress uses a modified on-line expectation-maximization algorithm to make probabilistic assignments. Its ability to handle data as they arrive makes the software fast and applicable to data sets of virtually any size. The approach also may predict a move toward real-time analysis for data generated by streaming methods such as third-generation single-molecule sequencing.

Brief Communication p71

Structurally annotated protein networks
Proteins are the workhorses of the cell, carrying out biological functions through highly regulated interactions. High-throughput approaches to map protein-protein interactions have generated large amounts of information about protein networks. With Interactome3D, Aloy and colleagues present a resource and web tool for annotating such networks with three-dimensional structural details. They provide a homology modeling pipeline to model protein-protein interactions using available structure information, and they present models for more than 12,000 such interactions in eight model organisms. Interactome3D will appeal to the bench biologist lacking bioinformatics expertise; the pipeline is fully automated and the web interface is user friendly. The resource will facilitate applications such as analysis of the effects of disease-causing mutations or the exploration of hypotheses about protein network dynamics.

Resource p47