Breaking boundaries in SSNMR

Solid-state nuclear magnetic resonance (SSNMR) spectroscopy can be used to characterize insoluble proteins such as membrane proteins or amyloid fibrils, which are difficult to crystallize and thus cannot readily be studied by X-ray crystallography. SSNMR spectroscopy has been limited, however, by low intrinsic sensitivity, so it has been a challenge to apply the technology to large and interesting biological targets. In this issue, Ishii and colleagues present a method to reduce the total time of SSNMR experiments by 5–20-fold while maintaining the same spectral quality. They managed this by applying paramagnetic doping, which decreases the longitudinal relaxation times of the nuclei, in conjunction with very fast magic angle spinning and fast recycling of low-radiofrequency power sequences. The method should expand the range of biological targets that can be studied at the atomic level using nuclear magnetic resonance spectroscopy.

Brief Communication p215, News and Views p197

Chemical labeling of glycoproteins

Glycoproteins containing post-translational sugar chain modifications are found on the cell surface and have important roles in cell-cell recognition. Several approaches to metabolically label glycoproteins have been developed, but such methods are not very efficient and often are toxic to living cells. Paulson and colleagues now introduce a chemical labeling method that is highly efficient and can be used to label sialic acid–containing glycoproteins on living mammalian cells, under mild conditions. The method applies mild periodate oxidation to introduce an aldehyde handle on sialic acid and then aniline-catalyzed oxime ligation to introduce a tag such as biotin or a fluorophore. The method should be useful for visualizing and tracking cell-surface glycoproteins as well as in glycoproteomics applications.

Brief Communication p203

Long-range haplotyping

A map of single-nucleotide polymorphisms (SNPs), a haplotype map, is very informative for determining the association of SNPs with complex traits, but obtaining haplotypes over long genomic distances in diploid individuals is still challenging. By first deriving long PCR fragments from each allele, then dye-labeling the SNPs on the individual DNA fragments, Xiao, Kwok and their colleagues can read the haplotype of single DNA molecules that span up to 50 kilobases, using total internal reflection microscopy. The simplicity of the method will allow its application to large-scale high-throughput genome-wide association studies.

Brief Communication p199

Quantitative interaction proteomics

Without absolute quantitative information, affinity purification–mass spectrometry–based analyses of protein complexes merely generate parts lists. Gstaiger and colleagues now present an approach to obtain absolute quantification of protein complex components via affinity purification–mass spectrometry. The method relies on the use of an affinity tag containing a unique reference peptide sequence, with which the bait protein is tagged. Defined amounts of two differentially isotope-labeled versions of the reference peptide are added to the affinity purified samples to absolutely quantify the amount of bait protein. The amounts of prey proteins pulled down with the bait are then calculated using label-free quantification. The researchers used the method to quantitatively model the human protein phosphatase 2A network.

Brief Communication p215, News and Views p197

Mapping the brain with light

Traditional approaches to motor mapping—identifying which parts of the motor cortex control particular body muscles—involve stimulation of the brain with electrodes. Murphy and colleagues now use the light-activated cation channel, channelrhodopsin-2, for light-based motor mapping in the mouse. An automated stage scanning system is used to precisely laser-photostimulate hundreds to thousands of predefined locations in the mouse cortex. Simultaneous electromyogram recordings or motion-sensing of limb muscles yield reproducible motor maps for forelimb and hindlimb muscles. The approach is much faster and less laborious than mapping using electrodes, and is likely to be more suitable for long-term studies. It will find application in studies of brain reorganization after learning or damage to the nervous system.

Article p219