

Photo-cross-linking amino acids go natural

Many methods have been developed to look for specific interactions between proteins in cells, but these have substantial limitations. Photo-cross-linking is one of the more specific methods for detecting interacting proteins, but it is no simple task to introduce a photoactivatable amino acid into a protein. Thiele and colleagues report the synthesis of cross-linkable, unnatural amino acids that, amazingly, are taken up by the natural mammalian translation machinery and incorporated into cellular proteins. They show that this has no adverse effects on the function of the proteins or on the cell as a whole. Upon photoactivation, only directly interacting proteins are cross-linked and they can be detected by simple western blotting. These extraordinary amino acids should be a powerful new tool to aid in elucidating signaling pathways in cells.

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whole-cell lysates with high specificity and sensitivity. This assay allows the study of kinase activities across different pathways in their natural environment, without the need for purification of individual kinases.

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Quantifying random mutations

The deleterious effects of genetic mutations are widely acknowledged. But even though this is an area of fundamental interest, there is little information about the background mutation rate in human cells or on how this rate may vary in different cells, during development and aging, or in diseases such as cancer. Bielas and Loeb have devised a clever new assay that relies on detecting changes within a restriction site in an attempt to provide more insight into this intractable problem. This assay is considerably more sensitive than earlier assays and provides what may be the first estimate of spontaneous neutral mutations in human cells.

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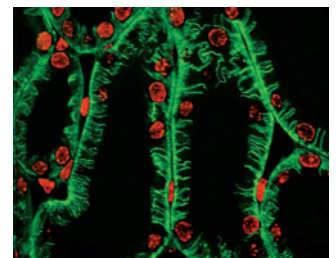
More viral microRNAs

With the discovery of an increasing number of genes for small regulatory microRNAs in evolutionarily diverse organisms, the awareness of their importance is also increasing. Recently Thomas Tuschl and colleagues have identified microRNAs encoded by a human virus; they now present a method for predicting microRNA genes in viral genomes and show, both computationally and experimentally, that several DNA viruses of the herpesvirus family contain microRNAs. This discovery will provide insight into viral evolution as well as the biogenesis and function of microRNAs.

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Biotinylating vessels *in vivo*

Comparing the proteome of diseased organs to those of their healthy counterparts yields valuable information about the genesis and progression of a



disease. Dario Neri, Giuliano Elia, and colleagues were interested in a subset of the proteome, namely proteins in the vasculature that are accessible from the bloodstream. They used an *in vivo* perfusion protocol with reactive biotin to label those proteins, purified them on streptavidin columns and analyzed them by mass spectrometry. Using this *in vivo* labeling strategy they identified proteins specific to certain tissues and compared their expression in normal versus diseased phenotypes. They confirmed the differential expression of several vascular proteins known to be associated with tumors and identified several new ones. As these proteins are easily accessible to any drug in the blood, a comprehensive list will be invaluable in designing new strategies for disease intervention.

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Finding active kinases in lysates

Protein phosphorylation is a key signal in numerous biological pathways. The study of pathways that run in parallel, requires detection of multiple active kinases simultaneously in the context of whole-cell lysates. Building on their previous work describing a substrate peptide whose fluorescence increases severalfold in response to phosphorylation, Barbara Imperiali, Doug Lauffenburger and their colleagues report a method of using these fluorescent peptides to monitor the activity of different kinases in