

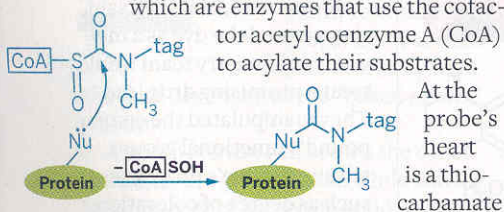
TAKING CONTROL OF TRANSCRIPTION

A small-molecule mimic of a protein transcription factor has been used to manipulate only a subset of its natural counterpart's web of genomic targets (*ACS Chem. Biol.* 2007, 2, 561). The result suggests that similar "artificial transcription factors" could be programmed to control subsets of genomic targets—say, only those related to disease. Peter B. Dervan and coworkers at Caltech used a DNA-binding polyamide to disrupt the interaction between DNA and hypoxia-inducible factor (HIF-1). HIF-1 activates several genes that help cells adapt to oxygen deficiencies that arise during normal physiological processes and during cancer progression. The researchers found that the polyamide affects only a handful of genes normally turned on by HIF-1, namely those that match the polyamide's specific DNA-binding preferences. In contrast, small interfering RNAs targeted against HIF-1 affect the expression of every gene controlled by HIF-1. Therefore, polyamides programmed to bind specific HIF-1-induced genes might be used to modulate only a desired subset of HIF-1 effects, the authors note.

TRACKING DOWN ACETYLTRANSFERASES

By employing a functional group never before used in protein labeling, a new chemical probe could enable closer scrutiny of an enormous and diverse enzyme family (*Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.200702485). A team led by Philip A. Cole at Johns Hopkins School of Medicine and Neil L. Kelleher of the University of Illinois, Urbana-Champaign, designed a probe for capturing acetyltransferases,

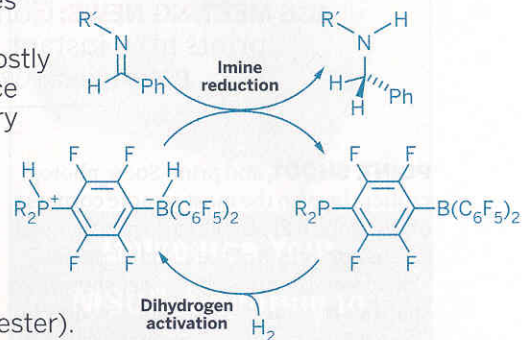
which are enzymes that use the cofactor acetyl coenzyme A (CoA) to acylate their substrates.



sulfoxide (shown, left), an electron-poor functional group that's attacked by the thiol group of acetyltransferases' nucleophilic cysteine residues (Nu). The reaction releases the CoA directing group and tags the enzyme with a biotin analog for detection and purification (right). The team anticipates that the probe will be useful in

METAL-FREE HYDROGENATIONS

Hydrogenation, the addition of hydrogen to unsaturated organic compounds, is broadly used in chemical production and usually mediated by precious-metal catalysts. Now, adding to a developing trend to go metal-free, Douglas W. Stephan and colleagues at the University of Windsor, in Ontario, report the first catalysts that eschew costly metals and can use H₂ directly to reduce imines, nitriles, and aziridines to primary and secondary amines under mild reaction conditions (*Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.200702908). Organocatalysts exist that can hydrogenate enones and imines, but these catalysts use a surrogate source of H₂, such as a Hantzsch ester (a pyridine diester). The Canadian researchers have instead created a phosphonium borate system that activates H₂ for direct hydrogenations. For example, they use their catalyst to hydrogenate imines (shown, R = 2,4,6-(CH₃)₃C₆H₂ or *tert*-butyl, R' = various groups, Ph = phenyl). The phosphonium group of the catalyst's zwitterion initially protonates an imine, thereby forming an intermediate that subsequently undergoes nucleophilic attack by the borohydride anion. Hydride transfer yields the amine.



identifying unknown CoA-binding proteins involved in signaling or gene regulation and that thiocarbamate sulfoxides will be broadly applicable in protein labeling.

PEPTIDE UNDERGOES 'JEKYLL-HYDE' MUTATION

A single mutation has been found to convert the function of a peptide in a "Jekyll and Hyde" manner—from a version that forms toxic amyloid fibrils to another that inhibits amyloid formation. In type 2 diabetes patients, islet amyloid polypeptide (amylin) forms amyloid fibrils that are believed to contribute to the loss of insulin-producing pancreatic β -cells and progression of the disease. Andisheh Abedini, Fanling Meng, and Daniel P. Raleigh at the State University of New York, Stony Brook, now find that a single point mutation converts amylin from one of the most aggregation-prone peptides known into a potent inhibitor of amyloid formation (*J. Am. Chem. Soc.* 2007, 129, 11300). Because mutated amylin retains binding affinity to natural amylin, the agent combines target recognition with aggregation-disrupting ability and thus represents a possible lead for the development of antidiabetic drugs.

PROBING FEMTOSECOND MOLECULAR DYNAMICS

With a new, fast, and high-energy laser spectroscopy method, researchers can now probe the dynamics of highly excited molecular species on the femtosecond timescale with angstrom-level spatial resolution (*Science* 2007, 317, 1374). Developed by Etienne Gagnon, Arvinder S. Sandhu, and coworkers at the University of Colorado, Boulder, and elsewhere, the procedure provides a way to probe atmospheric chemical processes stimulated by high-energy photons as well as interactions between ionizing radiation and various forms of matter. Using an optical method, the researchers converted an intense beam of infrared light into an ultrashort burst of soft X-rays and then trained the high-energy light onto a cold jet of nitrogen. That process ionized the N₂ molecules by ejecting electrons from their valence shells. Then, by using additional pulses of IR light, the team probed the molecular dynamics on the femtosecond timescale and found two main pathways leading to N₂ fragmentation—dissociation following photoejection of an electron and photoejection coupled with excitation of a second electron.