Open to Repair

The information stored in DNA underpins almost all life. It is therefore not surprising that there are multiple systems for rapidly sensing and repairing damage to genomic DNA within cells. The repair systems in eukaryotic cells have necessarily had to evolve to be able to correct such damage in the context of the chromatin proteins—principally histones—that compact DNA in the nucleus. Tolber et al. have studied the role of the SIRT6 histone deacytelase in the response of mammalian tissue culture cells to double-strand breaks in DNA. They find that SIRT6, which can bind to chromatin, interacts with the histone remodeling protein SNF2H and recruits it to sites of double-strand DNA breaks. The dual abilities of SIRT6 to deacetylate histone H3 at lysine 56 and to recruit SNF2H are necessary for DNA repair to occur and provide further evidence that remodeling chromatin to allow access by the repair machinery is critical for an effective DNA damage response. Both proteins act in the same DNA repair pathway, and their interaction shows tissue specificity, in the pancreas and brain, possibly consistent with the role of SIRT6 in brain function. —GR

Reining in Responses

In response to infections, dendritic cells acquire microbial antigens and present them to T cells, which leads to the induction of adaptive immunity. Although the dendritic–T cell interaction is essential to turn on the innate immune response, this interaction must also be turned off (or at least turned down) so as to avoid an overly aggressive response, as is observed in allergy and chronic inflammatory diseases. Carrera Silva et al. describe one such off switch that operates in mice and humans. Upon engagement of antigen-laden dendritic cells, T cells increased the expression of protein S (Pros1), which is a ligand for TAM-family receptor tyrosine kinases, which are expressed by dendritic cells. Conditional deletion of Pros1 in T cells in mice demonstrated that Pros1 was essential to keep dendritic cell activation in check, and the dendritic cells in these mice expressed more cytokines and activation markers. The loss of Pros1 on T cells in mice also led to worsened colitis and enhanced T cell–mediated immunity in vivo. Pros1 expressed on T cells did signal through TAM receptors; the deletion of TAM receptors in dendritic cells phenocopied mice with a T cell–specific deletion of Pros1. A similar expression and function of Pros1 were seen in human T cells, suggesting that this negative regulatory mechanism is evolutionarily conserved. —KLM

Carbenes in Their Natural Habitat

Over 50 years ago, Ronald Breslow suggested that thiamin may adopt a short-lived reactive carbone structure—with a divalent carbon center stabilized by flanking sulfur and nitrogen—during the enzymatic reaction cycle of vitamin B1. In the interim time, chemists have synthesized a huge range of stabilized cyclic carbenes, most of which are derived from imidazole (with two flanking nitrogens) rather than thiazole frameworks. These N-heterocyclic carbenes, or NHCs, are frequently stable and possible to isolate and have been applied as ligands in transition-metal catalysts. They are also versatile catalysts in their own right. Nonetheless, the question of whether thiamin itself reacts as a catalytic carbene in native context has remained open. Meyer et al. present a high-resolution (1.06 Å) crystal structure of pyruvate oxidase with bound phosphate (an unreactive analog of the pyruvate substrate), and the associated thiamin molecule shows clear evidence of carbone character. The carbon center in question appears to be deprotonated while lacking the excess electron density indicative of a carbanion. —JSY


MATERIALS SCIENCE

Nanoparticle Transformers

On the nanometer scale, small metal nanoparticles behave neither like atoms nor a bulk material, and hence their properties can be tuned by changing the sizes of the particles, which makes them of broad research interest. When used for catalytic purposes, they are often placed onto a supporting substrate, and both it and the presence of absorbed atoms may further alter the nanoparticle properties. Li et al. studied the structure of platinum nanoparticles in the size range of 0.6 to 5 nm by using a combination of transmission electron microscopy, x-ray absorption fine-structure spectroscopy, and first-principles calculations. In studying over 3000 nanoparticles, they were able to distinguish between noncrystalline and crystalline ones. They found that there was not a single size that marked the transition between the two. Rather, the transition was a statistical one, with the potential for both ordered and disordered particles of a certain size to coexist. The coexistence size region was found to be dependent on the nature of the substrate and the amount of H2 adsorbed. The authors believe that this effect is general for late 5d transition metals. —MSL

Reining in Responses
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