

New Tool for the TB Armory

There is an urgent need for new drugs to combat the advancing scourge of tuberculosis that is inexorably linked with the HIV epidemic. **Andries *et al.*** (p. 223, published online 9 December 2004; see the cover and Perspective by **Cole and Alzari**) have developed a lead compound from a series of recently patented diarylquinolines, known as R207910. This compound has good selectivity and potency for several mycobacterial species, including *Mycobacterium tuberculosis*, and retains activity against *M. tuberculosis* strains that are singly or multiply resistant to commonly used drugs. In contrast to other anti-mycobacterial drugs, R207910 targets an adenosine triphosphate synthase. R207910 enhanced mycobacterial killing in a mouse model of established infection compared with isoniazid, rifampicin, or pyrazinamide, which are used in current therapeutic regimens. It is hoped that this new drug candidate will allow the treatment of tuberculosis in as little as 2 months.

Variation on a Theme

The semaphorins and their plexin-neuropilin coreceptors are established players in axon guidance. More recently, they have also been implicated in vascular development. **Gu *et al.*** (p. 265, published online 18 November 2004) report that semaphorin 3E (Sema3E) does not require neuropilin as a coreceptor in patterning the developing mouse vascular system, but instead interacts directly with the plexin-D1-expressing cells. The repulsive effect of Sema3E-bearing somites on vascular endothelial cells expressing plexin-D1 was observed in the absence of neuropilins, indicating that neuropilins are not, after all, obligatory semaphorin coreceptors in mammalian vasculogenesis.

Spin Switching Nanomagnets

Injecting a polarized spin current into a magnetic material can exert a torque on the magnetic moment, causing it to precess. Under the right conditions, the magnetic moment can be flipped, potentially allowing electrically controlled magnetic memories. However, details of the dynamics of this precession and switching have been lacking. **Kirivortov *et al.*** (p. 228; see the Perspective by **Covington**) now present a time-domain technique for looking at these processes. Using a magnetic nanopillar sandwich structure, they show that the precession and magnetic reversal processes are coherent processes driven by polarized spin injection.

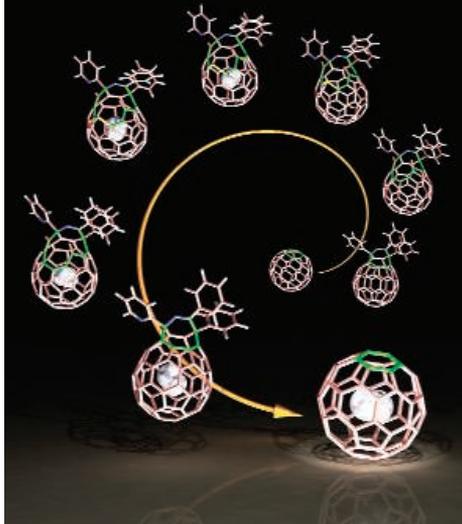
Tuning Superatom Chemistry

Much of chemical reactivity can be understood in terms of the driving force provided by the stability of bonding arrangements that provide each atom with a closed atomic shell of electrons. For small atomic clusters, the so-called "jellium" model predicts that stable superatom

clusters can form with a distinct number of valence-electrons (one such shell occurs at 40 electrons). **Bergeron *et al.*** (p. 231) build on recent work showing that Al_{13}^- forms such a superatom. They now show that Al_{13} cluster anions bearing an even number of iodine atoms show halogen-like stability, and that Al_{14} cluster anions bearing an odd number of iodine atoms show an alkaline earth-like stability. The delineation of these additional families indicates that other superatom systems may also be realized.

Caged Gas

Endohedral fullerenes contain guest atoms or molecules within their cages that are trapped during the synthesis of the fullerene. **Komatsu *et al.*** (p. 238) show that a C_{60} derivative that contained a large opening (a 13-membered ring) could be closed in a series of synthetic steps. In this manner, they are able to create C_{60} trapping H_2 in high yield.



A Tamed Radical

Radicals, or compounds in which a single electron is missing from the valence shell of one of the atoms, act as short-lived intermediates in many chemical reactions. A series of important oxidative enzymes stabilize O-centered phenoxyl radicals by coordination to a transition metal in the active site. Whether a comparable mechanism pertains with N-centered radicals has been an open question. Now **Büttner *et al.*** (p. 235; see the Perspective by **Kaim**) have prepared a rhenium complex with a coordinated N-centered aminyl radical. The complex is stable as a solid and in a room-temperature solution. Spectroscopy, theory, and its reactivity supports a structure in which it is mainly N, not the metal center, that has lost an electron, consistent with radical stabilization by the rhenium.

Resolved Bump

Astronomers have repeatedly noted a 2175 angstrom extinction feature (or bump) in spectra of dust in the interstellar medium. The unknown source of this bump must be

the most abundant species in the interstellar medium, as the feature is ubiquitous. **Bradley *et al.*** (p. 244) identified organic carbon and amorphous silica-rich material as the carriers of the 2175 angstrom bump in laboratory spectra of interplanetary dust particles that were collected in Earth's stratosphere.

An Albatross's Life

Albatrosses are well known for their extreme wide ranging foraging trips around the Southern Ocean from their colonies during the breeding season. Using leg-mounted loggers on 22 individual gray albatrosses over periods of 18 months, **Croxall *et al.*** (p. 249) provide evidence of the spectacular circumpolar migrations of albatrosses and reveal the underlying structure and strategies of these journeys. Migration strategies differed between individual birds. Some regularly circumnavigated the globe, while others either remained in the vicinity of the breeding grounds or migrated to a region in the Indian Ocean. Albatrosses are among the most endangered of all pelagic seabirds, and these data help to identify the critical habitats where protection is most required.

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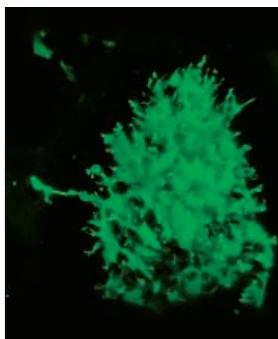
Retinoic Acid and Heart Development

Model systems such as the zebrafish heart can be used to shed light on the normal development and function of the cardiac system in vertebrates and to assist in our understanding of heart injury and disease. Retinoic acid is critical for late steps in heart development, including terminal myocardial differentiation, cardiac looping, and ventricular maturation and growth. Using zebrafish genetics and embryology, **Keegan *et al.*** (p. 247) now show that there is also an early function of retinoic acid in cardiac specification. Retinoic acid signaling is involved in selecting the number of cardiac progenitors from within a multipotential pool, and organ size is controlled by retinoic acid-mediated restriction of the early cardiac progenitor pool.

Gut Antigen Sampling and Host Defense

A complex interplay has evolved between the cells of the immune system and the mucosal barrier that interfaces with the intestinal lumen and its contents. A good

example of this are the specialised antigen-presenting dendritic cells (DC) that reside below the intestinal epithelium "sampling" luminal contents via dendritic extrusions as they extend through the epithelial barrier. **Niess *et al.*** (p. 254) examined the behavior and activity of these myeloid-derived DC. The DC were regulated in the extrusion of trans-epithelial dendrites and in their phagocytic activity by the chemokine receptor CX3CR1. Loss of these activities in the absence of CX3CR1 correlated with an increase in susceptibility to *Salmonella typhimurium*, suggesting a direct link between trans-epithelial sampling of antigen by DC and immune-mediated protection of the intestinal mucosa.



Anticonvulsant Medications and Aging in Worms

Drugs used to treat human seizures have been found to extend the life-span of worms. **Evason *et al.*** (p. 258; see the news story by **Wickelgren**) report that adult worms exposed to three structurally similar anticonvulsant drugs had a life-span increase of nearly 50%. In addition to delaying age-related degenerative changes in worms, the drugs also increased neuromuscular activity, a behavior associated with increased life-span in the worm. The drugs may act by a common mechanism both to affect neural activity and aging, and provide potential leads as therapeutics to treat human aging.

Another Route to Stat Regulation

Stats (signal transducers and activators of transcription) efficiently carry information from cell surface cytokine receptors (which cause Stat phosphorylation) to the nucleus (where Stats work as transcriptional activators). **Yuan *et al.*** (p. 269; see the Perspective by **O'Shea *et al.***) report that Stat3 is also regulated by acetylation of a specific lysine residue. Stat3 associated with the transcriptional coactivators CBP and p300, which have histone acetyltransferase activity and can modify Stat3 in vitro. Acetylation of the key lysine residue appears to be required for dimerization of Stat3 and for transcriptional activation of genes in cells treated with the cytokine, oncostatin M. Cells expressing a mutant form of Stat3 that is not acetylated were insensitive to gene regulation and growth promotion by oncostatin M.

Testing the Strength of Hypothesis

Whether a hypothesis gets credit for predicting new data versus for when it merely accommodates old data is a controversial matter among philosophers of science. **Lipton** (p. 219) reviews several attempts to answer this question before presenting his own arguments as to how and why the ability to predict trumps the ability to accommodate existing data.

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