The role of atomic motion in cuprate superconductivity

The precise nature of electron pairing in type II cuprate superconductors has fascinated physicists for over 2 decades. In type I superconductors, electron pairing arises from coupling to phonons, and the superconducting electronic energy gap is isotropically symmetric. Cuprates, however, possess a cloverleaf-shaped gap in 2 dimensions, and their pairing mechanism has remained a mystery. Researchers have postulated that magnetic interactions may play a role in tandem with phonons. Fabrizio Carbone et al. now present evidence for the importance of the 3D dynamics of cuprate superconductors. The authors observed the influence of structure in the superconductor Bi$_2$Sr$_2$CaCu$_2$O$_8$ by measuring the intensity of a reflected, diffracted electron beam after the material had been illuminated with femtosecond pulses of polarized light. They found that the intensity of the diffraction mark (correlated to dynamics perpendicular to the Cu–O plane) peaked when the polarized excitation was parallel to the Cu–O bonds. In addition, the authors report that the parallel orientation led to faster decay of energy from charge carrier to general lattice vibrations than did a nonparallel angle. The authors say that carrier–phonon coupling causes the Cu–O planes to buckle by $\sim 0.5\%$ of the unit cell height, suggesting that atomic motion plays a significant role in the mechanism of cuprate superconductivity. — K.M.

Modulating posttranscriptional regulation

The RNA-binding protein HuR regulates gene expression patterns in response to cell stimulation by stabilizing target mRNAs or by modulating their translation. Because HuR is also important in controlling the expression of proliferative genes, understanding the regulation of HuR levels has generated considerable interest. Kotb Abdelmohsen et al. identified a mechanism by which microRNA-519 (miR-519) regulates HuR levels by repressing translation of the protein, primarily by associating with the coding region of the HuR mRNA. The authors found that in several human cancer cell lines—including ovarian (A2780), cervical (HeLa), and colon (HCT116 and RKO) cancers—overexpression of a miR-519 precursor reduced HuR levels, whereas antisense RNA inhibition of miR-519 increased HuR abundance. Lowering HuR levels by miR-519 reduced the levels of proteins encoded by HuR target mRNAs and diminished cell proliferation, according to the authors. They suggest that the results highlight the complexity of the posttranscriptional regulatory systems that control the rate of cell division in human cancer cell lines. — C.A.

Genetic link to alcohol susceptibility

Geoff Joslyn et al. suggest that the intermediate phenotype—a genetically dictated trait—of an individual's level of response to alcohol intake can provide insight into the genetic factors that
affect a person’s susceptibility to alcohol abuse. A low level of response means that a person can tolerate many drinks before feeling the effects of alcohol intoxication. The authors genotyped 313 Caucasian siblings from the San Diego Sibling Pair project and analyzed the association of two sentinel single-nucleotide polymorphisms (SNPs) with three measures of level of response. The authors report that one SNP—RS1051730, which is strongly associated with swaying of the body—is significantly associated with a person’s level of response to alcohol. The authors investigated other SNPs but found none that provided similar physical evidence from alcohol’s effects. SNP RS1051730 is located on chromosome 15, which other studies have connected with alcohol use disorders. The specific region surrounding the SNP is in linkage disequilibrium, and several candidate genes could be responsible for the phenotype; however, the authors say the nicotinic receptor gene CHRNA5 is likely responsible for variation in the level of alcohol response. — K.M.

“Chromosome 15q25.1 genetic markers associated with level of response to alcohol in humans” by Geoff Joslyn, Gerry Brush, Margaret Robertson, Tom L. Smith, Jelger Kalmijn, Marc Schuckit, and Raymond L. White (see pages 20368–20373)

**GENETICS**

**High-throughput screening for cancer genes**

Identifying the subset of genes that drives tumor growth and development is vital to understanding the molecular basis of cancer. One strategy used to find these genes is to identify genetic alterations in tumors and the genes important for tumor growth. Biao Luo et al. identified genes required for cancer cell proliferation by infecting 12 human cancer cell lines with a pool of viruses carrying 45,000 different short hairpin RNAs (shRNAs). The authors then grew the cells and hybridized the shRNAs to assess the abundance of each shRNA. If an shRNA inhibited a gene essential to cell growth, the cells carrying that shRNA would die and be depleted from the population. Using a similar technique, Luo et al. identified 4 genes in chronic myelogenous leukemia required for response to imatinib, as well as 2 potent regulators of FAS-induced apoptosis. According to the authors, this strategy should allow for the rapid identification of oncogenes and genes involved in drug response. — C.A.


**IMMUNOLOGY**

**Blocking viral persistence**

Viral persistence requires the suppression of T-cell responses controlled by IL-10 and programmed death-ligand 1 (PD-L1). However, research has yet to determine whether IL-10 and PD-L1 act independently or jointly and whether the presence of both cytokines leads to a synergistic effect. David Brooks et al. report that IL-10 and PD-L1 act through independent immunosuppressive pathways and that blocking both pathways rapidly increased T-cells’ ability to remove a virus. The authors infected control mice and mice deficient in either IL-10 or PD-L1 with lymphocytic choriomeningitis virus to model a chronic viral infection. The up-regulation of PD-L1 did not require IL-10, and PD-L1 did not alter IL-10 expression in the spleen. Furthermore, the authors show that antibody inhibition of both IL-10 and PD-L1 resulted in a larger number of virus-specific CD8 T cells than inhibition of IL-10 or PD-L1 alone, which controlled an established persistent viral infection. Therapies that block the effects of IL-10 and PD-L1 may hold promise for treating chronic viral infections such as hepatitis C, according to the authors. — C.A.

“IL-10 and PD-L1 operate through distinct pathways to suppress T-cell activity during persistent viral infection” by David G. Brooks, Sang-Jun Ha, Heidi Elsaesser, Arlene H. Sharpe, Gordon J. Freeman, and Michael B. A. Oldstone (see pages 20428–20433)

**MICROBIOLOGY**

**A genetically diversified picornavirus genus**

The picornavirus family contains a wide range of small, positive-stranded RNA viruses, including enteroviruses such as polio, and is thought to be responsible for as many as a billion human infections a year. As part of the World Health Organization’s polio eradication campaign, researchers began screening the stool of children with acute flaccid paralysis for polio and other enteroviruses. Amit Kapoor et al. examined these samples using viral metagenomics and found a highly prevalent and genetically diverse genus in the Picornaviridae family, which they named Cosavirus. Nearly half of the children with acute flaccid paralysis had cosavirus RNA in their stool, as did otherwise healthy children. The authors suggest that some variants of this new picornavirus genus may cause symptoms in susceptible persons—symptoms as diverse as those associated with the similarly prevalent and genetically diverse human enteroviruses. The authors say the identification of Cosavirus can help expand knowledge of the viral flora commonly found in children. — C.A.

“A highly prevalent and genetically diversified Picornaviridae genus in South Asian children” by Amit Kapoor, Joseph Victoria, Peter Simmonds, Elizabeth Slikas, Thaweesak Chieochansin, Asif Naeeem, Shahzad Shaukat, Salmaan Sharif, Muhammad Masroor Alam, Mehar Angez, Chunlin Wang, Robert W. Shafer, Sohail Zaidi, and Eric L. Delwart (see pages 20482–20487)
Correction

IN THIS ISSUE, PHYSICS

The authors note that on page 20047, left column, line 20, the structure of the superconductor formula BiSr2Ca2Cu2O8 should instead have appeared as Bi2Sr2CaCu2O8. The online version has been corrected.

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