

The inside of a catheter.

## MICROBIOLOGY

## Biofilms and Medical Implants

A major problem that develops with implanted biomedical devices is that they become covered with biofilms that are made by microbes such as the fungus *Candida albicans*. The properties of biofilms make it difficult to defend against such infections, even with antifungals. *Candida* initially grow on surfaces as typical yeast-form cells and then mature into hyphal-like structures bearing adhesins and forming an extensive extracellular matrix of carbohydrate and protein.

Nobile *et al.* have been investigating the regulation of *Candida* biofilm formation. After their discovery that hyphal development and adhesion are coupled via Tec1 control of Bcr1, they find that adhesin expression is the specific target of Bcr1 in vivo. Yeast mutants deficient in *BCR1* cannot form biofilms on polyethylene catheters implanted in rats but can be rescued if an adhesin-encoding gene, *ALS3*, is overexpressed. Interestingly, *als3/als3* mutants do form biofilms, probably because other adhesins, including those similar to mating agglutinins, are under the influence of *BCR1* in this network and can compensate. — CA

*PLoS Pathol.* 2, e63 (2006).

## APPLIED PHYSICS

## X-rays Chopped to Order

High-intensity x-ray sources such as synchrotrons have recently facilitated many studies of the dynamical properties of materials, such as phase transitions, conformational changes, and other transient behavior. However, synchrotron geometries and operating parameters, as well as available mechanical chopper technology, have limited the repetition frequencies and durations of x-ray bunches deliverable to the samples under investigation.

Grigoriev *et al.* demonstrate a versatile diffractive switch to isolate x-ray pulses, based on the lattice shift induced in a piezoelectric  $\text{Pb}(\text{Zr}, \text{Ti})\text{O}_3$  thin film by an electric field. A 15-V applied field pulse, 10 ns in duration, induces 0.38% mechanical strain in the piezoelectric layer, thereby redirecting the x-rays; whether the diffraction blocks or transmits the radiation depends on the scattering angle chosen for the experiment. The switch is 50  $\mu\text{m}$  in diameter—a size window accessible to the focused output of a typical synchrotron—and can be driven by an arbitrary combination of signals spanning a range from 0 (dc) to 10 kHz.

Thus, a tailored x-ray pulse sequence can be delivered to suit the desired application. — ISO

*Appl. Phys. Lett.* 89, 21109 (2006).

## GENETICS

## Shoots and Leaves

Cascades of regulatory genes and signaling factors shape an indeterminate mass of cells into the complex morphologies we recognize as leaves.

But why are some leaves simple and round and others complicated and curly? Hay and Tsiantis analyze how genetic networks enable one plant, *Arabidopsis thaliana*, to have simple undissected leaves, and a closely related plant, *Cardamine hirsute*, to have complex dissected leaves. Both plants express the homeobox protein KNOX, which functions as a transcription factor and affects leaf development. Both also express AS1 proteins that repress KNOX expression. The difference lies in the territory: KNOX protein confined to the shoot apical meristem results in simple leaves, whereas KNOX protein expressed in later leaf primordia results in complex leaves. The promoter sequences upstream of the KNOX coding region are critical for determining pattern of expression and hence the shape of the leaf. Although the topology of the genetic network is unchanged, in terms of which gene represses which effector, the morphological outcome is altered by changing the expression domain of the repressor. — PJH

*Nat. Genet.* 38, 10.1038/ng1835 (2006).

## CHEMISTRY

## Ins and Outs of HCl

The capacity of porous solids, such as zeolites and metal organic frameworks, to adsorb gases reversibly has been studied extensively for storage and catalysis applications. In contrast, reversible gas incorporation that alters the covalent bonding structure of a solid is a much rarer phenomenon. Mínguez Espallargas *et al.*

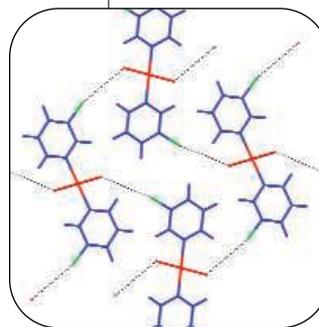
present a compound that stores and releases HCl through a complex sequence of bond cleavage and formation steps.

In the initial structure, two 3-halopyridinium cations [in which the halogen atom (X) can be either Cl or Br] form an ionic crystal through N-H hydrogen bonding to the chloride ligands of a  $[\text{CuCl}_4]$  dianion. If the crystals are ground and left open to air, the yellow powders turn blue after a few hours for the chloro species and a few days for the bromo species, indicative of a change in Cu coordination geometry from distorted tetrahedral to square planar. The transformation is accelerated if the vial is immersed in a silver nitrate solution that can capture gaseous HCl

through precipitation of AgCl. Powder x-ray diffraction confirms HCl elimination via cleavage of N-H and Cu-Cl bonds, leading to N-Cu coordination and rearrangement of the ionic chains into a two-dimensional network held together by Cu-Cl...X-C bonds. Reexposure of the solids to HCl vapor recovers the original ionic compounds. — PDS

*J. Am. Chem. Soc.* 128, 10.1021/ja0625733 (2006).

*Continued on page 413*



Lattice structure after HCl loss ( $\text{CuCl}_2$ , red; pyridine, blue; Cl or Br, green).

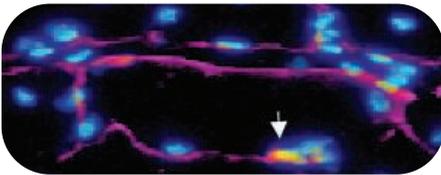
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## BIOMEDICINE

## Muscle Rejuvenation

It is already possible to treat some immune disorders by bone marrow transplantation, which can reconstitute defective tissues by introducing healthy cells. In the future, it is hoped that it will be possible to treat a variety of disorders by using cell therapy. One technical hurdle that must be overcome is the efficient delivery of injected cells to their correct target sites (homing), while maintaining, or perhaps even enhancing, successful incorporation and long-term survival of their progeny.

Galvez *et al.* have improved the delivery of mesoangioblasts, which are stem cells that are associated with blood vessels and are involved in



Donor cell (yellow) positioned as a reservoir of satellite cells.

muscle regeneration, to repair defective muscles in a mouse model of muscular dystrophy. Treating donor mesoangioblasts with cytokines and promoting the expression of specific adhesion proteins before injection into recipient animals resulted in the efficient colonization and supplementation of muscle tissue. In addition to migrating into growing muscles, the donor cells took up positions as satellite cells (committed muscle stem

cells) in the basal lamina of myofibers. It is hoped that similar strategies will be helpful in devising appropriate cell-based therapies in patients with muscular dystrophies. — SMH

*J. Cell Biol.* **174**, 245 (2006).

## IMMUNOLOGY

## Opposites Attach

Regulatory T cell activity depends on a course of gene expression and repression piloted by the Forkhead transcriptional factor FOXP3. Loss or impairment of FOXP3 disrupts the balancing of T cell responses and can lead to autoimmune disorders. The ability of FOXP3 to regulate the targets of the cytokine-activating transcription factor NFAT led Wu *et al.* to test whether the two factors cooperate directly. FOXP3 was found to complex with NFAT in a T cell line, resulting in the repressed activity of other complexes formed between NFAT and its cytokine-activating partner AP1, as well as in the enhanced binding of FOXP3 to its own DNA targets. The structure of a closely related factor, FOXP2, in a ternary complex with NFAT and DNA, was used to guide the introduction of mutations in FOXP3 that interfered with the interaction of NFAT and FOXP3; the levels of transcriptional repression of NFAT targets and activation of FOXP3-induced genes were thereby reduced. The inability of T cells carrying these mutations to control disease in a mouse model of autoimmune diabetes provides evidence that the formation of alternate transcriptional complexes by NFAT critically shapes the distinctive programs of effector and regulatory T cells. — SJS

*Cell* **126**, 10.1016/j.cell.2006.05.042 (2006).



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## &lt;&lt; A Peptidase Affecting Angiogenesis

Prostate-specific membrane antigen (PSMA) got its name because its expression is enhanced in advanced prostate carcinomas. It is also called glutamate carboxypeptidase II and is a transmembrane protein with peptidase activity. PSMA has been found in endothelial cells in tumor vasculature, and, given the involvement of other peptidases in angiogenesis,

Conway *et al.* explored such a possibility for PSMA. They used an angiogenesis assay in mice lacking PSMA to show that loss of PSMA inhibited formation of new blood vessels. Proteolysis contributes to a remodeling of the extracellular matrix that is necessary for angiogenesis, but the authors suggest that PSMA may instead be part of a complex regulatory loop that controls integrin signaling and activation of the p21-activated kinase 1 (PAK1). Cell invasion studies with PSMA-null cells showed that PSMA has an important role in cell invasion and in signaling from  $\beta$ 1 integrins to focal adhesion kinase (FAK) and PAK1. They confirmed that PSMA interacts with the actin-binding protein filamin A, and disruption of this interaction decreased the peptidase activity of PMSA and decreased phosphorylation of PAK1 in cultured cells. The interaction of PMSA and the cytoskeletal protein filamin A may allow a feedback signal from integrin  $\beta$ 1 and PAK to keep PMSA activity in check. Inhibition of PAK by expression of a peptide corresponding to its autoinhibitory domain enhanced the association of PMSA with filamin A, increasing its peptidase activity. Further understanding of how PMSA affects angiogenesis may lead to strategies to inhibit angiogenesis in cancers and other diseases. — LBR

*Mol. Cell Biol.* **26**, 5310 (2006).

# Q Who's making Science a household name?



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