GEOLOGY

Salty Fingers

Convection of groundwater through porous rock plays a critical role in many geological processes in the crust. It occurs whenever groundwater density decreases with depth (on account of either a temperature or salinity gradient relative to overlying water layers) and the rock permeability and pore connectivity are sufficient to allow flow. Convection at ocean ridges is responsible for altering the composition of ocean crust globally; locally, convection is the basis for most geothermal energy systems. Despite the wide-ranging implications of the phenomenon, clear-cut visualization of convection in the field has proven difficult. Laboratory experiments have shown that stratified systems, in which salty water overlies fresh water, should produce interfingering of the layers at a wavelength of about twice the thickness of the system. In this context, Van Dam *et al.* studied a sabkha aquifer near Abu Dhabi, United Arab Emirates, where evaporation produces salty groundwater perched above fresh ancient water at depth. Electrical resistivity measurements, sensitive to the salt content of the groundwater, revealed prominent fingers of descending salt water that were generally consistent with predictions. — BH

Geophys. Res. Lett. **36**, L11403 (2009).

MICROBIOLOGY

Resistance on Tap

Antibiotic-resistant bacteria have become so common in aquatic ecosystems that some researchers suggest their genes should be considered environmental contaminants. Efforts to uncover the means whereby antibiotic resistance propagates are crucial in confronting the overall problem. Using a combination of broad-spectrum culturing methods and quantitative molecular techniques, Xi *et al.* characterized the prevalence of antibiotic-resistant bacteria, as well as the genes conferring resistance, at various points within water supply networks in the midwestern United States. In most municipalities they sampled, the abundance of antibiotic-resistant bacteria was higher in tap water than in finished water (i.e., water sampled directly after treatment). The quantity of antibiotic-resistant genes in tap water was also greater than in finished water and, remarkably, exceeded the quantities in original source waters as well. Water treatment plants and distribution systems may therefore unintentionally serve as incubators for growth of antibiotic-resistant bacteria and selectively increase antibiotic resistance of bacterial communities through horizontal gene transfer. — NW

Appl. Environ. Microbiol. **75**, 10.1128/AEM.00382-09 (2009).

MICROBIOLOGY

Paracrine Parable

Bacillus subtilis is a soil-dwelling organism that forms biofilms—extracellular matrices harboring a bacterial community. One way in which bacteria are known to coordinate their activities is via signaling molecules that are produced when the colony reaches a certain density, a phenomenon known as quorum sensing. Lopez *et al.* describe a distinct mode of social networking, referred to as paracrine signaling. Many of the cells in a *B. subtilis* biofilm secrete a small peptide called ComX. This peptide binds to a membrane-bound kinase and triggers the phosphorylation of an intracellular transcription factor, which goes on to initiate the synthesis and secretion of the peptide surfactin in a small group of cells. The authors have discovered that apart from being a surfactant, surfactin evokes extracellular matrix production in another group of cells. Surfactin producers do not make extracellular matrix themselves, whereas matrix producers do not become surfactin producers, because their response to ComX is blocked by the presence of matrix. Thus, populations of independently minded cells develop and coexist for prolonged periods, alongside others with yet other functions, defying the notion that bacterial cells cannot differentiate and specialize like eukaryotic cells do. — CA

Genes Dev. **23**, 1631 (2009).

BIOCHEMISTRY

A Scaffold for Interactions

The mitogen-activated protein kinase (MAPK) signaling pathway provides an example of the elaborate controls that are necessary when a cellular module regulates a huge range of processes from proliferation and survival to metabolism and cell motility. The enzymes of the MAPK cascade—the protein kinase Raf, which phosphorylates the kinase MEK, which in turn phosphorylates the MAPK ERK—are localized in

CREDITS (TOP TO BOTTOM): LOPEZ *ET AL.*, *GENES DEV.* **23**, 1631 (2009); JUPITERIMAGES

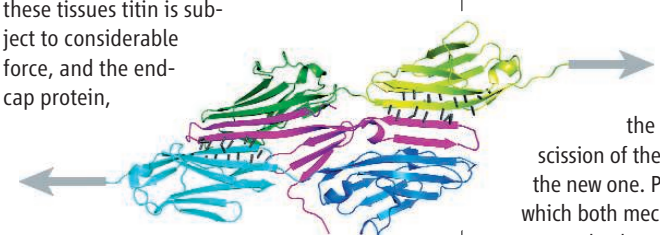
complexes by scaffold proteins, increasing the efficiency of interactions and stipulating the specificity of such events. McKay *et al.* have established the intricate choreography of interactions mediated by the scaffold protein KSR1. This protein was identified as a positive regulator of the small guanosine triphosphatase Ras, which initiates the activation of Raf and the rest of the MAPK cascade. KSR1 forms a ternary complex with Raf and MEK; this activates ERK, and the activation of ERK exposes a site that allows ERK to bind to KSR1, where it (ERK, that is) phosphorylates four sites each on KSR1 and Raf. When the binding site for ERK on KSR1 was disrupted or the sites that ERK phosphorylates on KSR1 were removed, though, the interaction of KSR with Raf1 was enhanced and signaling was prolonged. Thus, the authors conclude that ERK provides a negative-feedback signal that disrupts interaction of Raf and KSR1 and releases KSR1 from the cell membrane, thereby adjusting the intensity and duration of signaling through the MAPK cascade. — LBR

Proc. Natl. Acad. Sci. U.S.A. **106**, 11022 (2009).

BIOPHYSICS

Tugging at Heartstrings

One of the first lessons in learning to work with wood is that it exhibits a resistance to compression or tension that depends upon the direction in which force is applied. A macroscopic clue to this anisotropic behavior can be found by examining the wood grain. Bertz *et al.* demonstrate that this phenomenon can also be observed at the molecular level in their atomic force microscopy investigation of titin, a structural protein found in skeletal and cardiac muscle. In these tissues titin is subject to considerable force, and the end-cap protein,



telethonin (red), grasps two titin molecules, binding to the N-terminal domain Z1 (dark green and blue) and the next interior one Z2 (light green and blue). Pulling apart this joint requires a force of 700 pN when applied to Z2 (that is, the normal physiological direction of pulling), but only one-third as much force need be applied to Z1; the difference is accounted for by directionally oriented hydrogen bonds (gray) between telethonin and the Z2 domain. — GJC

Proc. Natl. Acad. Sci. U.S.A. **106**, 10.1073/pnas.0902312106 (2009).

CREDIT: BERTZ *ET AL., PROC. NATL. ACAD. SCI. U.S.A.* **106**, 10.1073/PNAS.0902312106 (2009)

BIOMEDICINE

Inhibiting Interactions

Although the genetic bases of many cancers have been identified, there remains the challenge of translating this knowledge into promising drug candidates. The discovery of the chromosomal translocation that fuses the *BCR* and *Abl* genes and leads to the development of chronic myeloid leukemia was followed by spectacular clinical data attesting the efficacy of the inhibitor imatinib mesylate in the late 1990s. Ewing's sarcoma family tumors are also caused by a chromosomal translocation, most commonly one that fuses the *EWS* and *FLI1* genes. The resulting EWS-FLI1 transcription factor both lacks enzymatic activity and is inherently disordered, making it difficult to screen chemical libraries for inhibitors. EWS-FLI1 does, however, bind to RNA helicase A, which acts as a transcriptional coactivator, and this interaction is important for tumorigenesis. Erkizan *et al.* designed a peptide to inhibit binding and used it to identify a small molecule (YK-4-279) that specifically blocked EWS-FLI1 binding to RNA helicase A and also decreased tumor growth in mouse xenograft assays. This strategy may be valuable for developing lead molecules in other cancers caused by similar types of fusion proteins. — HP

Nature Med. **15**, 750 (2009).

CHEMISTRY

Simultaneous Substitutions

There is a long-standing distinction in organic chemistry between unimolecular (S_N1) and bimolecular (S_N2) substitution mechanisms at carbon centers. The former involves departure of a substituent before arrival of its replacement, whereas the latter involves concomitant scission of the old bond and formation of the new one. Phan *et al.* explore a system in which both mechanisms appear to operate concurrently, depending on the identity of the attacking group, or nucleophile. Through careful kinetics measurements, they show that a series of benzhydryl bromides react with amines via an S_N2 pathway, while a competitive S_N1 pathway results in replacement of bromide with a dimethyl sulfoxide solvent molecule. Using a parameterized nucleophilicity/electrophilicity relation, the authors account for the results based on the lifetimes of benzhydrylium intermediates and the relative likelihood of having an amino or dimethyl sulfoxide molecule in the vicinity when bromide departs. — JSY

J. Am. Chem. Soc. **131**, 10.1021/ja903207b (2009).

Simultaneous Substitutions

Jake Yeston

Science **325** (5941), 657.
DOI: 10.1126/science.325_657c