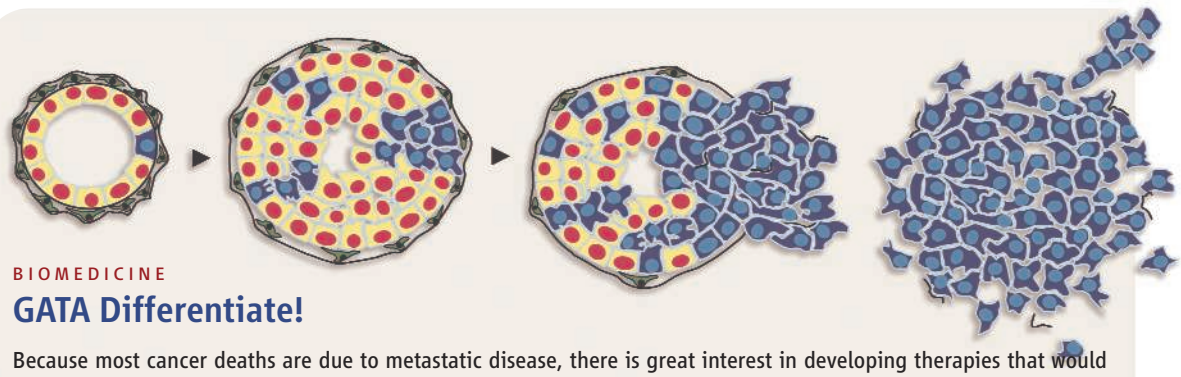


BIOMEDICINE

GATA Differentiate!

Because most cancer deaths are due to metastatic disease, there is great interest in developing therapies that would prevent cells in a primary tumor from undergoing the changes that confer the capacity to disseminate, or that would reverse such changes. Tumors that are destined to disseminate and metastasize display molecular markers that distinguish them from less aggressive cells, but it is not clear if these molecules play a causal role in tumor metastasis, and hence would be suitable drug targets.

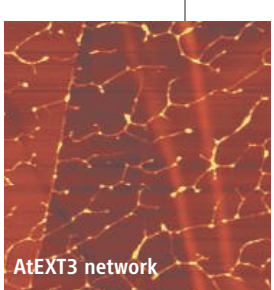
Kouros-Mehr *et al*. have explored the role of one intriguing predictive marker in human breast cancer, a transcription factor called GATA-3 that is required for the differentiation and proper function of normal mammary tissue. Breast tumors with low expression levels of GATA-3 typically are poorly differentiated, have a higher metastatic potential, and are associated with a worse clinical outcome than are tumors with high levels of GATA-3. Studying a mouse model of breast cancer, the authors found that GATA-3 expression and markers of differentiated epithelial cells (red-yellow) were lost very early in tumor progression and that this loss was likely due to the expanded growth of GATA-3–negative mammary stem cells (blue). Importantly, when they reintroduced GATA-3–positive cells into later-stage breast tumors, the tumors became more differentiated and showed a reduced capacity to disseminate. These results indicate that GATA-3 is not only a marker but also a causal factor in tumor metastasis, and that drugs activating GATA-3 itself or the molecules that regulate it could form the basis of differentiation therapy for breast cancer. — PAK

Cancer Cell **13**, 141 (2008).

PLANT SCIENCE

Constructing a Scaffold

Plant cells partition at cytokinesis by forming a new cell wall. These walls are composed of interpenetrating networks of the polysaccharides cellulose and pectin and of (hydroxy)proline-rich glycoproteins, notably the extensins. Cannon *et al.* show by electron microscopy that the *Arabidopsis* mutant *rsh* is defective in cell wall assembly and that the defect is likely due to the absence of the *rsh*-encoded extensin protein, AtEXT3. This protein contains 11 identical amphiphilic motifs that, besides being rich in hydroxyproline, contain an isodityrosine (Idt) cross-link motif (YXY) and an HYS motif. In vitro, extensin peroxidase catalyzed tyrosine cross-linking between purified AtEXT3 monomers and led to the inference that the monomers were offset such that intermolecular cross-linking occurred between Idt and HYS, rather than between two Idt motifs. Atomic force microscopy imaging shows that AtEXT3 forms a dendritic network displaying both end-on and lateral adhesion. The alternating hydrophilic and hydrophobic modules of AtEXT3 may induce like-to-like self-association with cross-linking stabilizing the network and favoring a staggered alignment that would permit two-dimensional growth. The authors suggest that such a positively charged extensin network may serve as a template for the orderly deposition of negatively charged pectin during cell wall assembly. — VV


AtEXT3 network

Proc. Natl. Acad. Sci. U.S.A. **105**, 2226 (2008).

APPLIED PHYSICS

Glimpsing Tiny Live Wires

The realization of molecular electronics requires reproducible methods for creating devices in which conduction occurs through individual molecules. Current methods rely on the fabrication of many devices to prove statistically that a single-molecule junction has been realized, but knowledge of the specific chemical environment of the conducting molecules tends to be limited, complicating the interpretation of the data. Ward *et al.* present a method for simultaneous electron transport measurements and single-molecule sensing using surface-enhanced Raman spectroscopy (SERS) on nanometer-scale structures (nanogaps) bridged by individual molecules. The metal electrodes that are used as contacts to the molecules also function as plasmonic antennae, resulting in an enormously enhanced vibrational signal. In about 1 in 10 junctions, changes in conductance with time correlate closely with changes in the SERS signal, supporting a link between electron transport and single-molecule conformational changes. The relation between conductance and SERS spectra remains complex, but steadily improving theoretical analyses paired with such measurements should shed light on the fundamental mechanisms at play. — JFU

Nano Lett. **8**, 10.1021/nl073346h (2008).

MOLECULAR BIOLOGY

Motoring Inside the Nucleus

The highly conserved protein actin not only functions as a critical cytoplasmic actor in cell shape and movement, but also, as shown recently, has a nuclear role in regulating gene expression. The

frequent companion of cytoplasmic actin is the motor protein myosin; therefore, it is not surprising that a myosin isoform (NM1) can be found in the nucleus. Ye *et al.* have examined the contributions of nuclear actin and myosin to transcription and find that NM1 and oligomeric (possibly filamentous) actin cooperate in the transcription of ribosomal RNA genes by RNA polymerase I. A series of experiments demonstrated that NM1 adenosine triphosphatase activity was necessary and that the cyclic actin-myosin interaction observed in skeletal muscle was likely to occur in the nucleus as well. The authors suggest that actin and myosin may collaborate in driving RNA polymerase and its target genes together. — BAP

Genes Dev. **22**, 322 (2008).

MATERIALS SCIENCE

A Graded Improvement

Refractive index is a key parameter to consider in selecting materials for optics and photonics applications, as it determines the extent of reflection and refraction when light impinges on an interface. Unfortunately, optimal choice of this parameter often necessitates compromising other material properties. Kim *et al.* show that they can conveniently tailor the refractive index of a single material—the transparent conductor indium tin oxide (ITO)—for device applications. Using oblique angle deposition, they are able to grow porous films consisting of arrays of oriented rods. The porosity can be controlled by changing the angle of the ITO vapor flux, thus tuning the refractive index from a bulk value of 2.19 to below 1.3. The authors exploit this tunability to grow a six-layer gradient coating on a light-emitting diode (LED), in which the ITO acts as both a coating and a conducting layer. By gradually reducing the refractive index, they eliminate almost all Fresnel reflection and thereby improve the output of the LED by 24% compared to a device made with a bulk ITO layer. — MSL

ITO gradient

CREDIT: KIM *ET AL.*, *ADV. MATER.* **20**, 801 (2008)

Adv. Mater. **20**, 801 (2008).

CHEMISTRY

Picking O over N

In general, amines react more rapidly with carbonyl electrophiles than do alcohols. Lipase enzymes manage to invert this tendency and efficiently catalyze ester formation even in the face of a nearby nitrogen group striving to form an amide. Artificial catalysts have been less successful for this purpose though, and laboratory amino ester syntheses therefore often require wasteful N protection and deprotection steps. Ohshima *et al.* have now prepared a tetranuclear zinc cluster that bucks this trend and affords selectivity along the same lines as the enzymes. At loadings as low as 1.25 mole percent, the oxophilic catalyst gives 82 to 99% yields of the ester in reactions of methyl benzoate with a range of terminal alkyl amino alcohols. Similarly, ester selectivities higher than 90:1 are observed when equal concentrations of various amines and alcohols compete intermolecularly. The authors posit a mechanism that entails dual activation of the alcohol and electrophile by cooperative Zn centers. — JSY

J. Am. Chem. Soc. **130**, 10.1021/ja073578i (2008).

Science Signaling

AAAS

<< A Receptor for Neurotrophins

Integrins are dimeric cell surface receptors composed of α and β subunits and interact with the extracellular matrix (ECM) to promote cell adhesion and survival. There are 18 α and 8 β subunits in mammals, and at least 24 heterodimers have been described. Given this complexity, it is not surprising that integrins have been observed to interact with molecules other than those in the ECM. For example, $\alpha_9\beta_1$, a widely distributed integrin, interacts with several classes of ligands, including ECM constituents (tenascin, thrombospondin 1, and osteopontin), metalloproteases (ADAM12 and 15), and vascular endothelial growth factor. Staniszewska *et al*. report that integrin $\alpha_9\beta_1$ also binds to the neurotrophins NGF, NT3, and BDNF. They found that an $\alpha_9\beta_1$–transfected colon cancer cell line adhered to mouse NGF, human recombinant NGF, BDNF, or NT3 with the same efficiency as to VCAM1, a known $\alpha_9\beta_1$ ligand. Adherence was blocked by an $\alpha_9\beta_1$-specific antibody and by a snake venom protein that selectively antagonizes $\alpha_9\beta_1$. Human recombinant NGF bound to $\alpha_9\beta_1$ with a K_d of about 5 nM, which is similar to the strength of the interaction between NGF and the low-affinity receptor $p75^{NTR}$. The responses of the transfected cells to NGF included proliferation (involving extracellular signal–regulated kinases 1 and 2) and migration (involving paxillin). — NRG

J. Cell Sci. **121**, 504 (2008).

Constructing a Scaffold

Science **319** (5867), 1162.
DOI: 10.1126/science.319.5867.1162b