

DEVELOPMENTAL BIOLOGY

A Loss of Flexibility with Age

As a cell transitions from an undifferentiated state to a differentiated cell type, its gene expression profile changes, which in part reflects physical changes in chromatin structure. In a complementary approach, Pajeroski *et al.* have examined the macroscopic properties of the nucleus during differentiation. Aspiration with a micropipette revealed that the nuclei of pluripotent human embryonic stem cells could be deformed relatively easily; however, as the cells differentiated, the nuclei became stiffer. Hematopoietic stem cells (from bone marrow) were able to differentiate into fewer cell types than embryonic stem cells and, similarly, showed an intermediate level of deformability. Progression toward the differentiated state was accompanied by an increase in the filamentous protein lamin A/C and greater condensation of chromatin. When lamin A/C was knocked down in epithelial cells, their flow behavior resembled that of hematopoietic stem cells. Further analysis showed that the fluid character of the nucleus is determined primarily by chromatin but that the degree of nuclear deformability is set by the lamina. Variations in the physical plasticity of the nucleus may be important for allowing less differentiated cells to move through tissues. — BAP

Proc. Natl. Acad. Sci. U.S.A. **104**, 15619 (2007).

ECOLOGY/EVOLUTION

Nasty, Brutish, and Short

Leaves are a vital organ for plants and for their environments. Their structure and life span influence photosynthesis, resource acquisition, and growth rates; they also influence the plant's ability to resist being eaten, for instance by insects. And leaves have important effects on the local ecosystem through leaf litter decomposition.

Knowing how leaves influenced paleoenvironments can provide key insights into past ecosystem functions. Leaf mass per area is a metric that correlates with various ecological traits but has not been applied systematically to fossil data. Royer *et al.* measure the petiole width (the petiole being the small stalk that attaches the leaf to the stem of the plant) and leaf area of fossil leaves and, through a scaling relationship they develop for these characteristics in extant leaves, use these to estimate fossil leaf mass per area. In a comparative analysis of two Eocene fossil lake floras (Republic, in the Klondike Mountains, and Bonanza, in Utah), the leaf mass per area was uniformly low at Republic, whereas Bonanza exhibited a broad range of values. These biosynthetic choices are consistent with the respective paleoclimates: The former was dominated by trees bearing short-lived leaves, which suffered fairly high levels of herbivory, and was associated with rapid leaf lit-

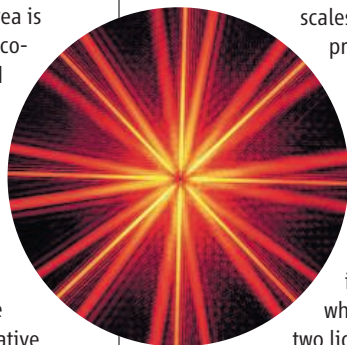
ter decomposition; whereas the latter showed wider ranges of these same traits. — GR

Paleobiology **33**, 574 (2007).

PHYSICS

Speeding Up Holography

The ability to produce ultrashort electron bunches and x-ray and optical pulses has allowed researchers to glimpse fleeting structural and electronic rearrangements occurring on femtosecond or shorter time scales. However, these pump-probe measurements often tend to provide a somewhat limited series of one- or two-dimensional (2D) snapshots of the processes at play. Two groups now show how holographic imaging—a technique in which the interference of two light beams encodes 3D information on a 2D detection surface—can be extended to the ultrafast regime, thereby raising the possibility of obtaining more detailed, fully dynamical 3D movies of processes taking place on these rapid time scales. Kubota *et al.* demonstrate the use of optical holography to track light images formed from femtosecond red light pulses as they are launched into an optical medium; the result is a spatially and tem-



porally continuous movie of the images propagating, converging into a focal point, and then diverging again. Schlotter *et al.* extend ultrafast holography to shorter wavelengths in the x-ray regime. Using patterned masks to provide multiple x-ray sources, they demonstrate the ability to record images simultaneously at different parts of the sample. They note that combining this multi-spatial sampling with gated pump-probe illumination could extend the technique to 3D imaging of ultrafast processes. — ISO

Opt. Express **15**, 14348 (2007);

Opt. Lett. **92**, 3110 (2007).

CELL BIOLOGY

To Spread or Not to Spread

When animal cells grow over a surface, they survey their surroundings and make decisions as to whether they should spread or retract from a certain path, processes that are central in cell migration and proliferation. Key to these decisions is the interaction of a group of membrane proteins, the integrins, with the surface on which the cells grow.

Flevaris *et al.* find that it is the calpain-dependent proteolytic cleavage of the integrin subunit β_3 at a specific tyrosine residue that acts as a molecular switch to help the cell change from spreading to retraction. In cells expressing a β_3 integrin that cannot be cleaved, spreading is enhanced in comparison to retraction. On the other hand, in cells expressing

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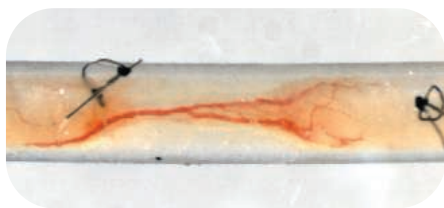
only the cleaved form of β_3 , retraction is favored—a defect that can be overcome by expressing the downstream signaling protein RhoA. The effects of β_3 appear to be mediated via an interaction of the intact integrin with the kinase c-Src at the plasma membrane, which in turn regulates RhoA-dependent contractile signaling. — SMH

J. Cell Biol. **179**, 553 (2007).

BIOMATERIALS

Nerves of Hair

Hair growth is a complex process involving more than 30 growth factors, cytokines, and signaling molecules. Both the alpha and gamma keratins, which respectively form the structure and cross-linking in the hair fibers, can be extracted from human hair. Sierpinski *et al.* explored the use of keratin-based hydrogels, which form on mixing extracts with water, for the rapid regeneration of peripheral nerves. At present, small nerve defects can be repaired using fillers to provide a structural support, but only short gaps are amenable to this approach. In vitro testing showed that the keratin hydrogels improved Schwann cell proliferation and migration and showed either no effect or some up-regulation in the production of certain



Regenerated nerve fiber.

key proteins. Using a nerve injury model in mice, the authors then proceeded to compare regeneration results from the keratin protocol with autografts (in which a different form of tissue is used to patch a defect site), as well as controls where no material was added to the defect site. The hair-based hydrogels outperformed the autografts in reducing electrical signal latency and showed a greater increase in overall nerve area, as well as comparable improvements in a number of other tests. The authors believe that the hydrogels provide a framework for the Schwann cells and also retain a number of the regulatory molecules needed for hair growth, which are also involved in nerve repair. — MSL

Biomaterials **29**, 118 (2008).

BIOTECHNOLOGY

Together We Shine

Green fluorescent protein (GFP) and its variants can be used in Förster resonance energy trans-

fer (FRET) experiments (where emission is a function of the distance between donor and acceptor fluorophores) to monitor dynamic processes such as protein folding or association in intact cells. These experiments come with limitations, however, as the changes in fluorescence intensity may be smaller than cell-to-cell variations, and fusing GFP to the target protein may interfere with function. An alternative readout strategy uses the biarsenical reagents FLAsH-EDT₂ and ReAsH-EDT₂. These reagents selectively label recombinant proteins containing a tetracysteine sequence (CCPGCC), and only the protein-bound forms fluoresce.

Luedtke *et al.* show that polypeptides containing a split sequence, with the two cysteine pairs separated in linear sequence but close together when folded, can be labeled with FLAsH or ReAsH to give a fluorescent complex. Labeling of a dimer, where the two pairs were contained on different monomers, was also successful. Fluorescence intensity correlated with the stability of either protein folding or dimerization and allowed the detection of protein folding and assembly in live cells. — VV

Nat. Chem. Biol. **3**, 10.1038/nchembio.2007.49 (2007).

CHEMISTRY

Linking Up Cleanly

Selective coupling of aryl molecules is a crucial step in the preparation of a wide range of commercial organic compounds. The requisite selectivity has traditionally been achieved by appending mutually reactive groups (such as halides and boron- or tin-based substituents) to each partner, but the addition and elimination of such groups generate considerable waste material. Recent advances in transition metal catalysis have offered a promising alternative approach, in which C-H bonds on the aryl rings are oxidatively cleaved directly to yield a C-C bonded biaryl product and (ideally) water as the sole byproduct. Li *et al.* extend this method to the coupling of acetylated anilines with alkyl benzenes. The acetamide group directs a palladium catalyst to react selectively with an adjacent ortho C-H bond, and a second C-H scission links up the benzene partner. In the case of NH(acetyl) substrates, a subsequent sequence involving N-H and C-H scission leads efficiently to carbazole products with a fused central C₄N ring connecting the aromatic cycles on either side. The reactions proceed under oxygen at 120°C, with varying amounts of a cupric salt added as a co-catalyst depending on the substrates. — JSY

Angew. Chem. Int. Ed. **46**, 10.1002/anie.200704092 (2007).