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In This Issue

APPLIED PHYSICAL SCIENCES, APPLIED BIOLOGICAL SCIENCES

How snakes slither

The physics behind the snake's slither has provoked much debate. Previous analyses suggested that snakes push against objects to propel themselves forward. This assumption has driven the design of search-and-rescue robotic snakes with wheels that go back and forth but not sideways. David Hu et al. propose that friction caused by the snake's belly scales plays a critical role in movement. The authors focused on "lateral undulation," a form of locomotion in which snakes apply lateral pressure against rocks and branches to move forward. To test their hypothesis, the authors used 10 juvenile pueblan milk snakes (*Lampropeltis triangulum campbelli*) and tested the sliding ability of the snakes covered in a cloth of similar thickness and roughness to their belly scales, and when they were covered in a slicker fiberboard. The authors also measured the snakes' ability to move on surfaces covered with the same 2 materials. After measuring the snakes' friction coefficients while slithering, the authors showed that the scales perform a vital function: they snag on rough surfaces and increase the resistance, which the snake uses for propulsion. — B.P.T.

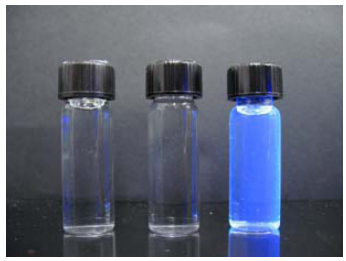
Boa constrictor on a flat, smooth surface. Image courtesy of Grace Pryor and David Hu.

"The mechanics of slithering locomotion" by David L. Hu, Jasmine Nirody, Terri Scott, and Michael J. Shelley (see pages 10081–10085)

CHEMISTRY

Biodegradable fluorescent polymers

Although fluorescent dyes and quantum dots are widely used in bench research, longer-term use of these reagents in vivo is made difficult by their toxicity. Fluorescent proteins, on the other hand, are nontoxic, but have low quantum yield and bleach easily. Jian Yang et al. introduce an alternative: aliphatic biodegradable fluorescent polymers that can be crosslinked into membranes. The polymers may serve as scaffolds in tissue engineering and drug delivery, and permit in vivo monitoring of structure. The authors modified the fabrication process for polymers that they had previously developed by reacting citric acid with 1,8-octanediol. In the new process, an amino acid is introduced at the same time as the citric acid and joins the polymer as a side chain. Based on structural characterization, the authors propose that a 6-member ring forms when the carboxylic acid, alpha carbon, and amino moieties of the amino acid bend back to join the polymer backbone. The ring is essential for fluorescence, although the amino acid side chain influences both fluorescence frequencies and quantum yield. The fluorescent polymers, which can be further processed into membranes, were nontoxic to fibroblasts and induced only mild inflammation in mice over a 5-month period, according to the authors. — K.M.



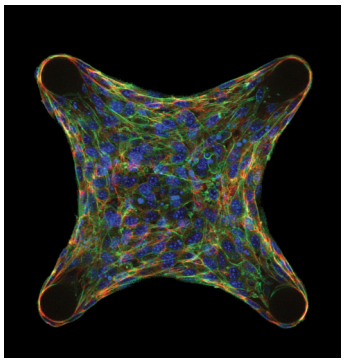
Aliphatic biodegradable photoluminescent polymer solution.

"Development of aliphatic biodegradable photoluminescent polymers" by Jian Yang, Yi Zhang, Santosh Gautam, Li Liu, Jagannath Dey, Wei Chen, Ralph P. Mason, Carlos A. Serrano, Kevin A. Schug, and Liping Tang (see pages 10086–10091)

ENGINEERING

Studying forces within tissue

The physical forces present within tissues are of interest to biophysicists and to researchers investigating biological processes such as morphogenesis, wound healing, and hypertension. Many studies of cellular mechanics are carried out in 2D cultures of cells on elastic substrates, the deformation of which provides a measure of force. Wesley Legant et al. fabricated microscale cantilevers to study the mechanics of a tissue as it develops in a 3D setting and also designed a computational model of their system. The authors microfabricated arrays of individual wells, each containing flexible pillars; cells and collagen were centrifuged into the wells. Over several hours, the cells in each well



Immunofluorescence sections of cells embedded within a micropatterned collagen gel.

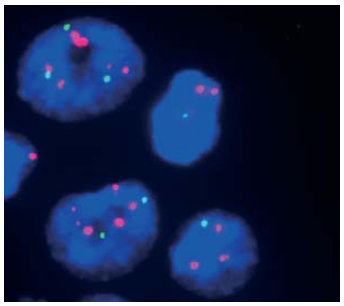
contracted the collagen into a coherent band of tissue, drawing the pillars closer together. The experiments and model, while focused on the contraction of relatively simple masses of fibroblasts, reveal how gradients of mechanical stress dictate the spatial expression of structural proteins in multicellular tissues. In subsequent experiments, the authors developed a bio-chemo-mechanical computer model of the system and used it to predict the distribution of stress, and, therefore, the density of structural proteins such as actin. — K.M.

"Microfabricated tissue gauges to measure and manipulate forces from 3D microtissues" by Wesley R. Legant, Amit Pathak, Michael T. Yang, Vikram S. Deshpande, Robert M. McMeeking, and Christopher S. Chen (see pages 10097–10102)

MEDICAL SCIENCES

A second molecular target for breast cancer treatment

Breast cancer can arise because of myriad mutations or changes in gene expression level. Ideally doctors would be able to analyze a tumor, identify its cause and target the molecular source.



Breast carcinoma cells with extra copy of AGTR1 (green).

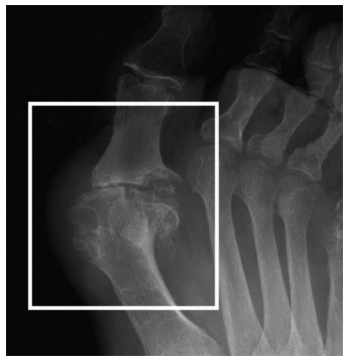
This is possible for tumors that overexpress the receptor ERBB2; clinicians have had success using trastuzumab, a monoclonal antibody, to inactivate ERBB2. Daniel Rhodes et al. conducted a metastudy to analyze genes overexpressed in breast cancer and found that AGTR1, the angiotensin II receptor type I, is overexpressed in a subset of tumors and could prove a valuable clinical target—especially because a commonly prescribed drug, losartan, is known to inhibit AGTR1. The authors analyzed overexpressed genes in 31 breast cancer-profiling datasets obtained in other studies. ERBB2 was most commonly expressed in the metastudy; AGTR1, which has been linked to cancer in previous work, was the second-most frequently found compound. The authors also conducted cellular and xenotransplant studies to examine the effect of AGTR1 overexpression and found that AGTR1 appears not to affect proliferation, but to increase invasive behavior. — K.M.

"AGTR1 overexpression defines a subset of breast cancer and confers sensitivity to losartan, an AGTR1 antagonist" by Daniel R. Rhodes, Bushra Ateeq, Qi Cao, Scott A. Tomlins, Rohit Mehra, Bharathi Laxman, Shanker Kalyana-Sundaram, Robert J. Lonigro, Beth E. Helgeson, Mahaveer S. Bhojani, Alnawaz Rehemtulla, Celina G. Kleer, Daniel F. Hayes, Peter C. Lucas, Sooryanarayana Varambally, and Arul M. Chinnaiyan (see pages 10284–10289)

PHYSIOLOGY

A mutation that causes gout

Genome-wide association studies can detect statistical associations between single nucleotide polymorphisms (SNPs) and diseases, but cannot show that a mutation causes a condition. A recent genome-wide association study found a missense SNP on chromosome 4 associated with gout, a painful condition resulting from the buildup of urate. This genomic region contains the *ABCG2* gene, known to encode a multidrug transporter. Owen Woodward et al. conducted experiments that show that ABCG2 protein transports urate, and that the mutation encoded by this missense SNP in *ABCG2* strongly inhibits urate transport. The mutation was significantly associated with serum urate levels and gout in >14,000 adults in the United States and could be responsible for 10% of gout cases, the authors estimate. The authors expressed human ABCG2 in oocytes and found that accumulation of urate was greatly decreased, because the protein was transporting it out of the cells. Mutated ABCG2 transports urate at 46% of the rate of wild-type protein. Chemically inhibiting ABCG2 in kidney cells impaired urate export. Fluorescent labeling showed that ABCG2 is expressed in kidney tubule cells, consistent with its function as a secretory urate transporter, according to the authors. — K.M.



Gout disease shown in human foot. Image courtesy of Janet Maynard.

"Identification of a urate transporter, ABCG2, with a common functional polymorphism causing gout" by Owen M. Woodward, Anna Köttgen, Josef Coresh, Eric Boerwinkle, William B. Guggino, and Michael Köttgen (see pages 10338–10342)