EDITORS' CHOICE

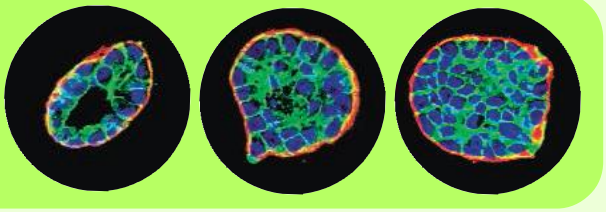
edited by Gilbert Chin

CELL BIOLOGY

A ROCK, a Tumor Cell, and a Hard Place

Tumors are generally stiffer than surrounding healthy tissue, a characteristic that has been exploited in certain diagnostic procedures such as breast self-examination. Tumor rigidity reflects not only intrinsic properties of the tumor cells but also an increased stiffness of the extracellular matrix (ECM). Whether ECM stiffening plays an active role in tumor cell growth or is an innocent bystander has been unclear.

Paszek *et al.* investigated this question by monitoring the behavior of human mammary epithelial cells cultured with ECM components that had been cross-linked to polyacrylamide gels of varying stiffness. These experiments revealed that even a small increase in matrix rigidity enhanced epithelial cell growth. Mechanistically, this effect was traced to a mechano-regulatory circuit that links physical cues from the matrix to transmembrane ECM receptors (integrins), to intracellular regulators of cell contractility such as ROCK (Rho-associated protein kinase), and to a key signaling pathway for cell growth, the mitogen-activated protein kinase pathway. These results suggest that factors causing a sustained increase in matrix stiffness—for example, a chronic inflammatory response—may promote malignant transformation. — PAK



Cell growth with increasing stiffness.

Cancer Cell, in press.

MEDICINE

New Routes to Drugs

Twentieth-century dogma was that drug development for neglected diseases is neglected because there is not enough (or no) profit to be made from the generally impoverished populations who suffer these infections. A recent analysis by Moran reveals a more optimistic turn of events for this century with the burgeoning of public-private partnerships (PPPs), such as the Medicines for Malaria Venture, the Drugs for Neglected Diseases Initiative, and the TB Alliance. PPPs are becoming pivotal in coordinating the efforts of Western multinational pharmaceutical firms, with a range of contacts and clinical experience in academia, with the efforts of smaller biotech and developing-country firms. Moran points out that multinationals are not motivated solely by profit; they also want to burnish their reputations and gain strategic access to developing-country markets and labor skills. By integrating and screening projects and expertise, PPPs synergistically reduce drug development costs from about $1 billion for a Western market to tens of millions for a neglected disease. The good news is that the PPPs will get better and more efficient as their experience grows. — CA

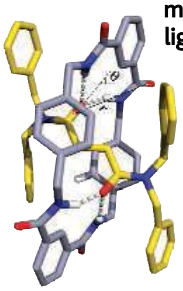
PLoS Med. 2, e302 (2005).

CHEMISTRY

Fast Vibrational Coupling

Multipulse nuclear magnetic resonance (NMR) spectroscopy is useful for determining the conformations of proteins and other large molecules in solution, but its temporal resolution is limited to microseconds. Recently synthesized nanoscale switches and motors operate on a picosecond time scale, and so require a faster method to gauge their operation. In principle, two-dimensional infrared (2D IR) spectroscopy offers the necessary increase in resolution because it measures coupling between atomic vibrations, rather than nuclear spins.

Larsen *et al.* have taken the preliminary step of showing that a 2D IR pulse sequence effectively reveals the static structure of a rotaxane in solution. This common molecular switch motif consists of a macrocycle that is suspended on an axle via hydrogen bonding; elaborations of this basic structure allow the ring to move when light, current, or chemical reagents are applied. The spectroscopic study quantified coupling between vibrating carbonyl (C=O) groups on the ring and those on the shaft. Analysis of the data through modeling yielded the distance (r = 6.9 Å) and angle (θ = 48°) between these groups, opening the door to a real-time dynamics study of switch and motor operations. — JSY



The rotaxane with the carbonyl oxygens in red.

Proc. Natl. Acad. Sci. U.S.A. 10.1073/pnas.0505313102 (2005).

APPLIED PHYSICS

Highly Heat-Sensitive

The most severe tests of calorimetry are surface processes, where the small number of reaction, binding, or adsorption events limits the amount of heat available for measurement. Fon *et al.* have constructed a cryogenic suspended SiN calorimeter that has a heat capacity resolution of 0.5 attojoule per Kelvin, compared with a typical state-of-the-art resolution of 1 femtojoule per Kelvin. The fast response of interdigitated AuGe resistance thermometers allows sampling every few microseconds, so that temperature changes can be followed via the fast relaxation of the calorimeter. The authors measured the enthalpy change associated with adsorbing 0.16 monolayers of ^{4}He on a device area of 1.2 x 10^{-9} m^2. The measured value at 2 K corresponds to a heat capacity of 1.4 k_B per helium atom, which agrees well with the measured value for He adsorbed on Grafoil. — PDS

Nano Lett. 10.1021/nl051345o (2005).

BIOCHEMISTRY

A Frozen Giant

Mimivirus (so-named because when subjected to Gram staining it, resembles or mimics a microbe) was first identified a decade ago as a virus growing within amoebae during an outbreak of pneumonia. Since then, its genome has been sequenced

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CREDITS: (TOO) PASZEK *ET AL.*, *CANCER CELL*, IN PRESS; (BOTTOM) LARSEN *ET AL.*, *PROC. NATL. ACAD. SCI. U.S.A.* 10.1073/PNAS.0505313102 (2005)

Published by AAAS