September 15, 2009 | vol. 106 | no. 37 | 15515–16004

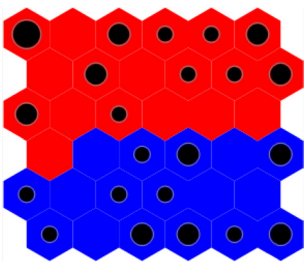
In This Issue

PNAS
Proceedings of the National Academy of Sciences of the United States of America
www.pnas.org

ENVIRONMENTAL SCIENCES

Genomes reveal bacterial lifestyles

Researchers have used genomic sequence comparisons to predict an ocean bacterium's trophic strategies, which may provide a technique to analyze the diversity of ocean bacteria, many of which are difficult to culture in the lab. Federico Lauro et al. compared the genomes of two common ocean bacteria: the copiotrophic *Photobacterium angustum*, which lives in warm, nutrient-rich waters and is fast to grow and divide, and the oligotrophic *Sphingopyxis alaskensis*, which lives in nutrient-poor, Arctic waters and grows more slowly. The authors analyzed the number, patterns, and variations in gene families. In one family, copiotrophic bacteria had many selective transporter proteins to quickly absorb plentiful nutrients, whereas oligotrophic bacteria had a smaller number of highly efficient transporter proteins to extract what little nutrition is available in Arctic oceans. The authors found differences in other genes related to nutrient and energy usage, reflecting the bacteria's adaptation to their environments. The authors used their technique to analyze 124 other oceanic bacteria, and found that oligotrophic bacteria outnumbered copiotrophic bacteria in worldwide samples of ocean water, despite the fact that copiotrophic bacteria are easier to culture in the lab. — P.D.



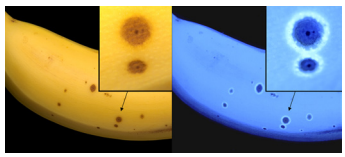
Self-organizing map showing two clusters of organisms.

"The genomic basis of trophic strategy in marine bacteria" by Federico M. Lauro, Diane McDougald, Torsten Thomas, Timothy J. Williams, Suhelen Egan, Scott Rice, Matthew Z. DeMaere, Lily Ting, Haluk Ertan, Justin Johnson, Steven Ferriera, Alla Lapidus, Iain Anderson, Nikos Kyrpides, A. Christine Munk, Chris Detter, Cliff S. Han, Mark V. Brown, Frank T. Robb, Staffan Kjelleberg, and Ricardo Cavicchioli (see pages 15527–15533)

CHEMISTRY, PLANT BIOLOGY

Glowing markers of cell death in bananas

As a banana transitions from ripe to rotten, the yellow peel develops brown and black spots that grow rapidly, eventually enveloping the whole fruit. The spots are a sign of local cell death and reveal necrotic tissue. Simone Moser et al. found that aging bananas glow blue under UV light, and the black spots are surrounded by bright blue halos. The fluorescent blue color is caused by the breakdown of chlorophyll into fluorescent chlorophyll catabolites (FCCs). In bananas, the authors show that FCCs accumulate and are persistent molecules that reveal a previously unknown pathway for chlorophyll breakdown and may prove particularly useful to researchers as noninvasive markers of cell death. The authors note that nonfluorescent chlorophyll catabolites are antioxidants and may extend the viability of aging tissues, although it is not known whether FCCs would do the same for bananas. Whereas the biological role of these fluorescent molecules is unclear, the authors speculate that fruit-eating animals may detect the fluorescent halos as a sign of ripe food. — B.P.T.



Ripening bananas exhibit luminescent blue halos.

"Fluorescent chlorophyll catabolites in bananas light up blue halos of cell death" by Simone Moser, Thomas Müller, Andreas Holzinger, Cornelius Lütz, Steffen Jockusch, Nicholas J. Turro, and Bernhard Kräutler (see pages 15538–15543)

PSYCHOLOGICAL AND COGNITIVE SCIENCES

Media multitaskers pay a cognitive price

Media multitasking is becoming ubiquitous as technology proliferates and people are able to simultaneously consume multiple forms of media, including music, e-mail, video, and other applications. How the human brain copes with this shift is unclear.

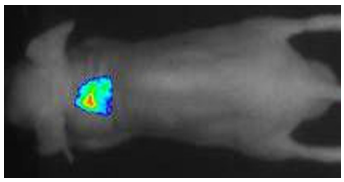
Eyal Ophir et al. created a media multitasking index and administered it to 262 college students. Heavy and light media multitaskers (HMMs and LMMs) were defined as those who fell one standard deviation above or below the scale's mean, respectively. The authors compared groups of HMMs and LMMs on several cognitive tasks and found that HMMs had greater difficulty filtering out irrelevant information from the environment and from memory. HMMs also had more trouble switching from task to task. The data suggest that LMMs pay closest attention to information relevant to their primary task whereas HMMs may sacrifice performance on a primary task to let in other sources of information. The study does not show whether media multitasking causes cognitive differences or whether people with these differences tend to be predisposed to multitasking, the authors say. This study is a step toward understanding how the technological landscape will affect cognition in the 21st century, according to the authors. — B.A.

"Cognitive control in media multitaskers" by Eyal Ophir, Clifford Nass, and Anthony D. Wagner (see pages 15583–15587)

APPLIED BIOLOGICAL SCIENCES

Red bioluminescent protein detects tumors in live animals

To aid in the fight against cancer, researchers have manufactured monoclonal antibodies that recognize antigens expressed on malignant cells, which can reveal minute and otherwise unidentifiable tumors. Visualization of these malignancies, however, typically relies on expensive and toxic radioisotope imaging. Chun Wu et al. developed a method to detect the spread of cancer in live animals that relies on bioluminescence resonance energy transfer, which is safer and less costly than radioisotope imaging. The authors created a red bioluminescent protein by conjugating a far-red fluorescent, indocyanine-derivative dye to the luciferase enzyme from the sea firefly, *Cypridina*. Except for the color red, most bioluminescence spectra occur in the visible range where they overlap with the absorption spectrum of hemoglobin, attenuating bioluminescence intensity. The authors attached the red bioluminescent molecule to an antibody against human delta-like protein, which is an embryonic antigen expressed on the surface of many cancer cells. In the presence of luciferin, energy transfer in the bioluminescent protein produced a fluorescence that identified hepatoma tumors in live mice. With the commercial availability of anticancer antibodies, this work may aid in the early detection of many types of malignancies, according to the authors. — F.A.



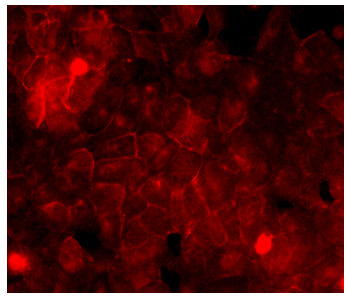
In vivo tumor imaging using a far-red bioluminescent protein-antibody probe.

"In vivo far-red luminescence imaging of a biomarker based on BRET from Cypridina *bioluminescence to an organic dye" by Chun Wu, Kazuhiro Mino, Hidetoshi Akimoto, Makiko Kawabata, Koji Nakamura, Michitaka Ozaki, and Yoshihiro Ohmiya* (see pages 15599–15603)

CELL BIOLOGY, ENGINEERING

Cultured hepatocytes aid in drug screening

Model systems that aid in toxicity screening and drug clearance can likely reduce the high cost of drug development. Srivatsan Kidambi et al. developed a method to culture human and rat hepatocytes that sustains their metabolic competence, allowing for the cells to be used in drug studies. The liver functions as the body's hub for nutrient metabolism and plays a central role in the clearance of most therapeutic agents. However, freshly cultured or primary liver cells rapidly lose their metabolic competence under standard culture methods. The authors grew primary hepatocytes together with endothelial cells under a 95% oxygen environment in media that lacked animal-derived serum. The isolated cells quickly regained metabolic competence, with gene expression profiles on par with normal hepatocytes and with high activity levels of cytochrome P450—the enzyme responsible for the liver's metabolic ability. The cell co-cultures predicted in vivo drug clearance rates for both rapid- and slow-clearing drugs and maintained a high level of metabolic activity for weeks. Further development of a rapid and predictive preclinical screening method may reduce a drug's cost as well as its time to market compared with current screening methods, thus allowing greater access to therapeutics for patients, according to the authors. — F.A.



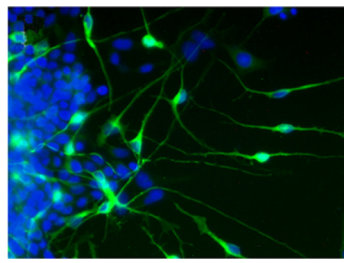
Immunofluorescence micrograph of 3-O-sulfated heparan sulfate.

"Oxygen-mediated enhancement of primary hepatocyte metabolism, functional polarization, gene expression, and drug clearance" by Srivatsan Kidambi, Rubin S. Yarmush, Eric Novik, Piyun Chao, Martin L. Yarmush, and Yaakov Nahmias (see pages 15714–15719)

CELL BIOLOGY

Using fat to generate stem cells

The search to reprogram adult cells into multi-use stem cells for research or disease treatment has largely focused on skin cells. Research has now revealed an easily and safely acquired source of cells that can be quickly and efficiently coaxed into adult stem cells: human fat. Whereas skin fibroblasts can be induced to produce lines of stem cells, the process with adult cells takes a long time and is inefficient. Ning Sun et al. looked for a more workable source of adult stem cells and identified adult fat, or adipose tissue, which is made up of cells with different lineages and cells that can be easily isolated in prodigious quanti-



Pluripotent hASC-iPS cells.

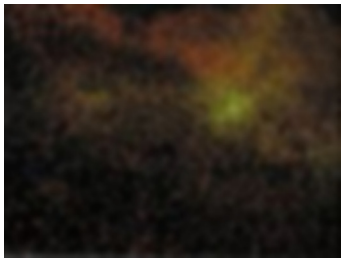
ties. The authors isolated adipose cells from adults between the ages of 45 and 60 and attempted to reprogram the cells into stem cells using an established genetic targeting method. At the same time, they began the same procedure with adult skin cells. The adipose cells produced adult stem cells twice as fast and 20 times more efficiently than skin cells. In addition, the fat cells did not require addition of mouse feeder cells, which could complicate the method's future use, according to the authors. — T.H.D.

"Feeder-free derivation of induced pluripotent stem cells from adult human adipose stem cells" by Ning Sun, Nicholas J. Panetta, Deepak M. Gupta, Kitchener D. Wilson, Andrew Lee, Fangjun Jia, Shijun Hu, Athena M. Cherry, Robert C. Robbins, Michael T. Longaker, and Joseph C. Wu (see pages 15720–15725)

DEVELOPMENTAL BIOLOGY

Insulin-producing β cells created from patients with Type 1 diabetes

Type 1 diabetes, also known as juvenile diabetes, is an autoimmune disease that destroys the insulin-producing β cells in the pancreas. The molecular or genetic defects that trigger T1D are unknown. Animal models have been useful, but it is unclear to what extent they replicate the human disease. René Maehr et al. developed a tool for studying T1D that may also work as a cell replacement therapy. Using three transcription factors—OCT4, SOX2, and KLF4—the authors reprogrammed adult fibroblast cells taken from T1D patients and transformed them into induced pluripotent stem cells (iPS). These T1D iPS cells are a genetic match to the patient from which they are derived and have the potential to develop into many cell types in the body. The authors coaxed the T1D iPS cells to become insulin-producing β cells—though the process was not very efficient. Still, the work provides proof of principle that genetically matched, insulin-producing cells can be made from patients with T1D. If coupled with a method to block rejection, these cells could be useful for transplantation, but their principal value is as a tool to study how and why diabetes occurs, according to the authors. — B.P.T.



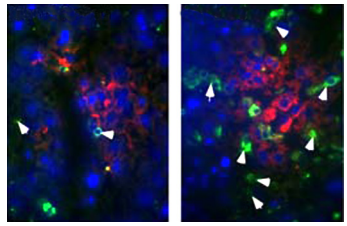
Differentation of human pluripotent stem cells to β-like cells.

"Generation of pluripotent stem cells from patients with type 1 diabetes" by René Maehr, Shuibing Chen, Melinda Snitow, Thomas Ludwig, Lisa Yagasaki, Robin Goland, Rudolph L. Leibel, and Douglas A. Melton (see pages 15768–15773)

MEDICAL SCIENCES

Free heme may contribute to severe malaria

Malaria remains one of the world's deadliest diseases, responsible for up to 3 million deaths annually. The causative parasites, which are from the *Plasmodium* family of protozoans, infect and replicate in red blood cells. When the pathogens emerge, they rupture these cells, and hemoglobin and other normally sequestered molecules enter the blood stream where they can be oxidized and produce deleterious chemicals such as free heme, hemoglobin's iron center. Elsa Seixas et al. report that free heme's pro-oxidant properties can lead to the death of *Plasmodium*-infected mice. The survival of an infected host relied on the heme-catabolyzing enzyme, heme oxygenase-1 (HO-1), which prevented the cytotoxic effects of free heme; *plasmodium*-infected mice that lacked the enzyme developed a lethal form of hepatic failure. Although HO-1 did not inhibit the protozoan's ability to replicate, the enzyme prevented free heme from provoking TNF-mediated programmed cell death in hepatocytes, affording so-called host "tolerance" against *Plasmodium* infection. A pharmacological antioxidant, N-acetylcysteine (NAC), mimicked protective effect of HO-1 and suppressed the development of liver failure in infected mice. This research may lead to therapeutics that promote host tolerance against *Plasmodium* infection and could reduce the protozoan's ability to cause severe forms of malaria, according to the autors. — F.A.



Liver of noninfected (*Left*) or Pcc-infected (*Right*) mice.

"Heme oxygenase-1 affords protection against noncerebral forms of severe malaria" by Elsa Seixas, Raffaella Gozzelino, Ângelo Chora, Ana Ferreira, Gabriela Silva, Rasmus Larsen, Sofia Rebelo, Carmen Penido, Neal R. Smith, Antonio Coutinho, and Miguel P. Soares (see pages 15837–15842)