EDITORS' CHOICE

edited by Gilbert Chin

IMMUNOLOGY

Animating Regulatory T cells

The importance of regulatory T lymphocytes in maintaining self-tolerance and suppressing autoimmunity has long been apparent, yet a clear functional definition of these cells remains difficult to pin down. Several reports now provide evidence that CTLA-4—a molecule already established in the down-modulation of immune responses—may operate by the provision of signals to a distinct subset of regulatory T cells.

Using different disease models, Read *et al.* and Takahashi *et al.* define comparable $CD25^+$ $CD4^+$ T cells, whose pivotal functions in preventing T cell–mediated pathology depend on the constitutive expression of CTLA-4. These findings bear an interesting similarity to those of Salomon *et al.* who observed that the CD28/B7 co-stimulatory pathway is required for the development and function of $CD25^+CD4^+$ regulatory T cells in a mouse model of diabetes. Collectively, these studies may adjust the way CTLA-4 and CD28 are viewed. Thus, in addition to their direct influence on effector T cell function, CTLA-4 and CD28 may fulfill an equally important role as mediators of signals to those T cells responsible for maintaining the immunological status quo. — SJS

J. Exp. Med. **192**, 295 (2000); *J. Exp. Med.* **192**, 303 (2000); *Immunity* **12**, 431 (2000).

OCEANS

Reading Planktonic History

Many reconstructions of sea surface temperatures are based on foraminiferal "transfer functions," which combine counts of the relative numbers of different kinds of forams found in marine sediments with knowledge of the environmental conditions in which those species live now, in order to estimate water temperatures in earlier times. In the high-latitude Norwegian-Greenland Sea, modern carbonate sediments are dominated by a single polar-adapted planktonic foraminifer,

"N pachy left."

Neogloboquadrina pachyderma sinistral. Plankton-based paleotemperature reconstructions for this area depend on the abundance of this foram, whose presence or absence is interpreted as indicating warm or cold conditions, respectively. However, if the ecological preferences of this foram were different in the past than they are now, then its utility as a paleoenvironmental proxy would be compromised.

Huber *et al.* have measured how the shell size of this foraminifer has varied over the past 1.3 million years in six sediment cores from the Norwegian-Greenland Sea. They find that the maximum diameter has increased over that interval, and interpret this as evidence of adaptation to cold water environments. This would mean, among other things, that the carbonate-poor intervals before 1.1 million years ago do not necessarily indicate severe glacial conditions, and that sea surface temperature reconstructions using transfer functions for periods older than that may be inaccurate. — HJS

Palaeogeogr. Palaeoclimatol Palaeoecol. **160**, 193 (2000).

APPLIED PHYSICS

Bacterial Cantilever

Much effort is being expended in exploiting micro- and nano-electromechanical systems for potential applications as miniaturized biological sensors and actuators. For example, the sensitive electromechanical properties of these systems can be used to shed light on cell adhesion and the dynamics of specific molecular interactions. Ilic *et al.* introduce a bacterial detection system based on the resonant-frequency shift of a microcantilever. Their cantilever is coated with an immobilizing antibody layer (specific in this case for the *Escherichia coli* O157:H7 serotype) and then exposed to solutions containing *E. coli.* Under ambient conditions, the technique is sensitive enough to detect just 16 bacterial cells ($\sim 6 \times 10^{-12}$ g). Exposure to other bacteria, such as *Salmonella*, caused no shift in the resonant frequency. Arrays of such cantilevers, each one coated with a different antibody, may offer a simple multibacterial detection system. — ISO

Appl. Phys. Lett. **77**, 450 (2000).

CHEMISTRY

A Bone-Supported Catalyst

Although alcohol oxidations are among the most versatile of synthetic reactions, traditionally the reagents that perform these reactions have been stoichiometric rather than catalytic, and often produce environmental waste. Recently, homogenous transition metal catalysts for oxidizing alcohols have been reported (ten Brink *et al.*, Reports, 3 March, p. 1636); these minimize production of waste products.

Yamaguchi *et al.* have developed a heterogenous catalyst for partially oxidizing alcohols to the corresponding carbonyl compounds by taking a familiar transition metal—ruthenium—and placing it on an unusual support—hydroxyapatite, the main component of bone. Replacement of the Ca^{2+} ions with Ru^{3+} produced a monomeric active species, as deter-

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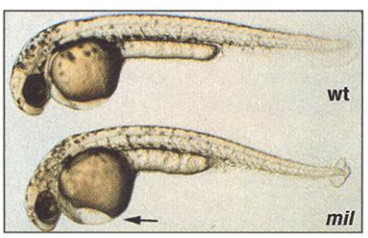
DEVELOPMENT

Orchestrating a Heart-to-Heart

The vertebrate heart originates from two separate groups of myocardial precursor cells located on opposite sides of the embryo's dorsal midline. These cells migrate along the midline and eventually fuse to form the heart. How do the cells find each other? An important clue comes from the work of Kupperman *et al.*, who identified the culprit gene in a zebrafish mutant *miles apart*, which shows defective migration of the myocardial cells. The gene encodes a lysosphingolipid G-protein–coupled receptor that most likely is activated by a lipid ligand, sphingosine-1-phosphate. Cell transplant experiments indicate that signaling through the Miles apart receptor occurs not in the myocardial precursors themselves but in surrounding cells, perhaps causing changes in the cell surfaces on which the myocardial cells migrate. Thus lipids may be important developmental signaling molecules in vertebrates. — PAK



Cardia bifida in zebrafish.

Nature **406**, 192 (2000).

SOURCE: (LEFT TO RIGHT) KUPPERMAN *ET AL.*, *NATURE* **406**, 192 (2000); RUSTY LOTTI BOND/LAMONT-DOHERTY EARTH OBSERVATORY

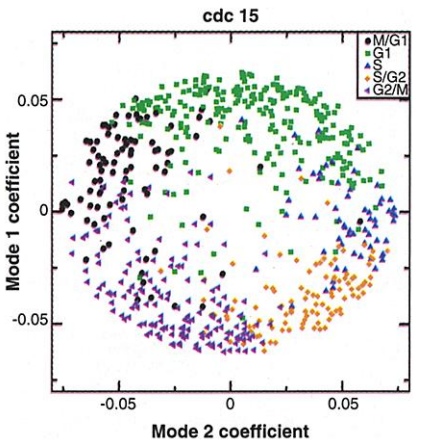
mined by analysis of x-ray adsorption fine structure. The catalyst gave high yields (often greater than 90%) for a wide variety of alcohols, and no leaching of the Ru species was observed, which allows the catalyst to be reused many times. — PDS

J. Am. Chem. Soc., in press.

COMPUTATIONAL BIOLOGY

Clocking the Cell Cycle

One of the consequences of genomic sequencing projects and subsequent gene annotations is the development of DNA microarrays, which offer a facile method for rapidly analyzing the temporal patterns of gene expression in whole organisms. Holter *et al.* have adapted a standard analysis to organize and thus simplify these large data sets, as exemplified by



Clustered gene expression during the cell cycle.

applying this analysis to previously published observations of the yeast cell cycle (cellcycle-www.stanford.edu). They are able to characterize the patterns as consisting largely of two sinusoidal modes, each with a period of 2 hours and about 30 minutes out of phase. Plotting the weights of these two functions for each gene monitored provides a graphical representation of a relatively gradual sequence of which genes turn on and off (starting at about 9 o'clock and moving clockwise) as a yeast cell progresses through the mitotic cell cycle. — GJC

Proc. Natl. Acad. Sci. U.S.A. **97**, 8409 (2000).

GEOPHYSICS

Formation of Earth's Crust

A mystery in the evolution of Earth's surface is the origin and timing of growth of the continental crust. It is generally accepted that the majority of the continental crust formed within the first 2 to 3 billion years of Earth's history. The two proposed modes of growth are (i) rapid formation of the crust soon after Earth formed followed by steady-state recycling or (ii) gradual growth of the crust over 2 to 3 billion years with episodes of punctuated growth and minimal recycling. A special issue in *Tectonophysics* focuses on this debate.

De Smet *et al.* use a thermal convection model to show that rapid growth of the crust occurred within the first 0.6 billion years, and supporting geochemical evidence from the Australian craton is described by Green *et al.* and Krapez *et al.* However, Condie has modeled a few periods of punctuated growth caused by episodic collapse of layered convection between 3 to 1 billion years ago (Ga), which supports the gradual growth model. Although there is no compelling resolution of this debate, Abbott *et al.* provide a useful inventory of the amount of continental crust that may have formed early in Earth's history; they estimate that 29 to 45% of the total volume of continental crust was formed by 2.7 Ga and 51 to 79% was formed by 1.8 Ga. — LR

Tectonophysics **322**, 19; 69; 89; 153; 163 (2000).

CELL BIOLOGY

Cholesterol Trafficking

The role of elevated circulating cholesterol levels has been highlighted by an increased awareness of its role in causing heart disease. The cellular biology of cholesterol in normal cells is much less well understood, partly due to technical difficulties in assaying cholesterol synthesis and localization in intact cells.

Heino *et al.* developed techniques to allow them to examine the rate of transport of newly synthesized cellular cholesterol from its site of synthesis inside the cell—the endoplasmic reticulum—to the cell surface. They compared the rate at which cholesterol was transported to the cell surface with the delivery of a model cell surface protein. Their findings suggest that cholesterol follows at least two routes to the cell surface: 20% of newly synthesized cholesterol follows the classical secretory pathway from the endoplasmic reticulum through the Golgi complex to the cell surface, and the remainder follows another less well characterized pathway that appears to bypass the Golgi complex. The challenge remains to identify the membrane carriers for the bulk of newly synthesized cholesterol. — SMH

Proc. Natl. Acad. Sci. U.S.A. **97**, 8380 (2000).

CREDIT: HOLTER *ET AL.*, *PROC. NATL. ACAD. SCI. U.S.A.* **97**, 8409 (2000).