Mammalian fatty acid synthase, a multienzyme that catalyzes all steps of fatty acid biosynthesis. A blueprint of its atomic structure is shown in three views, and the extent of its functional domains is indicated by colored bars. The versatile segmental construction is also used in other members of this large family of multienzymes, which synthesize natural products such as antibiotics. See page 1315.

Image: Marc Leibundgut and Timm Maier/ETH Zurich

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P. A. Lee
**NEUROSCIENCE**

Internally Generated Reactivation of Single Neurons in Human Hippocampus During Free Recall

H. Gelbard-Sagiv, R. Mukamel, M. Harel, R. Malach, J. Fried

The firing patterns of brain neurons recorded from people watching a video episode were the same as those recorded during later recall of the same show.

>> News story p. 1280; Research Article p. 1322

10.1126/science.1164685

**CHEMISTRY**

Merging Photoredox Catalysis with Organocatalysis: The Direct Asymmetric Alkylation of Aldehydes

D. A. Nicewicz and D. W. C. MacMillan

When irradiated by light, a ruthenium-organic catalyst creates intermediates with unpaired electrons that undergo otherwise intractable asymmetric reactions.

10.1126/science.1161976

**CELL BIOLOGY**

TMEM16A, A Membrane Protein Associated with Calcium-Dependent Chloride Channel Activity

A. Caputo et al.

A transmembrane protein induced in cytokine-treated bronchial epithelial cells seems to be a long-sought primary carrier of a voltage- and calcium-dependent chloride current.

10.1126/science.1163518

**MEDICINE**

An Integrated Genomic Analysis of Human Glioblastoma Multiforme

D. W. Parsons et al.

Comprehensive analysis of mutations in a brain cancer identifies previously unrecognized cancer genes and a frequently mutated protein that may serve as a therapeutic marker.

>> News story p. 1280; Science Express Research Article by S. Jones et al.

10.1126/science.1164382

Core Signaling Pathways in Human Pancreatic Cancers Revealed by Global Genomic Analyses

S. Jones et al.

Analysis of genome alterations shows that the same 12 signaling pathways are disrupted in most pancreatic tumors, suggesting these as key to tumor development.

>> News story p. 1280; Science Express Research Article by D. W. Parsons et al.

10.1126/science.1164368

**ECOLOGY**

Comment on “Fire-Derived Charcoal Causes Loss of Forest Humus”

J. Lehmann and S. Sohi

full text at www.sciencemag.org/cgi/content/full/321/5894/1295c

Response to Comment on “Fire-Derived Charcoal Causes Loss of Forest Humus”

D. A. Wardle, M.-C. Nilsson, O. Zackrisson

full text at www.sciencemag.org/cgi/content/full/321/5894/1295d

**RESEARCH ARTICLES**

**STRUCTURAL BIOLOGY**

The Crystal Structure of a Mammalian Fatty Acid Synthase

T. Maier, M. Leibundgut, N. Ban

A high-resolution structure of mammalian fatty acid synthase reveals that this enzyme is derived from an iterative polyketide synthase and has five active catalytic domains.

10.1126/science.1163518

**NEUROSCIENCE**

Internally Generated Cell Assembly Sequences in the Rat Hippocampus

E. Pastalkova, V. Itskov, A. Amarasingham, G. Buzsáki

As rats perform a memory task, cells in their hippocampus fire in self-generated sequences that correspond to and presage the animals’ subsequent choices.

>> News story p. 1280; Science Express Report by H. Gelbard-Sagiv et al.; Science Podcast

**REPORTS**

**GEOCHEMISTRY**

Experimental Test of Self-Shielding in Vacuum Ultraviolet Photodissociation of CO

S. Chakraborty, M. Ahmed, T. L. Jackson, M. H. Thiemens

The anomalous variation of oxygen isotopes in early meteorites is produced by excited states during photodissociation of carbon monoxide, not by self-shielding, as was thought.
REPORTS CONTINUED...

CHEMISTRY
Identification of Active Gold Nanoclusters on Iron Oxide Supports for CO Oxidation
A. A. Herzing et al.
High-resolution microscopy showed that the most effective catalytic gold species on an iron oxide support were those forming bilayer clusters of just 10 atoms.

ASTRONOMY
Laser Frequency Combs for Astronomical Observations
T. Steinmetz et al.
Accurate spectroscopy of the sun with a laser frequency comb shows that it can improve astronomical observations and may yield direct evidence of the universe’s expansion.

PALEOCLIMATE
Regional Synthesis of Mediterranean Atmospheric Circulation During the Last Glacial Maximum
J. Kuhlemann et al.
A three-dimensional reconstruction of atmospheric temperatures in the Mediterranean during glacial times is analogous to one of winter during the Little Ice Age.

CLIMATE CHANGE
Kinematic Constraints on Glacier Contributions to 21st-Century Sea-Level Rise
Evaluation of glacier dynamics implies that melting of the Greenland and Antarctic Ice Sheets could raise sea level by up to 2 meters by 2100, although a rise of 0.8 meters is more likely.

IMMUNOLOGY
Apobec3 Encodes Rfv3, a Gene Influencing Neutralizing Antibody Control of Retrovirus Infection
M. L. Santiago et al.
A resistance factor known to protect mice from retroviral infection is unexpectedly identified as Apobec3, a deoxycytidine deaminase that controls somatic hypermutation.

GENETICS
Human-Specific Gain of Function in a Developmental Enhancer
S. Prabhakar et al.
When transferred to a mouse, a conserved regulatory element that has been positively selected in humans is robustly expressed at the base of its developing thumb and wrist.

CELL BIOLOGY
Wnt3a-Mediated Formation of Phosphatidylinositol 4,5-Bisphosphate Regulates LR6 Phosphorylation
W. Pan et al.
The interaction of the signaling molecule Wnt to its receptor triggers accumulation of a lipid regulator, which stimulates phosphorylation of the receptor and cellular responses.

BIOCHEMISTRY
Helical Structures of ESCRT-III Are Disassembled by VPS4
S. Lata et al.
A protein responsible for the final separation of daughter cells or budding viruses forms heteromeric complexes on the inside of the membrane to regulate the abscission step.

MEDICINE
A Neoplastic Gene Fusion Mimics Trans-Splicing of RNAs in Normal Human Cells
H. Li, J. Wang, G. Mor, J. Sklar
A chimeric messenger RNA generated in a tumor by a DNA rearrangement is also, unexpectedly, expressed in healthy cells, as a result of splicing together two separate messenger RNAs.

MEDICINE
Germline Allele-Specific Expression of TGFBR1 Confers an Increased Risk of Colorectal Cancer
L. Valle et al.
In patients with colorectal cancer, one allele of the transforming growth factor–β gene produces less messenger RNA and thus less protein, a likely contributor to disease risk.
Skeletal development requires the CaSR.

SCIENCE SIGNALING
www.sciencesignaling.org
THE SIGNAL TRANSDUCTION KNOWLEDGE ENVIRONMENT

EDITORIAL GUIDE: Seeing the Signaling Forest and the Trees
M. B. Yaffe
Science Signaling launches primary research to meet the needs of the signal transduction community.

Development

RESEARCH ARTICLE: The Extracellular Calcium-Sensing Receptor (CaSR) Is a Critical Modulator of Skeletal Development
The extracellular calcium-sensing receptor (CaSR) is essential for embryonic and postnatal skeletal development.

PERSPECTIVE: New Insights in Bone Biology—Unmasking Skeletal Effects of the Extracellular Calcium-Sensing Receptor
E. M. Brown and J. B. Lian
The extracellular calcium-sensing receptor (CaSR) is essential for embryonic and postnatal skeletal development.

RESEARCH ARTICLE: Linear Motif Atlas for Phosphorylation-Dependent Signaling
Created with both in vitro and in vivo data, NetPhorest is an atlas of consensus sequence motifs for 179 kinases and 104 phosphorylation-dependent binding domains and reveals new insight into phosphorylation-dependent signaling.

REVIEW: Alternative Wnt Signaling Is Initiated by Distinct Receptors
R. van Amerongen, A. Mikels, R. Nusse
The traditional classification of Wnts into canonical or noncanonical proteins may be misleading.

A particle physicist at the Large Hadron Collider.

SCIENCE CAREERS
www.sciencecareers.org/career_development
FREE CAREER RESOURCES FOR SCIENTISTS

Working in Industry: Taken for Granted—Fitting the Job Market to a ‘T’
B. Benderly
Scientists need more than bench expertise to find work in industry.

Working in Industry: Mastering Your Ph.D.—Is Industry Right for You?
B. Noordam
Research in industry differs from academic research in several ways.

Triggermeister
C. Reed
Particle physicist Bilge Demirkoz will make sure colleagues see what happens when CERN’s Large Hadron Collider starts this month.

September 2008 Funding News
J. Fernández
Learn about the latest in research funding, scholarships, fellowships, and internships.