COVER

Mammalian fatty acid synthase, a multi-enzyme 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 multifunctional enzymes, which synthesize natural products such as antibiotics. See page 1315.

Image: Marc Leibundgut and Timm Maier/ETH Zurich

NEWS OF THE WEEK

Whole-Genome Data Not Anonymous, Challenging Assumptions 1278
China Plans $3.5 Billion GM Crops Initiative 1279
A Detailed Genetic Portrait of the Deadliest Human Cancers 1280

>> Science Express Research Articles by D. W. Parsons et al. and S. Jones et al.

Hippocampal Firing Patterns Linked to Memory Recall 1280

>> Science Express Report by H. Gelbard-Sagiv et al.; Research Article p. 1322

SCIENCESCOPE 1281
MathFest 2008 Meeting 1282
Shapeshifting Made Easy
Sweet Inspiration
A Royal Squeeze
Taking the Edge Off

NEWS FOCUS 1284

Investigating the Psychopathic Mind

>> Science Podcast

Large Hadron Collider 1287
The Overture Begins
Researchers, Place Your Bets!
Bracing for a Maelstrom of Data, CERN Puts Its Faith in the Grid
Is the LHC a Doomsday Machine?

LETTERS 1293

Reading Between the Number Lines R. E. Núñez
Response V. Izard, S. Dehaene, P. Pica, E. Spelke
The Risks of Pigging Out on Antibiotics
R. Goldberg, S. Roach, D. Wallinga, M. Mellon
Battle of the Bugs R. D. Slatker and C. Hill
DOE Should Keep Education in Mind L. A. Kull
Call for an Objective DOE Decision C. Cassapakis

CORRECTIONS AND CLARIFICATIONS 1295

BOOKS ET AL. 1296

Doubt Is Their Product How Industry’s Assault on Science Threatens Your Health
D. Michaels, reviewed by C. F. Cranor

A Taste of the Gonzo Scientist

>> Online Feature p. 1267

POLICY FORUM 1298

Life Cycle of Translational Research for Medical Interventions
D. G. Contopoulos-Ioannidis et al.

PERSPECTIVES 1300

Enhancing Gene Regulation
G. A. Wray and C. C. Babbitt
>> Brevia p. 1314; Report p. 1346

The Universe Measured with a Comb
S. Lopez >> Report p. 1335

The Cart Before the Horse
J. D. Rowley and T. Blumenthal >> Report p. 1357

An Enzyme Assembly Line
J. L. Smith and D. H. Sherman >> Research Article p. 1315

How to Infect a Mimivirus
H. Ogata and J.-M. Claverie

An End to the Drought of Quantum Spin Liquids
P. A. Lee

Published by AAAS
www.sciencemag.org SCIENCE VOL 321 5 SEPTEMBER 2008
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NEUROSCIENCE
Internally Generated Reactivation of Single Neurons in Human Hippocampus During Free Recall
H. Gelbard-Sagiv, R. Mukamel, M. Harel, R. Malach, I. 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

TECHNICAL COMMENT ABSTRACTS
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

REVIEW
ATMOSPHERIC SCIENCE
Flood or Drought: How Do Aerosols Affect Precipitation?
D. Rosenfeld et al.
1309

DEVELOPMENTAL BIOLOGY
Shadow Enhancers as a Source of Evolutionary Novelty
J.-W. Hong, D. A. Hendrix, M. S. Levine
Some developmentally important genes can be regulated via two enhancers, one located nearby and the other, a “shadow” enhancer, 10 to 20 kilobases away.
>> Perspective p. 1300; Report p. 1346

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.
>> Perspective p. 1304

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

MEDICINE
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

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.
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.

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.

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.

Kinematic Constraints on Glacier Contributions to 21st-Century Sea-Level Rise
W. T. Pfeffer, J. T. Harper, S. O’Neel
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.

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.

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.

Wnt3a-Mediated Formation of Phosphatidylinositol 4,5-Bisphosphate Regulates LRP6 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.

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.

Apobec3, a deoxycytidine deaminase that a likely contributor to disease risk.

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

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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
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.

SCIENCE ONLINE FEATURE

THE GONZO SCIENTIST: How Astronomers Have Fun (and Nearly Die Trying)
In western Mongolia, a solar eclipse has mythic meaning (with audio slideshow).
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A particle physicist at the Large Hadron Collider.

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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.

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