



COVER

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

DEPARTMENTS

- 1267 Science Online
- 1268 This Week in *Science*
- 1272 Editors' Choice
- 1274 Contact *Science*
- 1275 Random Samples
- 1277 Newsmakers
- 1366 Gordon Research Conferences
- 1374 New Products
- 1375 Science Careers

EDITORIAL

- 1271 Scientific Publishing Standards
by Bruce Alberts

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*

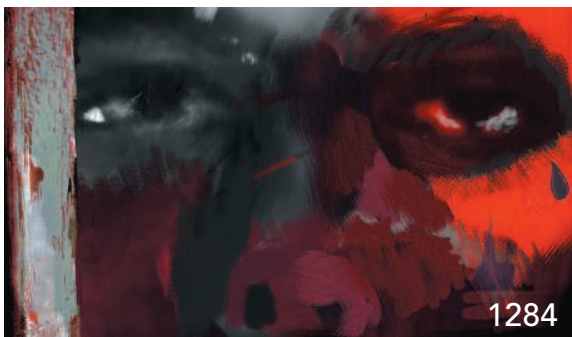
- SCIENTESCOPE 1281
- MathFest 2008 Meeting 1282
- Shapeshifting Made Easy
- Sweet Inspiration
- A Royal Squeeze
- Taking the Edge Off

NEWS FOCUS

- Investigating the Psychopathic Mind 1284
- >> *Science Podcast*

Large Hadron Collider

- The Overture Begins 1287
- Researchers, Place Your Bets!
- Bracing for a Maelstrom of Data, CERN Puts Its Faith in the Grid 1289
- Is the LHC a Doomsday Machine?



1284

LETTERS

- Reading Between the Number Lines *R. E. Núñez* 1293
- Response *V. Izard, S. Dehaene, P. Pica, E. Spelke*
- The Risks of Piggling Out on Antibiotics
- R. Goldberg, S. Roach, D. Wallinga, M. Mellon*
- Battle of the Bugs *R. D. Sleator 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.

- Doubt Is Their Product How Industry's Assault on Science Threatens Your Health 1296
- D. Michaels, reviewed by C. F. Cranor*
- A Taste of the Gonzo Scientist 1297
- >> *Online Feature p. 1267*

POLICY FORUM

- Life Cycle of Translational Research for Medical Interventions 1298
- D. G. Contopoulos-Ioannidis et al.*

PERSPECTIVES

- Enhancing Gene Regulation 1300
- G. A. Wray and C. C. Babbitt*
- >> *Brevia p. 1314; Report p. 1346*
- The Universe Measured with a Comb 1301
- S. Lopez* >> *Report p. 1335*
- The Cart Before the Horse 1302
- J. D. Rowley and T. Blumenthal* >> *Report p. 1357*
- An Enzyme Assembly Line 1304
- J. L. Smith and D. H. Sherman*
- >> *Research Article p. 1315*
- How to Infect a Mimivirus 1305
- H. Ogata and J.-M. Claverie*
- An End to the Drought of Quantum Spin Liquids 1306
- P. A. Lee*

Downloaded from <http://science.sciencemag.org/>



1297 April 21, 2018

CONTENTS continued >>

SCIENCE EXPRESS

www.sciencexpress.org

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

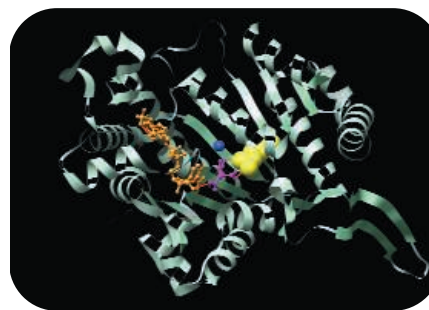
CELL BIOLOGY

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



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

TECHNICAL COMMENT ABSTRACTS

ECOLOGY

Comment on "Fire-Derived Charcoal Causes Loss of Forest Humus" 1295

J. Lehmann and S. Sohi

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

REVIEW

ATMOSPHERIC SCIENCE

Flood or Drought: How Do Aerosols Affect Precipitation? 1309

D. Rosenfeld et al.



BREVIA

DEVELOPMENTAL BIOLOGY

Shadow Enhancers as a Source of Evolutionary Novelty 1314

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*

RESEARCH ARTICLES

STRUCTURAL BIOLOGY

The Crystal Structure of a Mammalian Fatty Acid Synthase 1315

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*

NEUROSCIENCE

Internally Generated Cell Assembly Sequences in the Rat Hippocampus 1322

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 1328

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.

CONTENTS continued >>

REPORTS CONTINUED...

CHEMISTRY

Identification of Active Gold Nanoclusters on Iron Oxide Supports for CO Oxidation 1331

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 1335

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.

>> *Perspective p. 1301*

PALEOCLIMATE

Regional Synthesis of Mediterranean Atmospheric Circulation During the Last Glacial Maximum 1338

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 1340

W. T. Pfeffer, J. T. Harper, S. O'Neil

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.

>> *Science Podcast*

IMMUNOLOGY

Apobec3 Encodes *Rfv3*, a Gene Influencing Neutralizing Antibody Control of Retrovirus Infection 1343

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 1346

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.

>> *Perspective p. 1300; Brevia p. 1314*

CELL BIOLOGY

Wnt3a-Mediated Formation of Phosphatidylinositol 4,5-Bisphosphate Regulates LRP6 Phosphorylation 1350

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 1354

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 1357

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, a result of splicing together two separate messenger RNAs.

>> *Perspective p. 1302*

MEDICINE

Germline Allele-Specific Expression of *TGFBR1* Confers an Increased Risk of Colorectal Cancer 1361

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.



1343



ADVANCING SCIENCE. SERVING SOCIETY

SCIENCE (ISSN 0036-8075) is published weekly on Friday, except the last week in December, by the American Association for the Advancement of Science, 1200 New York Avenue, NW, Washington, DC 20005. Periodicals Mail postage (publication No. 484460) paid at Washington, DC, and additional mailing offices. Copyright © 2008 by the American Association for the Advancement of Science. The title SCIENCE is a registered trademark of the AAAS. Domestic individual membership and subscription (51 issues): \$144 (\$74 allocated to subscription). Domestic institutional subscription (51 issues): \$770; Foreign postage extra: Mexico, Caribbean (surface mail) \$55; other countries (air assist delivery) \$85. First class, airmail, student, and emeritus rates on request. Canadian rates with GST available upon request, GST #1254 88122. Publications Mail Agreement Number 1069624. SCIENCE is printed on 30 percent post-consumer recycled paper. Printed in the U.S.A.

Change of address: Allow 4 weeks, giving old and new addresses and 8-digit account number. Postmaster: Send change of address to AAAS, P.O. Box 96178, Washington, DC 20090-6178. Single-copy sales: \$10.00 current issue, \$15.00 back issue prepaid includes surface postage; bulk rates on request. Authorization to photocopy material for internal or personal use under circumstances not falling within the fair use provisions of the Copyright Act is granted by AAAS to libraries and other users registered with the Copyright Clearance Center (CCC) Transactional Reporting Service, provided that \$20.00 per article is paid directly to CCC, 222 Rosewood Drive, Danvers, MA 01923. The identification code for Science is 0036-8075. Science is indexed in the Reader's Guide to Periodical Literature and in several specialized indexes.



Printed on
30% post-consumer
recycled paper.

CONTENTS continued >>>



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

W. Chang, C. Tu, T.-H. Chen, D. Bikle, D. Shoback

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

M. L. Miller, L. J. Jensen, F. Diella, C. Jørgensen, M. Tinti, L. Li, M. Hsiung, S. A. Parker, J. Bordeaux, T. Sicheritz-Ponten, M. Olhovsky, A. Pasculescu, J. Alexander, S. Knapp, N. Blom, P. Bork, S. Li, G. Cesareni, T. Pawson, B. E. Turk, M. B. Yaffe, S. Brunak, R. Linding

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).

www.sciencemag.org/sciext/gonzoscientist/

SCIENCE NOW

www.sciencenow.org

HIGHLIGHTS FROM OUR DAILY NEWS COVERAGE

Taking One for the Team

Selflessness might be bad for the warrior but good for the tribe.

Fancy Footwork Helps Flies Cheat Death

High-speed videos reveal surprising sophistication in insect's escape response.

Why Men Cheat

Study chalks up promiscuous behavior to a single genetic change.

A particle physicist at the Large Hadron Collider.



SCIENCE CAREERS

www.sciencereers.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 Demirköz 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.

SCIENCE PODCAST

www.sciencemag.org/about/podcast.dtl

FREE WEEKLY SHOW



Download the 5 September Science Podcast to hear about organizing memory in the hippocampus, ice level rise, criminal psychopathy, and more.

Separate individual or institutional subscriptions to these products may be required for full-text access.

Science

321 (5894)

Science **321** (5894), 1268-1374.

ARTICLE TOOLS

<http://science.sciencemag.org/content/321/5894>

PERMISSIONS

<http://www.sciencemag.org/help/reprints-and-permissions>

Use of this article is subject to the [Terms of Service](#)

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. 2017 © The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. The title *Science* is a registered trademark of AAAS.