



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

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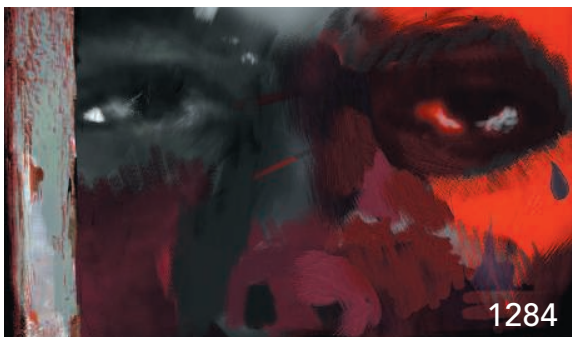
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www.sciencexpress.org

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

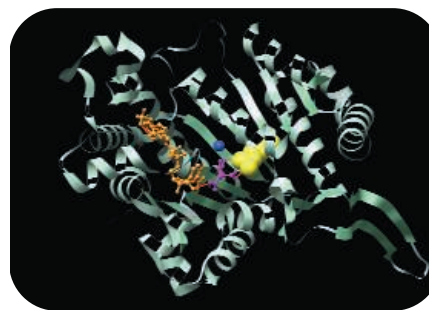
CELL BIOLOGY

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

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J. Lehmann and S. Sohi

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

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

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

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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*

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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*

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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*

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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.

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W. T. Pfeffer, J. T. Harper, S. O'Neil
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>> *Perspective p. 1300; Brevia p. 1314*

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S. Lata et al.
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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*

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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.



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Skeletal development requires the CaSR.

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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

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).

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Study chalks up promiscuous behavior to a single genetic change.



A particle physicist at the Large Hadron Collider.

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B. Benderly

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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

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