COVER
A metaphorical USB cable transmitting genetic information to “reprogram” cells symbolizes the Breakthrough of the Year for 2008. Advances in the burgeoning field of cellular reprogramming have brought scientists closer to the goal of using stem cells to better understand and someday treat disease. See the special section beginning on page 1766.

Image: Chris Bickel

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Breakthrough of the Year

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www.sciencemag.org SCIENCE VOL 322 19 DECEMBER 2008
Foraminiferal Isotope Evidence of Reduced Nitrogen Fixation in the Ice Age Atlantic Ocean

H. Ren et al.

Nitrogen fixation in the tropical Atlantic increased during deglaciation and, along with increased denitrification, helped to stabilize the ocean nitrogen reservoir.

10.1126/science.1165787

Glucosinolate Metabolites Required for an Arabidopsis Innate Immune Response

N. K. Clay, A. M. Adio, C. Denoux, G. Jander, F. M. Ausubel

A Glucosinolate Metabolism Pathway in Living Plant Cells Mediates Broad-Spectrum Antifungal Defense

P. Bednarek et al.

Plant cells defend against fungal attack through an innate immunity pathway in which infection triggers glucosinolate synthesis, stimulating formation of a protective callose.

10.1126/science.1164627

Rapid Membrane Disruption by a Perforin-Like Protein Facilitates Parasite Exit from Host Cells

B. F. C. Kafsack et al.

The human and animal parasite that causes toxoplasmosis escapes from host cells by using a perforin-like protein to make holes in the intracellular vacuole in which it resides.

10.1126/science.1165740

Electron Cryomicroscopy of E. coli Reveals Filament Bundles Involved in Plasmid DNA Segregation

J. Salje, B. Zuber, J. Löwe

The actin-like filaments that power movement of DNA during bacterial cell division form small bundles of three to five filaments near the nucleoid.

10.1126/science.1164346

Making Waves with the Clean Water Act

L. S. Fore et al.

The State of Global Hunger

J. Sastre

Bird Brains Key to the Functions of Sleep

S. M. H. Gobes and J. J. Bolhuis

Old Seeds Coming in from the Cold

F. Gugerli

Response

S. Sallon et al.

Comment on "Declining Wild Salmon Populations in Relation to Parasites from Farm Salmon"

B. E. Riddell, R. J. Beamish, L. J. Richards, J. R. Candy

full text at www.sciencemag.org/cgi/content/full/322/5909/1790b

Response to Comment on "Declining Wild Salmon Populations in Relation to Parasites from Farm Salmon"

M. Krkosěk et al.

full text at www.sciencemag.org/cgi/content/full/322/5909/1790c

Spiral Jetta: A Road Trip Through the Land Art of the American West

E. Hogan, reviewed by M. Parrish

The Tragedy of Thomas Hobbes

A. Shaplin, Royal Shakespeare Theatre, London

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Nuclear Reprogramming in Cells

J. B. Gurdon and D. A. Melton

Reports

Matching Glass-Forming Ability with the Density of the Amorphous Phase

Y. Li, Q. Guo, J. A. Kalb, C. V. Thompson

The change in density during crystallization predicts which copper-zirconium alloys can most easily form a metallic glass.

Stable Prenucleation Calcium Carbonate Clusters

D. Gebauer, A. Völkel, H. Cölfen

Even unsaturated solutions contain stable neutral clusters of calcium carbonate, which may aid in crystallization and biomineralization.

>> Perspective p. 1802
**REPORTS CONTINUED...**

**MATERIALS SCIENCE**

Shock-Wave Exploration of the High-Pressure Phases of Carbon

M. D. Knudson, M. P. Desjarlais, D. H. Dolan

A magnetically driven plate shocks diamond to extreme pressures and temperatures, allowing resolution of its melting regime and a possible higher-pressure phase.

**PALEONTOLOGY**

Avian Paternal Care Had Dinosaur Origin

D. J. Varricchio et al.

The large egg clutches of troodontid and oviraptor dinosaurs and evidence that fossils of brooding dinosaurs were males shows that paternal care was ancestral to birds. >> Perspective p. 1799

**PLANETARY SCIENCE**

Orbital Identification of Carbonate-Bearing Rocks on Mars

B. L. Ehlmann et al.

Despite widespread acidic weathering on Mars, detection of carbonate-bearing rocks indicates that nonacidic waters existed in the past.

**PLANT SCIENCE**

The Circadian Clock in Arabidopsis Roots Is a Simplified Slave Version of the Clock in Shoots

A. B. James et al.

A simpler plant circadian clock, which normally has three interlocking feedback loops, is used in the roots, with one feedback loop regulating only a few genes.

**DEVELOPMENTAL BIOLOGY**

Human Fetal Hemoglobin Expression Is Regulated by the Developmental Stage-Specific Repressor BCL11A

V. G. Sankaran et al.

A way to reactivate a fetal form of γ-globin in adults—by releasing it from repression by an inhibitor—may prove useful for treating certain genetic anemias. >> Perspective p. 1803

**MOLECULAR BIOLOGY**

CRISPR Interference Limits Horizontal Gene Transfer in Staphylococci by Targeting DNA

L. A. Marraffini and E. J. Sontheimer

The small CRISPR RNAs in Staphylococci bacteria that protect against phage infection are complementary to foreign phage DNA and target it for destruction.

**CELL BIOLOGY**

Nascent RNA Sequencing Reveals Widespread Pausing and Divergent Initiation at Human Promoters

L. J. Core, J. J. Waterfall, J. T. Lis

RNA sequencing identifies antisense transcription immediately upstream of genes with transcriptionally engaged RNA polymerase.

> Perspective p. 1804

**CELL BIOLOGY**

Divergent Transcription from Active Promoters

A. C. Sella et al.

Active genes produce promoter-localized sense and antisense short RNAs, suggesting frequent transcription by divergently oriented RNA polymerase II complexes at mammalian promoters. >> Perspective p. 1804

**CELL BIOLOGY**

RNA Exosome Depletion Reveals Transcription Upstream of Active Human Promoters

P. Preker et al.

Highly unstable transcripts exist upstream of active human promoters. >> Perspective p. 1804

**CELL BIOLOGY**

The Antisense Transcriptomes of Human Cells

Y. He et al.

The abundance and nonrandom genomic origin of antisense transcripts in human cells suggest that these RNAs are an important feature of gene regulation. >> Perspective p. 1804

**MEDICINE**

Label-Free Biomedical Imaging with High Sensitivity by Stimulated Raman Scattering Microscopy

C. W. Freudiger et al.

Three-dimensional imaging based on stimulated Raman scattering can detect lipids in living cells and monitor the movement of drugs through the skin.

**MEDICINE**

Leukemic Cells Create Bone Marrow Niches That Disrupt the Behavior of Normal Hematopoietic Progenitor Cells

A. Colmone et al.

Cancerous immune cells create abnormal microenvironments in bone marrow that attract normal immune precursor cells, disrupting their function and exacerbating disease.

**NEUROSCIENCE**

Representation of Geometric Borders in the Entorhinal Cortex

T. Solstad et al.

A previously unknown cell type in the brain’s cortex encodes geometric boundaries of the nearby environment, perhaps providing a frame of reference.
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A horse can peg another’s identity by whinny alone.

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2000-year-old site suggests Romans returned to area of massive defeat.

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Intelligence marks a man as a good match.

Science in translation.

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Programs Aim to Train Translational Scientists
B. Vastag
New Ph.D. programs in translational medicine provide basic science training and clinical experience.

A Young Scientist at the Forefront of Cell Reprogramming
E. Pain
Curiosity, boldness, and single-mindedness won Austrian scientist Konrad Hochedlinger a place in cell reprogramming, Science’s Breakthrough of the Year for 2008.

Tooling Up: The ABCs of Transitioning to Leadership
D. Jensen
“Activator,” “behavior,” and “consequence” are key concepts in this simple management theory.

From the Archives: Translational Research Careers
K. Travis
Translational researchers are pushing a fundamental change in the way science has operated for decades.

Visualizing gene expression dynamics.

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MEETING REPORT: Ontologies of Cellular Networks
R. Arp and B. Smith
A meeting of philosophers and biologists reveals the great diversity in ideas about how pathway information can be organized.

PODCAST
J. F. Foley and A. M. VanHook
Binding of CD3ε subunits to plasma membrane lipids blocks T cell receptor signaling.

NETWATCH: GEDI, the Gene Expression Dynamics Inspector
Convert microarray data into visual portraits to identify genes that share dynamic expression profiles; in Bioinformatics Resources.

NETWATCH: NIH VideoCasting and Podcasting
Watch live and archived NIH-sponsored events; in Web Broadcasts.

SCIENCE ONLINE FEATURE

VIDEO: 2008 Breakthrough of the Year
An introduction to some of the work that led studies in reprogramming cells to be tagged the top scientific story for 2008.

From the Archives: Translational Research Careers
K. Travis
Translational researchers are pushing a fundamental change in the way science has operated for decades.

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