COVER

The many layers of gene regulation in a eukaryotic cell, envisioned as a video game. Transcription in the nucleus (green circle) proceeds to translation in the cytoplasm via genome topology, polymerase pausing, microRNA repression, RNA splicing, and riboswitch regulation. See the special section beginning on page 1781.

Illustration: Carin L. Cain

SPECIAL SECTION

Gene Regulation

INTRODUCTION
Freedom of Expression

NEWS
MicroRNAs Make Big Impression in Disease After Disease

PERSPECTIVES
Gene Regulation by Transcription Factors and MicroRNAs
O. Hobert

The Eukaryotic Genome as an RNA Machine

Multilevel Regulation of Gene Expression by MicroRNAs
E. V. Makeyev and T. Maniatis

Transcription Regulation Through Promoter-Proximal Pausing of RNA Polymerase II
L. J. Core and J. T. Lis

Gene Regulation in the Third Dimension
J. Dekker

Complex Riboswitches
R. R. Breaker

Evolution of Eukaryotic Transcription Circuits
B. B. Tuch, H. Li, A. D. Johnson

>> Editorial p. 1733; for online content, see p. 1727 or go to www.sciencemag.org/generegulation/

NEWS OF THE WEEK

Roads, Ports, Rails Aren’t Ready for Changing Climate, Says Report

Study Fingers Soot as a Major Player in Global Warming

Smart Birds Lend a Beak for Food

NIH Reports Breach of Patient Records

Elusive Pathogen Cornered at Last

SCIENCESCOPE
China’s Modern Medical Minister

Saudi Start-Up Hopes Grants Will Buy Time

NEWS FOCUS

Science by the Masses

Weighing the Climate Risks of an Untapped Fossil Fuel

With New Disease Genes, a Bounty of Questions

Lunar and Planetary Science Conference

Cooking Up the Solar System From the Right Ingredients

New Piece of the Solar System Puzzle Fits In

What Was a ‘Wet and Warm’ Early Mars Really Like?

Snapshots From the Meeting

DEPARTMENTS

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1856 New Products
1857 Science Careers

EDITORIAL

1733 Shortcuts to Medical Progress?
by Bruce Alberts

>> Gene Regulation special section p. 1781
MATERIALS SCIENCE
Stretchable and Foldable Silicon Integrated Circuits
D.-H. Kim et al.
High-performance, bendable, and stretchable electronic devices are fabricated on an elastic plastic substrate by placing the critical electronic components in the neutral bending plane.

10.1126/science.1154367

APPLIED PHYSICS
Silica-on-Silicon Waveguide Quantum Circuits
A. Politi et al.
Quantum circuits—in which individual photons interfere, entangle, and form logic gates—have been realized on silicon chips.

10.1126/science.1155441

BIOCHEMISTRY
Reconstitution of P ilus Assembly Reveals a Bacterial Outer Membrane Catalyst
M. Nishiyama, T. Ishikawa, H. Rechsteiner, R. Glockshuber
The cell-free formation of the protruberant pilus of a pathogenic bacteria is accelerated by a protein that catalyzes supramolecular assembly without input of cellular energy.

10.1126/science.1154994

GENETICS
Rare Structural Variants Disrupt Multiple Genes in Neurodevelopmental Pathways in Schizophrenia
T. Walsh et al.
Patients with schizophrenia carry multiple small deletions and duplications in their DNA that are associated nonrandomly with neuronal signaling and brain development pathways.

10.1126/science.1155174

LETTERS
The Last Inventor of the Telephone J. Schmidhuber
Thinking Outside the Reef E. L. Peterson, M. Beger, Z. T. Richards
Putting Ant-Acacia Mutualisms to the Fire R. Cochard and D. Agosti Response T. M. Palmer et al.

BOOKS ET AL.
Proust Was a Neuroscientist J. Lehrer
Artsience Creativity in the Post-Google Generation D. Edwards, reviewed by J. Labinger
Victorian Popularizers of Science Designing Nature for New Audiences B. Lightman, reviewed by P. J. Pauly

POLICY FORUM
The Planet Debate Continues M. V. Sykes

PERSPECTIVES
Multitasking in Tissues and Materials P. B. Messersmith >> Report p. 1816
A Milestone in Time Keeping D. Kleppner >> Reports pp. 1805 and 1808
When a Commodity Is Not Exactly a Commodity N. Folbre
Recording Earth’s Vital Signs R. F. Keeling
A Postgenomic Visual Icon J. N. Weinstein

REVIEW
MATERIALS SCIENCE
Doped Nanocrystals D. J. Norris, A. L. Efros, S. C. Erwin

BREVIA
PLANETARY SCIENCE
Dynamics of Saturn’s South Polar Vortex U. A. Dyudina et al.
Observations from Cassini show that the cloud vortex at Saturn’s south pole shares some features with hurricanes (such as an eye wall), but forms by a different mechanism.

REPORTS
ASTROPHYSICS
Magnetar-Like Emission from the Young Pulsar in Kes 75 F. P. Gavriil et al.
A pulsar exhibits x-ray bursts like that seen only in magnetars, which have ultrahigh magnetic fields, implying that neutron stars exhibit a continuum of magnetic activity.
REPORTS CONTINUED...

PHYSICS
Sr Lattice Clock at $1 \times 10^{-16}$ Fractional Uncertainty by Remote Optical Evaluation with a Ca Clock
A. D. Ludlow et al.
Two clocks based on optical transitions in single trapped ions, set 4 kilometers apart, are able to keep time within a fractional error of $1 \times 10^{-16}$, better than the standard atomic clock. >> Perspective p. 1768

PHYSICS
Frequency Ratio of Al$^+$ and Hg$^+$ Single-Ion Optical Clocks; Metrology at the 17th Decimal Place
T. Rosenband et al.
Precise measurements of the frequency ratio of two single ion clocks indicate that the fine-structure constant is fine and constant to an uncertainty of $10^{-17}$. >> Perspective p. 1768

CHEMISTRY
Self-Assembly of Large and Small Molecules into Hierarchically Ordered Sacs and Membranes
R. M. Capito et al.
Mixing of a high–molecular weight polymer with a low–molecular weight peptide amphiphile instantly forms repairable membrane sacs large enough to encapsulate cells.

MATERIALS SCIENCE
The Transition from Stiff to Compliant Materials in Squid Beaks
A. Mizeretz, T. Schneberk, C. Sun, F. W. Zok, J. H. Waite
The squid beak, sharp and hard only at the tip, exhibits a chemical gradient that tailors its mechanical properties to prevent damage to the attached soft muscle tissue. >> Perspective p. 1767

CHEMISTRY
Determining Transition-State Geometries in Liquids Using 2D-IR
J. F. Cohoon, K. R. Sawyer, J. P. Schlegel, C. B. Harris
Tracking vibrational modes through a transition state by spectroscopy reveals an iron compound’s thermal ligand rearrangement, which was previously too fast to monitor.

CHEMISTRY
Surface Trapping of Atoms and Molecules with Dipole Rings
H. Dil et al.
Holes in a boron nitride surface ringed by in-plane dipoles form a nanometer-scale pore network with a trapping potential that can hold weakly adsorbed molecules.

MOLECULAR BIOLOGY
Nutritional Control of Reproductive Status in Honeybees via DNA Methylation
R. Kucharski, J. Maleszka, S. Foret, R. Maleszka
Epigenetic modifications that involve methylation cause female honeybee larvae to become queens rather than workers when they are fed royal jelly.

STRUCTURAL BIOLOGY
The Flavivirus Precursor Membrane-Envelope Protein Complex: Structure and Maturation
L. Li et al.

Structure of the Immature Dengue Virus at Low pH
I.-M. Yu et al.

Dengue and West Nile viruses mature when the envelope protein precursor is cleaved at low pH, and then the cleavage product dissociates outside the cell, allowing infection.

NEUROSCIENCE
Insect Odorant Receptors Are Molecular Targets of the Insect Repellent DEET
M. Ditzen, M. Pellegrino, L. B. Vosshall
The widely used insect repellent DEET acts by inhibiting olfactory neurons that respond to odors such as those that attract insects to their hosts.

NEUROSCIENCE
Aversive Learning Enhances Perceptual and Cortical Discrimination of Indistinguishable Odor Cues
W. Li, J. D. Howard, T. B. Parrish, J. A. Gottfried
After association of negative stimuli to one of a pair of initially indistinguishable odors, human participants learn to tell the two odors apart and show altered brain representations.

NEUROSCIENCE
Electric Fields Due to Synaptic Currents Sharpen Excitatory Transmission
S. Sylantyev et al.
The electrical field set up by currents within the synaptic cleft can influence diffusion of negatively charged neurotransmitters, such as glutamate, and prolong excitatory events.

NEUROSCIENCE
Rule Learning by Rats
R. A. Murphy, E. Mondragón, V. A. Murphy
Rats can learn the rules governing simple sequences of stimuli and then unexpectedly can generalize these rules to new situations.
SPECIAL SECTION

Gene Regulation

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

EDITORIAL GUIDE: Focus Issue—Mechanisms of Gene Regulation
J. F. Foley
Multilayered mechanisms control various aspects of gene expression.

PERSPECTIVE: Silent Assassin—Oncogenic Ras Directs Epigenetic Inactivation of Target Genes
X. Cheng
Oncogenic Ras directs a program that epigenetically silences genes that inhibit tumorigenesis.

PERSPECTIVE: NFAT Is Well Placed to Direct Both Enhancer Looping and Domain-Wide Models of Enhancer Function
P. N. Cockerill
Inducible intrachromosomal looping between the tumor necrosis factor-α (TNF-α) gene promoter and two NFAT-dependent enhancers activates TNF-α gene expression.

PERSPECTIVE: SRC-3 Transcription-Coupled Activation, Degradation, and the Ubiquitin Clock—Is There Enough Coactivator to Go Around in Cells?
D. M. Lonard and B. W. O’Malley
The critical factor in estrogen-dependent growth of breast cancer cells appears to be the abundance of the coactivator protein SRC-3.