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COVER

Artist's conception of the complex network of relationships between disease and the human genome. Hundreds of diseases and traits (represented by colored dots) have been mapped to specific chromosomal positions in the genome. Most disease-associated genetic variants fall outside of protein-coding genes, instead affecting the genome's regulatory circuitry by modifying the DNA "switches" (some of which are depicted here as gray triangles, many others not shown) that control gene activity. See page 1190.

Image: Rachael Ludwig and John Stamatoyannopoulos

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M. T. Maurano et al.
Genetic variants that have been associated with diseases are concentrated in regulatory regions of the genome.
>> *News story p. 1159; Perspective p. 1179; Science Podcast*

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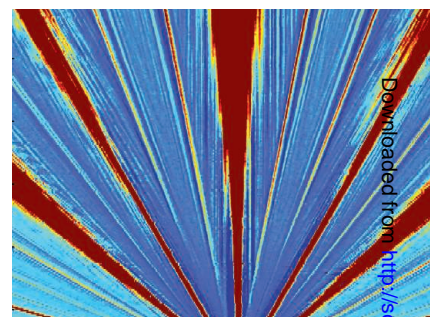
- 1196 **Unconventional Sequence of Fractional Quantum Hall States in Suspended Graphene**
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Duplication of a central protein in mitosis facilitated the evolution of a highly related protein required for meiosis.
- 1225 **The Molecular Mechanism of Thermal Noise in Rod Photoreceptors**
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In rhodopsin, the transition state for thermal activation has the same electronic structure as that for photoexcitation.
- 1228 **Ecological Populations of Bacteria Act as Socially Cohesive Units of Antibiotic Production and Resistance**
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Natural antibiotics enforce competition between, rather than within, bacterial populations.
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D. Singh et al.
A fusion gene detected in a small subset of human brain tumors encodes a potentially druggable target.

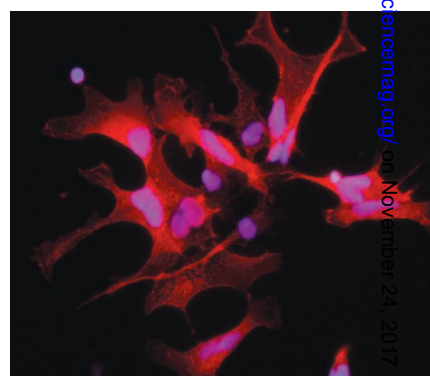
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SCIENCEONLINE

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Systematic Localization of Common Disease-Associated Variation in Regulatory DNA

M. T. Maurano et al.

Genetic variants that have been associated with diseases are concentrated in regulatory regions of the genome.

10.1126/science.1222794

A GPS for Navigating DNA

E. Schadt and R. Chang

10.1126/science.1227739

Evidence of Abundant Purifying Selection in Humans for Recently Acquired Regulatory Functions

L. D. Ward and M. Kellis

Diversity in human-specific regions of the genome has been reduced by functional constraints.

10.1126/science.1225057

>> *News story p. 1159*

Wnt5a Potentiates TGF- β Signaling to Promote Colonic Crypt Regeneration After Tissue Injury

H. Miyoshi et al.

Repair of the intestinal epithelium requires both cell proliferation and replacement of crypt stem cells.

10.1126/science.1223821

Mutations in *BCKD-kinase* Lead to a Potentially Treatable Form of Autism with Epilepsy

G. Novarino et al.

When the balance of branched-chain amino acids transported into the brain goes awry, neurological deficits can ensue.

10.1126/science.1224631

>> *Science Podcast*

Relaxation and Prethermalization in an Isolated Quantum System

M. Gring et al.

Two halves of a split ultracold gas of rubidium atoms retain memory of the initial state for an extended time.

10.1126/science.1224953

TECHNICALCOMMENTS

Comment on "Orthographic Processing in Baboons (*Papio papio*)"

W. Bains

Full text at www.sciencemag.org/cgi/content/full/337/6099/1173-b

Response to Comment on "Orthographic Processing in Baboons (*Papio papio*)"

J. Grainger et al.

Full text at www.sciencemag.org/cgi/content/full/337/6099/1173-c

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Highlights From Our Daily News Coverage

Microbe-Free Beaches, Thanks to Dogs

Canine patrols can cut down on harmful bacteria from seagull poop.

<http://scim.ag/Harmful-Bacteria>

Drinking Too Much? Blame Your Glass

A new study finds that the shape of beer glasses affects how fast we drink.

<http://scim.ag/Beer-Glasses>

Genome Brings Ancient Girl to Life

A Denisovan child sheds light on the evolution of humans and Neandertals.

http://scim.ag/Ancient_Girl

SCIENCE SIGNALING

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The Signal Transduction Knowledge Environment

4 September issue: <http://scim.ag/ss090412>

RESEARCH ARTICLE: FAM123A Binds to Microtubules and Inhibits the Guanine Nucleotide Exchange Factor ARHGEF2 to Decrease Actomyosin Contractility

P. F. Siesser et al.

Unlike related proteins, FAM123A interacts with microtubule-associated proteins and alters microtubule dynamics.

RESEARCH ARTICLE: Guanylyl Cyclases A and B Are Asymmetric Dimers That Are Allosterically Regulated by ATP Binding to the Catalytic Domain

J. W. Robinson and L. R. Potter

PERSPECTIVE: Allosteric Regulation of Nucleotidyl Cyclases—An Emerging Pharmacological Target

R. Seifert and K. Y. Beste

An ATP-binding allosteric site could be pharmacologically targeted to alter the activity of membrane guanylyl cyclases.

SCIENCE TRANSLATIONAL MEDICINE

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Integrating Medicine and Science

5 September issue: <http://scim.ag/stm090512>

RESEARCH ARTICLE: Structural Basis for Benzothiazinone-Mediated Killing of *Mycobacterium tuberculosis*

J. Neres et al.

FOCUS: Bridging the Gap Between a TB Drug and Its Target

G. M. Cook and A. Heikal

The crystal structure of the mycobacterial DprE1 reveals how the TB drug benzothiazinone BTZ043 blocks this microbial enzyme target.

RESEARCH ARTICLE: Disruption of the Sleep-Wake Cycle and Diurnal Fluctuation of Amyloid- β in Mice with Alzheimer's Disease Pathology

J. H. Roh et al.

FOCUS: The Nexus of A β , Aging, and Sleep

J. R. Gerstner et al.

Decreased sleep and attenuation of circadian fluctuations in A β reflect amyloid-associated pathology in Alzheimer's disease.

RESEARCH ARTICLE: An Intravaginal Ring That Releases the NNRTI MIV-150 Reduces SHIV Transmission in Macaques

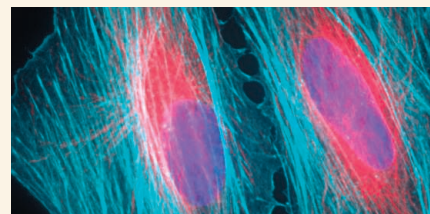
R. Singer et al.

An intravaginal ring loaded with the NNRTI MIV-150 prevents transmission of the HIV/SIV chimera SHIV-R1 in macaques.

FOCUS: Regulatory Science Innovation—A Rate-Limiting Step in Translation

N. S. Sung and J. Burris

Sustained funding for academic regulatory science will drive innovation and implementation, forge a viable career path, and build an educated workforce.



SCIENCE SIGNALING

The actomyosin cytoskeleton.

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J. A. Hobin et al.

Introducing myIDP, the first comprehensive, online tool to help you choose and pursue a science career.

<http://scim.ag/myIDPGamePlan>

>> *Editorial p. 1149*

Taken for Granted: Rethinking the Ph.D.

B. L. Benderly

Overlong and insufficiently focused on available careers, traditional Ph.D. programs clearly need reform: What changes make sense?

http://scim.ag/TGF_Rethinking

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Free Weekly Show

On the 7 September *Science* Podcast: disease and regulatory DNA, treatable autism, reverse brain drain, and more.

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