### Commentary and Review

**Perspective**

Raising the estimate of functional human sequences  
Michael Pheasant and John S. Mattick

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### Research

**Articles**

Reconstruction of the vertebrate ancestral genome reveals dynamic genome reorganization in early vertebrates  
Yoichiro Nakatani, Hiroyuki Takeda, Yuji Kohara, and Shinichi Morishita

Gene copy number variation spanning 60 million years of human and primate evolution  
Laura Dumas, Young H. Kim, Anis Karimpour-Fard, Michael Cox, Janet Hopkins, Jonathan R. Pollack, and James M. Sikela

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### Letters

Human gene organization driven by the coordination of replication and transcription  
Maxime Huvet, Samuel Nicolay, Marie Touchon, Benjamin Audit, Yves d’Aubenton-Carafa, Alain Arneodo, and Claude Thermes

Domain-wide regulation of gene expression in the human genome  
Hinco J. Gierman, Mireille H.G. Indemans, Jan Koster, Sandra Goetze, Jurgen Seppen, Dirk Geerts, Roel van Driel, and Rogier Versteeg

Architectures of somatic genomic rearrangement in human cancer amplicons at sequence-level resolution  

A multidimensional analysis of genes mutated in breast and colorectal cancers  
Jimmy Lin, Christine M. Gan, Xiaosong Zhang, Siân Jones, Tobias Sjöblom, Laura D. Wood, D. Williams Parsons, Nickolas Papadopoulos, Kenneth W. Kinzler, Bert Vogelstein, Giovanni Parmigiani, and Victor E. Velculescu

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(continued)
Functional conservation of Rel binding sites in drosophilid genomes  
Richard R. Copley, Maxim Totrov, Jane Linnell, Simon Field, 
Jiannis Ragoussis, and Irina A. Udalova

Genes under positive selection in *Escherichia coli*  
Lise Petersen, Jonathan P. Bollback, Matt Dimmic, Melissa Hubisz, 
and Rasmus Nielsen

Analysis of the VSG gene silent archive in *Trypanosoma brucei* reveals 
that mosaic gene expression is prominent in antigenic variation 
and is favored by archive substructure  
Lucio Marcello and J. David Barry

Unique genes in giant viruses: Regular substitution pattern 
and anomalously short size  
Hiroyuki Ogata and Jean-Michel Claverie

**Methods and Resources**

Whole proteome analysis of post-translational modifications:  
Applications of mass-spectrometry for proteogenomic annotation  
Nitin Gupta, Stephen Tanner, Navdeep Jaitly, Joshua N. Adkins, 
Mary Lipton, Robert Edwards, Margaret Romine, Andrei Osterman, 
Vineet Bafna, Richard D. Smith, and Pavel A. Pevzner

Quantification of the synaptosomal proteome of the rat 
cerebellum during post-natal development  
Daniel B. McClatchy, Lujian Liao, Sung Kyu Park, John D. Venable, 
and John R. Yates

Conrad: Gene prediction using conditional random fields  
David DeCaprio, Jade P. Vinson, Matthew D. Pearson, 
Philip Montgomery, Matthew Doherty, and James E. Galagan

**Cover**  
Regulation of gene expression by chromosomal domains. An artist impression of 
a cell nucleus with human chromosomes (blue DNA helices) illustrating how chromosomal 
domains modulate the expression of genes. Green viruses depict green fluorescent protein 
(GFP) gene introduction by lentivirus into human chromosomes. The virus in the fore-
ground represents a poorly expressed GFP gene within an inactive domain (anti-ridge), 
whereas the bright fluorescent light emitted from the virus in the background (center left) 
represents the up-regulation of GFP expression via a GFP gene embedded in an active 
domain (ridge). (Cover illustration by Esteban Aravena and Hinco J. Gierman. [For details, 
see Gierman et al., pp. 1286–1295.])

**OA**Open Access paper.