

	Commentary and Review	
<i>Commentary</i>	2× genomes—Does depth matter? Phil Green	1547 ^{OA}
	Research	
<i>Articles</i>	A comprehensive ChIP–chip analysis of E2F1, E2F4, and E2F6 in normal and tumor cells reveals interchangeable roles of E2F family members Xiaoqin Xu, Mark Bieda, Victor X. Jin, Alina Rabinovich, Mathew J. Oberley, Roland Green, and Peggy J. Farnham	1550
	Breed relationships facilitate fine-mapping studies: A 7.8-kb deletion cosegregates with Collie eye anomaly across multiple dog breeds Heidi G. Parker, Anna V. Kukekova, Dayna T. Akey, Orly Goldstein, Ewen F. Kirkness, Kathleen C. Baysac, Dana S. Mosher, Gustavo D. Aguirre, Gregory M. Acland, and Elaine A. Ostrander	1562
	Reductive evolution of architectural repertoires in proteomes and the birth of the tripartite world Minglei Wang, Liudmila S. Yafremava, Derek Caetano-Anollés, Jay E. Mittenthal, and Gustavo Caetano-Anollés	1572
<i>Letters</i>	Altered adenosine-to-inosine RNA editing in human cancer Nurit Paz, Erez Y. Levanon, Ninette Amariglio, Amy B. Heimberger, Zvi Ram, Shlomi Constantini, Zohar S. Barbash, Konstantin Adamsky, Michal Safran, Avi Hirschberg, Meir Krupsky, Issachar Ben-Dov, Simona Cazacu, Tom Mikkelsen, Chaya Brodie, Eli Eisenberg, and Gideon Rechavi	1586
	Information capture using SNPs from HapMap and whole-genome chips differs in a sample of inflammatory and cardiovascular gene-centric regions from genome-wide estimates Chris Wallace, Richard J. Dobson, Patricia B. Munroe, and Mark J. Caulfield	1596
	Comparative analysis of chicken chromosome 28 provides new clues to the evolutionary fragility of gene-rich vertebrate regions Laurie Gordon, Shan Yang, Mary Tran-Gyamfi, Dan Baggott, Mari Christensen, Aaron Hamilton, Richard Crooijmans, Martien Groenen, Susan Lucas, Ivan Ovcharenko, and Lisa Stubbs	1603
	An <i>Arabidopsis</i> gene network based on the graphical Gaussian model Shisong Ma, Qingqiu Gong, and Hans J. Bohnert	1614
	Systematic condition-dependent annotation of metabolic genes Tomer Shlomi, Markus Herrgard, Vasily Portnoy, Efrat Naim, Bernhard Ø. Palsson, Roded Sharan, and Eytan Ruppin	1626
	Functional and evolutionary implications of enhanced genomic analysis of rhomboid intramembrane proteases Marius K. Lemberg and Matthew Freeman	1634

(continued)

The rise and spread of a new pathogen: Seroresistant *Moraxella catarrhalis* 1647
Thierry Wirth, Giovanna Morelli, Barica Kusecek, Alex van Belkum, Cindy van der Schee, Axel Meyer, and Mark Achtman

Lateral gene transfer between obligate intracellular bacteria: Evidence from the *Rickettsia massiliae* genome 1657
Guillaume Blanc, Hiroyuki Ogata, Catherine Robert, Stéphane Audic, Jean-Michel Claverie, and Didier Raoult

Methods and Resources

Methods PennCNV: An integrated hidden Markov model designed for high-resolution copy number variation detection in whole-genome SNP genotyping data 1665

Kai Wang, Mingyao Li, Dexter Hadley, Rui Liu, Joseph Glessner, Struan F.A. Grant, Hakon Hakonarson, and Maja Bucan

Resources Initial sequence and comparative analysis of the cat genome 1675

Joan U. Pontius, James C. Mullikin, Douglas R. Smith, Agencourt Sequencing Team, Kerstin Lindblad-Toh, Sante Gnerre, Michele Clamp, Jean Chang, Robert Stephens, Beena Neelam, Natalia Volfovsky, Alejandro A. Schäffer, Richa Agarwala, Kristina Narfström, William J. Murphy, Urs Giger, Alfred L. Roca, Agostinho Antunes, Marilyn Menotti-Raymond, Naoya Yuhki, Jill Pecon-Slattey, Warren E. Johnson, Guillaume Bourque, Glenn Tesler, NISC Comparative Sequencing Program, and Stephen J. O'Brien

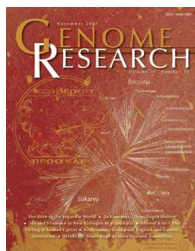
Islands of euchromatin-like sequence and expressed polymorphic sequences within the short arm of human chromosome 21 1690

Robert Lyle, Paola Prandini, Kazutoyo Osoegawa, Boudewijn ten Hallers, Sean Humphray, Baoli Zhu, Eduardo Eyra, Robert Castelo, Christine P. Bird, Sarantos Gagos, Carol Scott, Antony Cox, Samuel Deutsch, Catherine Ucla, Marc Cruts, Sophie Dahoun, Xinwei She, Frederique Bena, Sheng-Yue Wang, Christine Van Broeckhoven, Evan E. Eichler, Roderic Guigo, Jane Rogers, Pieter J. de Jong, Alexandre Reymond, and Stylianos E. Antonarakis

SHARCGS, a fast and highly accurate short-read assembly algorithm for de novo genomic sequencing 1697

Juliane C. Dohm, Claudio Lottaz, Tatiana Borodina, and Heinz Himmelbauer

^{OA}Open Access paper.



Cover Taming of Cerberus and the origins of the diversified world. A detailed phylogenomics analysis of the structure of protein architectures in proteomes reveals reductive tendencies in Archaea that are suggestive of the very early diversification of this lineage and establishes that the universal common ancestor of all life was architecturally complex and already harbored numerous biological functions. The study uncovers deep phylogenetic signals in the structure of proteins that root the Universal Tree of Life in Archaea. The image shows a universal phylogenomic tree chiseled on a fresco with proteomes grouping organisms into the three superkingdoms of life, Archaea, Bacteria, and Eukarya. The fresco captures the allegory of the monstrous three-headed Cerberus that guarded the gates to the underworld and its capture by Heracles in the last of his twelve labors. The symbolism embedded in the allegory conveys the discovery of the origins of a three-headed world that is reported in this issue. (Cover illustration by Derek Caetano-Anollés. [For details, see Wang et al., pp. 1572–1585.])