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Research

Unique mutation portraits and frequent *COL2A1* gene alteration in chondrosarcoma 1411
Yasushi Totoki, Akihiko Yoshida, Fumie Hosoda, Hiromi Nakamura, Natsuko Hama, Koichi Ogura, Aki Yoshida, Tomohiro Fujiwara, Yasuhito Arai, Junya Toguchida, Hitoshi Tsuda, Satoru Miyano, Akira Kawai, and Tatsuhiro Shibata

Reconfiguration of nucleosome-depleted regions at distal regulatory elements accompanies DNA methylation of enhancers and insulators in cancer 1421$^{\mathrm{OA}}$
Phillippa C. Taberlay, Aaron L. Statham, Theresa K. Kelly, Susan J. Clark, and Peter A. Jones

Interactive transcriptome analysis of malaria patients and infecting *Plasmodium falciparum* 1433
Junya Yamagishi, Anna Natori, Mohammed E.M. Tolba, Arthur E. Mongan, Chihiro Sugimoto, Toshiaki Katayama, Shuichi Kawashima, Wojciech Makalowski, Ryuichiro Maeda, Yuki Eshita, Josef Tuda, and Yutaka Suzuki

Error-prone polymerase activity causes multinucleotide mutations in humans 1445
Kelley Harris and Rasmus Nielsen

Novel H3K4me3 marks are enriched at human- and chimpanzee-specific cytogenetic structures 1455
Giuliana Giannuzzi, Eugenia Migliavacca, and Alexandre Reymond

Noncoding origins of anthropoid traits and a new null model of transposon functionalization 1469$^{\mathrm{OA}}$
Ricardo C.H. del Rosario, Nirmala Arul Rayan, and Shyam Prabhakar

Extreme expansion of the olfactory receptor gene repertoire in African elephants and evolutionary dynamics of orthologous gene groups in 13 placental mammals 1485
Yoshihito Niimura, Atsushi Matsui, and Kazushige Touhara

Gene length and expression level shape genomic novelties 1497
Vladislav Grishkevich and Itai Yanai

Microbiota modulate transcription in the intestinal epithelium without remodeling the accessible chromatin landscape 1504
J. Gray Camp, Christopher L. Frank, Colin R. Lickwar, Harendra Guturu, Tomas Rube, Aaron M. Wenger, Jenny Chen, Gill Bejerano, Gregory E. Crawford, and John F. Rawls

Methane yield phenotypes linked to differential gene expression in the sheep rumen microbiome 1517
Weibing Shi, Christina D. Moon, Sinead C. Leahy, Dongwan Kang, Jeff Froula, Sandra Kittelmann, Christina Fan, Samuel Deutsch, Dragana Gagic, Henning Seedorf, William J. Kelly, Renee Atua, Carrie Sang, Priya Soni, Dong Li, Cesar S. Pinares-Patiño, John C. McEwan, Peter H. Janssen, Feng Chen, Axel Visel, Zhong Wang, Graeme T. Attwood, and Edward M. Rubin

(continued)

Methods

Seamless gene correction of β-thalassemia mutations in patient-specific iPSCs using CRISPR/Cas9 and *piggyBac* 1526
Fei Xie, Lin Ye, Judy C. Chang, Ashley I. Beyer, Jiaming Wang, Marcus O. Muench, and Yuet Wai Kan

High resolution mapping of modified DNA nucleobases using excision repair enzymes 1534^OA
D. Suzi Bryan, Monica Ransom, Biniam Adane, Kerri York, and Jay R. Hesselberth

Selective enrichment of damaged DNA molecules for ancient genome sequencing 1543
Marie-Theres Gansauge and Matthias Meyer

MultiBLUP: improved SNP-based prediction for complex traits 1550^OA
Doug Speed and David J. Balding

^OA Open Access paper

Cover An artistic depiction of the complex interactions occurring between bacteria and host cells at the intestinal epithelium interface, highlighting the mechanics of host transcriptional regulation by RNA polymerases, DNA-binding transcription factors, and nucleosome occupancy. The intestinal epithelium is the primary interface between animal hosts and their microbiota, and it encounters dynamic environmental stimuli along the length of the gut. In this issue, the mechanisms by which microbiota regulate intestinal gene expression are explored by profiling the accessible chromatin and transcriptome landscapes in the ileal and colonic epithelia of mice living in the presence or total absence of microbiota. On the *left* is a small intestinal (*top*) and colonic (*bottom*) epithelium lacking microbiota (yellow); on the *right* is epithelium colonized with microbiota (brown). Comparison between these microbiota-free and colonized states suggests that the chromatin landscape in intestinal epithelial cells is preprogrammed by the host in a region-specific manner and is poised to permit transcriptional responses to microbiota through the binding of accessible regulatory elements by specific transcription factors. (Cover illustration by Barbara Treutlein, Max Planck Institute for Evolutionary Anthropology. [For details, see Camp et al., pp. 1504–1516.])