

Leading Edge

Cell Volume 147 Number 1, September 30, 2011

IN THIS ISSUE

SELECT

- 5 Cancer's Epigenome

VOICES

- 9 Human Genome: What's Been Most Surprising?

ANALYSIS

- 11 Genomics in Africa:
Avoiding Past Pitfalls *M. Kaplan*

COMMENTARIES

- 14 Genomics Reaches the Clinic:
From Basic Discoveries to Clinical Impact *T.A. Manolio and E.D. Green*
- 17 Genetics and Genomics to the Clinic:
A Long Road ahead *D. Ginsburg*

PREVIEWS

- 20 Translocation Mapping Exposes
the Risky Lifestyle of B Cells *R.P. McCord and J. Dekker*
- 22 Splicing up Pluripotency *B.R. Graveley*
- 24 Unweaving the Autism Spectrum *C. Lord*

ESSAY

- 26 A Blueprint for Advancing
Genetics-Based Cancer Therapy *W.R. Sellers*

PERSPECTIVES

- 32 Clan Genomics and the Complex
Architecture of Human Disease *J.R. Lupski, J.W. Belmont, E. Boerwinkle,
and R.A. Gibbs*
- 44 Metagenomics and Personalized Medicine *H.W. Virgin and J.A. Todd*

(continued)

PRIMER

- 57 Mapping Rare and Common Causal Alleles
for Complex Human Diseases *S. Raychaudhuri*

REVIEW

- 70 Modeling Human Disease
in Humans: The Ciliopathies *G. Novarino, N. Akizu, and J.G. Gleeson*

SNAPSHOT

- 248 Human Biomedical Genomics *E.E. Kenny and C.D. Bustamante*

Articles

Cell Volume 147 Number 1, September 30, 2011

- 81 The *Lin28/let-7* Axis Regulates Glucose Metabolism
H. Zhu, N. Shyh-Chang, A.V. Segrè, G. Shinoda, S.P. Shah,
W.S. Einhorn, A. Takeuchi, J.M. Engreitz, J.P. Hagan,
M.G. Kharas, A. Urbach, J.E. Thornton, R. Triboulet,
R.I. Gregory, DIAGRAM Consortium, MAGIC Investigators,
D. Altshuler, and G.Q. Daley
- 95 Translocation-Capture Sequencing Reveals the Extent and Nature of Chromosomal Rearrangements in B Lymphocytes
I.A. Klein, W. Resch, M. Jankovic, T. Oliveira, A. Yamane,
H. Nakahashi, M. Di Virgilio, A. Bothmer, A. Nussenzweig,
D.F. Robbiani, R. Casellas, and M.C. Nussenzweig
- 107 Genome-wide Translocation Sequencing Reveals Mechanisms of Chromosome Breaks and Rearrangements in B Cells
R. Chiarle, Y. Zhang, R.L. Frock, S.M. Lewis, B. Molinie,
Y.-J. Ho, D.R. Myers, V.W. Choi, M. Compagno,
D.J. Malkin, D. Neuberg, S. Monti, C.C. Giallourakis,
M. Gostissa, and F.W. Alt
- 120 A DNA Repair Complex Functions as an Oct4/Sox2 Coactivator in Embryonic Stem Cells
Y.W. Fong, C. Inouye, T. Yamaguchi, C. Cattoglio,
I. Grubisic, and R. Tjian
- 132 An Alternative Splicing Switch Regulates Embryonic Stem Cell Pluripotency and Reprogramming
M. Gabut, P. Samavarchi-Tehrani, X. Wang,
V. Slobodeniuc, D. O'Hanlon, H.-K. Sung, M. Alvarez,
S. Talukder, Q. Pan, E.O. Mazzoni, S. Nedelec,
H. Wichterle, K. Wolfjen, T.R. Hughes, P.W. Zandstra,
A. Nagy, J.L. Wrana, and B.J. Blencowe
- 147 Selective Translation of Leaderless mRNAs by Specialized Ribosomes Generated by MazF in *Escherichia coli*
O. Vesper, S. Amitai, M. Belitsky, K. Byrgazov,
A.C. Kaberdina, H. Engelberg-Kulka, and I. Moll
- 158 Regulatory Control of the Resolution of DNA Recombination Intermediates during Meiosis and Mitosis
J. Matos, M.G. Blanco, S. Maslen, J.M. Skehel,
and S.C. West
- 173 Saturated Fatty Acids Induce c-Src Clustering within Membrane Subdomains, Leading to JNK Activation
R.G. Holzer, E.-J. Park, N. Li, H. Tran, M. Chen, C. Choi,
G. Solinas, and M. Karin
- 185 Conformation-Sensing Antibodies Stabilize the Oxidized Form of PTP1B and Inhibit Its Phosphatase Activity
A. Haque, J.N. Andersen, A. Salmeen, D. Barford,
and N.K. Tonks
- 199 Crystal Structure of the Mammalian GIRK2 K⁺ Channel and Gating Regulation by G Proteins, PIP₂, and Sodium
M.R. Whorton and R. MacKinnon

(continued)

- 209 A Pseudoatomic Model of the Dynamin Polymer Identifies a Hydrolysis-Dependent Powerstroke
J.S. Chappie, J.A. Mears, S. Fang, M. Leonard,
S.L. Schmid, R.A. Milligan, J.E. Hinshaw, and F. Dyda
- 223 Beclin1 Controls the Levels of p53 by Regulating the Deubiquitination Activity of USP10 and USP13
J. Liu, H. Xia, M. Kim, L. Xu, Y. Li, L. Zhang, Y. Cai,
H.V. Norberg, T. Zhang, T. Furuya, M. Jin, Z. Zhu, H. Wang,
J. Yu, Y. Li, Y. Hao, A. Choi, H. Ke, D. Ma, and J. Yuan
- 235 Absence of CNTNAP2 Leads to Epilepsy, Neuronal Migration Abnormalities, and Core Autism-Related Deficits
O. Peñagarikano, B.S. Abrahams, E.I. Herman,
K.D. Winden, A. Gdalyahu, H. Dong, L.I. Sonnenblick,
R. Gruver, J. Almajano, A. Bragin, P. Golshani,
J.T. Trachtenberg, E. Peles, and D.H. Geschwind

CORRECTION

- 247 AKT/FOXO Signaling Enforces Reversible Differentiation Blockade in Myeloid Leukemias
S.M. Sykes, S.W. Lane, L. Bullinger, D. Kalaitzidis, R. Yusuf,
B. Saez, F. Ferraro, F. Mercier, H. Singh, K.M. Brumme,
S.S. Acharya, C. Scholl, Z. Tothova, E.C. Attar, S. Fröhling,
R.A. DePinho, D.G. Gilliland, S.A. Armstrong,
and D.T. Scadden

ANNOUNCEMENTS

POSITIONS AVAILABLE

On the cover: Chromosomal rearrangements disrupt the integrity of the genome and are involved in producing leukemias and lymphomas. Klein et al. (pp. 95–106) implement translocation capture sequencing (TC-Seq) to document genome-wide chromosomal rearrangements in primary B cells. Their results reveal that double-strand break location, transcriptional activity, chromosome territories, and activation-induced cytidine deaminase (AID) activity influence the extent of genome rearrangement and favor recurrent oncogenic translocations. The cover image depicts AID as a spider and a TC-Seq-generated translocation map to the immunoglobulin heavy-chain locus as its web. The cover was designed by Rafael Casellas and Ethan Tyler.

