

Contents of Volume 64

January 1999

i This Month in the *Journal*

John Ashkenas

1998 ASHG Presidential Address

1 Making Genomic Medicine a Reality

Arthur L. Beaudet

1998 ASHG Award for Excellence in Education

14 Professor Ching Chun Li, Courageous Scholar and Educator

Aravinda Chakravarti

16 Remarks on Receiving the ASHG Award: Science and Science Education

C. C. Li

Molecular Evolution '99

18 When Less Is More: Gene Loss as an Engine of Evolutionary Change

Maynard V. Olson

24 Concerted Evolution: Molecular Mechanism and Biological Implications

Daiqing Liao

31 The Genomic Record of Humankind's Evolutionary Roots

Morris Goodman

Insights from Model Systems

40 Mice and the Role of Unequal Recombination in Gene-Family Evolution

John C. Schimenti

Invited Editorial

46 Multiple ATM-Dependent Pathways: An Explanation for Pleiotropy

Kevin D. Brown, Carolee Barlow, and Anthony Wynshaw-Boris

Original Articles

51 Structure of the Gene for Congenital Nephrotic Syndrome of the Finnish Type (NPHS1) and Characterization of Mutations

Ulla Lenkkeri, Minna Männikkö, Paula McCready, Jane Lamerdin, Olivier Gribouval, Patrick Niaudet, Corinne Antignac, Clifford E. Kashtan, Christer Holmberg, Anne Olsen, Marjo Kestilä, and Karl Tryggvason

62 LINE-1 Elements at the Sites of Molecular Rearrangements in Alport Syndrome–Diffuse Leiomyomatosis

Yoav Segal, Bernard Peissel, Alessandra Renieri, Mario de Marchi, Andrea Ballabio, York Pei, and Jing Zhou

- 70 Prader-Willi Syndrome Is Caused by Disruption of the SNRPN Gene**
C. D. Kuslich, J. A. Kobori, G. Mohapatra, C. Gregorio-King, and T. A. Donlon
- 77 Spectrum of Mutations in α -Mannosidosis**
Thomas Berg, Hilde Monica Frostad Riise, Gaute Martin Hansen, Dag Malm, Lisbeth Tranebjærg, Ole Kristian Tollersrud, and Øivind Nilssen
- 89 Recurrence of the T666M Calcium Channel CACNA1A Gene Mutation in Familial Hemiplegic Migraine with Progressive Cerebellar Ataxia**
A. Ducros, C. Denier, A. Joutel, K. Vahedi, A. Michel, F. Darcel, M. Madigand, D. Guerouaou, F. Tison, J. Julien, E. Hirsch, F. Chedru, C. Bisgård, G. Lucotte, P. Després, C. Billard, M. A. Barthez, G. Ponsot, M. G. Bousser, and E. Tournier-Lasserre
- 99 Peroxisomal Bifunctional Protein Deficiency Revisited: Resolution of Its True Enzymatic and Molecular Basis**
E. G. van Grunsven, E. van Berkel, P. A. W. Mooijer, P. A. Watkins, H. W. Moser, Y. Suzuki, L. L. Jiang, T. Hashimoto, G. Hoefler, J. Adamski, and R. J. A. Wanders
- 108 Rh_{mod} Syndrome: A Family Study of the Translation-Initiator Mutation in the Rh50 Glycoprotein Gene**
C.-H. Huang, G.-J. Cheng, M. E. Reid, and Y. Chen
- 118 Williams Syndrome: Use of Chromosomal Microdeletions as a Tool to Dissect Cognitive and Physical Phenotypes**
Mayada Tassabehji, Kay Metcalfe, Annette Karmiloff-Smith, Martin J. Carette, Julia Grant, Nick Dennis, W. Reardon, Miranda Splitt, Andrew P. Read, and Dian Donnai
- 126 Assignment of the Muscle-Eye-Brain Disease Gene to 1p32-p34 by Linkage Analysis and Homozygosity Mapping**
Bru Cormand, Kristiina Avela, Helena Pihko, Pirkko Santavuori, Beril Talim, Haluk Topaloglu, Albert de la Chapelle, and Anna-Elina Lehesjoki
- 136 Refinement of the Chromosome 5p Locus for Familial Calcium Pyrophosphate Dihydrate Deposition Disease**
L. J. Andrew, V. Brancolini, L. Serrano de la Pena, M. Devoto, F. Caeiro, R. Marchegiani, A. Reginato, A. Gaucher, P. Netter, P. Gillet, D. Loeuille, D. J. Prockop, A. Carr, B. F. Wordsworth, M. Lathrop, S. Butcher, E. Considine, K. Everts, A. Nicod, S. Walsh, and C. J. Williams
- 146 A Quantitative-Trait Locus on Chromosome 6p Influences Different Aspects of Developmental Dyslexia**
Simon E. Fisher, Angela J. Marlow, Janine Lamb, Elena Maestrini, Dianne F. Williams, Alex J. Richardson, Daniel E. Weeks, John F. Stein, and Anthony P. Monaco
- 157 Quantitative-Trait Locus for Specific Language and Reading Deficits on Chromosome 6p**
Javier Gayán, Shelley D. Smith, Stacey S. Cherny, Lon R. Cardon, David W. Fulker, Amy M. Brower, Richard K. Olson, Bruce F. Pennington, and John C. DeFries
- 165 Localization of a Gene for Familial Hemophagocytic Lymphohistiocytosis at Chromosome 9q21.3-22 by Homozygosity Mapping**
Mina Ohadi, Michel R. A. Lalloz, Pak Sham, Jinghua Zhao, Andrew M. Dearlove, Caroline Shiach, Sally Kinsey, Michael Rhodes, and D. Mark Layton
- 172 Linkage of Familial Hemophagocytic Lymphohistiocytosis to 10q21-22 and Evidence for Heterogeneity**
Rémi Dufourcq-Lagelouse, Nada Jabado, Françoise Le Deist, Jean-Louis Stéphan, Gérard Souillet, Marrie Bruin, Etienne Vilmer, Marion Schneider, Gritta Janka, Alain Fischer, and Geneviève de Saint Basile
- 180 Hereditary Isolated Renal Magnesium Loss Maps to Chromosome 11q23**
Iwan C. Meij, Kathrin Saar, Lambert P. W. J. van den Heuvel, Gudrun Nuernberg, Martin Vollmer, Friedhelm Hildebrandt, André Reis, Leo A. H. Monnens, and Nine V. A. M. Knoers

- 189 Localization of Familial Benign Hypercalcemia, Oklahoma Variant (FBH_{Ok}), to Chromosome 19q13**
Sarah E. Lloyd, Anna A. J. Pannett, Peter H. Dixon, Michael P. Whyte, and Rajesh V. Thakker
- 196 Genome Scan for Human Obesity and Linkage to Markers in 20q13**
Joseph H. Lee, Danielle R. Reed, Wei-Dong Li, Weizhen Xu, Eun-Jeong Joo, Robin L. Kilker, Elizabeth Nanthakumar, Michael North, Hakan Sakul, Callum Bell, and R. Arlen Price
- 210 A Comprehensive Linkage Analysis of Chromosome 21q22 Supports Prior Evidence for a Putative Bipolar Affective Disorder Locus**
Vincent M. Aita, Jianjun Liu, James A. Knowles, Joseph D. Terwilliger, Romulo Baltazar, Adina Grunn, Jo Ellen Loth, Kyra Kanyas, Bernard Lerer, Jean Endicott, Zhenyuan Wang, Graciela Penchaszadeh, T. Conrad Gilliam, and Miron Baron
- 218 Rapid Clearance of Fetal DNA from Maternal Plasma**
Y. M. Dennis Lo, Jun Zhang, Tse N. Leung, Tze K. Lau, Allan M. Z. Chang, and N. Magnus Hjelm
- 225 Inbreeding Effects on Fertility in Humans: Evidence for Reproductive Compensation**
Carole Ober, Terry Hyslop, and Walter W. Hauck
- 232 The Emerging Tree of West Eurasian mtDNAs: A Synthesis of Control-Region Sequences and RFLPs**
Vincent Macaulay, Martin Richards, Eileen Hickey, Emilce Vega, Fulvio Cruciani, Valentina Guida, Rosaria Scozzari, Batsheva Bonn -Tamir, Bryan Sykes, and Antonio Torroni
- 250 Molecular Genetic Analysis of Remains of a 2,000-Year-Old Human Population in China—and Its Relevance for the Origin of the Modern Japanese Population**
Hiroki Oota, Naruya Saitou, Takayuki Matsushita, and Shintaroh Ueda
- 259 Combined Linkage and Association Sib-Pair Analysis for Quantitative Traits**
D. W. Fulker, S. S. Cherny, P. C. Sham, and J. K. Hewitt
- 268 A Simulation Study of the Effects of Assignment of Prior Identity-by-Descent Probabilities to Unselected Sib Pairs, in Covariance-Structure Modeling of a Quantitative-Trait Locus**
Conor V. Dolan, Dorret I. Boomsma, and Michael C. Neale
- 281 Further Evidence for the Increased Power of LOD Scores Compared with Nonparametric Methods**
Martina Durner, Veronica J. Vieland, and David A. Greenberg
- Letters to the Editor**
- 290 The Glu318Gly Substitution in Presenilin 1 Is Not Causally Related to Alzheimer Disease**
Bart Dermaut, Marc Cruts, Arjen J. C. Slooter, Sofie Van Gestel, Chris De Jonghe, Hugo Vanderstichele, Eugene Vanmechelen, Monique M. Breteler, Albert Hofman, Cornelia M. van Duijn, and Christine Van Broeckhoven
- 292 p53 Variants Predisposing to Cancer Are Present in Healthy Centenarians**
Massimiliano Bonaf , Fabiola Olivieri, Daniela Mari, Giovannella Baggio, Rosario Mattace, Paolo Sansoni, Giovanna De Benedictis, Maria De Luca, Stefano Bertolini, Cristiana Barbi, Daniela Monti, and Claudio Franceschi
- 295 Maternally Inherited Cardiomyopathy: An Atypical Presentation of the mtDNA 12S rRNA Gene A1555G Mutation**
Filippo M. Santorelli, Kurenai Tanji, Panagiota Manta, Carlo Casali, Sindu Krishna, Arthur P. Hays, Donna M. Mancini, Salvatore DiMauro, and Michio Hirano
- 300 An *Alu*-Mediated 6-kb Duplication in the *BRCA1* Gene: A New Founder Mutation?**
Nadine Puget, Olga M. Sinilnikova, Dominique Stoppa-Lyonnet, Carole Audouy, Sabine Pag s, Henry T. Lynch, David Goldgar, Gilbert M. Lenoir, and Sylvie Mazoyer

- 303 Cystic Fibrosis Mutations in Heterozygous Newborns with Hypertrypsinemia and Low Sweat Chloride**
C. Castellani, M. G. Benetazzo, A. Bonizzato, P. F. Pignatti, and G. Mastella
- 304 A Loss-of-Function Mutation in the Endothelin-Converting Enzyme 1 (ECE-1) Associated with Hirschsprung Disease, Cardiac Defects, and Autonomic Dysfunction**
Robert M. W. Hofstra, Olivier Valdenaire, Ellen Arch, Jan Osinga, Hester Kroes, Bernd-Michael Löffler, Ada Hamosh, Carel Meijers, and Charles H. C. M. Buys
- 308 Variant Manifestation of Cowden Disease in Japan: Hamartomatous Polyposis of the Digestive Tract with Mutation of the *PTEN* Gene**
Keisuke Kurose, Tsutomu Araki, Tsuyoshi Matsunaka, Yasuharu Takada, and Mitsuru Emi
- 310 Failure to Detect Linkage of Preeclampsia to the Region of the *NOS3* Locus on Chromosome 7q**
Ian Lewis, Guus Lachmeijer, Sarah Downing, Gustaaf Dekker, Clive Glazebrook, David Clayton, Nick H. Morris, and Kevin M. O'Shaughnessy
- 313 Exclusion of Chromosome 7 for Kartagener Syndrome but Suggestion of Linkage in Families with Other Forms of Primary Ciliary Dyskinesia**
Michal Witt, Yue-fen Wang, Shengbiao Wang, Cui-e Sun, Jacek Pawlik, Ewa Rutkiewicz, Jerzy Zebrak, and Scott R. Diehl
- 318 A New Locus for Nonsyndromic Hereditary Hearing Impairment, *DFNA17*, Maps to Chromosome 22 and Represents a Gene for Cochleosaccular Degeneration**
Anil K. Lalwani, William M. Luxford, Anand N. Mhatre, Ali Attaie, Edward R. Wilcox, and Caley M. Castelein
- 323 Two Novel Single-Base-Pair Substitutions Adjacent to the CAG Repeat in the Huntington Disease Gene (*IT15*): Implications for Diagnostic Testing**
Russell L. Margolis, O. Colin Stine, Colleen Callahan, Adam Rosenblatt, Margaret H. Abbott, Meeia Sherr, and Christopher A. Ross
- 326 The Interpretation of the Parameters in the Transmission/Disequilibrium Test**
Hongyu Zhao
- 328 Cancer Genetics and Insurance**
M. F. Niermeijer
- 329 Reply to Niermeijer**
Miguel A. Rodriguez-Bigas, Mary-Jo T. Rosenblatt, and Carolyn Farrell

Book Review

- 330 *Organelle Diseases*. Edited by Derek A. Applegarth, James E. Dimmick, and Judith G. Hall**
Reviewed by Michael G. Hanna

Announcements

- 331 Employment and Fellowship Opportunities; Course; Meetings; Workshops**

Errata

- 334 Gene Localization for Aculeiform Cataract, on Chromosome 2q33-35**
Héon et al. (September 1998 [63:921–926])
- 334 Genome Screens Using Linkage Disequilibrium Tests: Optimal Marker Characteristics and Feasibility**
Chapman and Wijsman (December 1998 [63:1872–1885])

334 Absence of Linkage of Phonological Coding Dyslexia to Chromosome 6p23-p21.3 in a Large Family Data Set

Field and Kaplan (November 1998 [63:1448–1456])

Information for Contributors

February 1999

i This Month in the *Journal*

John Ashkenas

ASHG Statement

335 Eugenics and the Misuse of Genetic Information to Restrict Reproductive Freedom

Board of Directors of the American Society of Human Genetics

Human Genetics '99: Trinucleotide Repeats

339 Protein Fate in Neurodegenerative Proteinopathies: Polyglutamine Diseases Join the (Mis)Fold

Henry L. Paulson

346 Biological Implications of the DNA Structures Associated with Disease-Causing Triplet Repeats

Richard R. Sinden

354 Fragile Sites—Cytogenetic Similarity with Molecular Diversity

Grant R. Sutherland and Robert I. Richards

360 Myotonic Dystrophy: The Role of RNA CUG Triplet Repeats

Lubov T. Timchenko

Insights From Model Systems

365 The Yeast Connection to Friedreich Ataxia

Simon A. B. Knight, Roy Kim, Debkumar Pain, and Andrew Dancis

Invited Editorial

372 Overgrowth Syndromes and the Regulation of Signaling Complexes by Proteoglycans

Scott B. Selleck

Original Articles

378 Inherited Colorectal Polyposis and Cancer Risk of the *APC I1307K* Polymorphism

Robert Gryfe, Nando Di Nicola, Geeta Lal, Steven Gallinger, and Mark Redston

385 Molecular Mechanism of Angelman Syndrome in Two Large Families Involves an Imprinting Mutation

T. Ohta, K. Buiting, H. Kokkonen, S. McCandless, S. Heeger, H. Leisti, D. J. Driscoll, S. B. Cassidy, B. Horsthemke, and R. D. Nicholls

397 Imprinting-Mutation Mechanisms in Prader-Willi Syndrome

T. Ohta, T. A. Gray, P. K. Rogan, K. Buiting, J. M. Gabriel, S. Saitoh, B. Muralidhar, B. Bilienska, M. Krajewska-Walasek, D. J. Driscoll, B. Horsthemke, M. G. Butler, and R. D. Nicholls

- 414 High Prevalence of Mutations in the Microtubule-Associated Protein Tau in a Population Study of Frontotemporal Dementia in the Netherlands**
Patrizia Rizzu, John C. Van Swieten, Marijke Jooisse, Masato Hasegawa, Martijn Stevens, Aad Tibben, Martinus F. Niermeijer, Marcel Hillebrand, Rivka Ravid, Ben A. Oostra, Michel Goedert, Cornelia M. van Duijn, and Peter Heutink
- 422 Genotype/Phenotype Analysis of a Photoreceptor-Specific ATP-Binding Cassette Transporter Gene, ABCR, in Stargardt Disease**
Richard Alan Lewis, Noah F. Shroyer, Nanda Singh, Rando Allikmets, Amy Hutchinson, Yixin Li, James R. Lupski, Mark Leppert, and Michael Dean
- 435 Molecular Analysis of SALL1 Mutations in Townes-Brocks Syndrome**
Jürgen Kohlhase, Peter E. M. Taschner, Peter Burfeind, Bastian Pasche, Bill Newman, Christopher Blanck, Martijn H. Breuning, Leo P. ten Kate, Petra Maaswinkel-Mooy, Beate Mitulla, Jörg Seidel, Susan J. Kirkpatrick, Richard M. Pauli, David S. Wargowski, Koen Devriendt, Willem Proesmans, Orazio Gabrielli, Giovanni V. Coppa, Eveline Wesby-van Swaay, Richard C. Trembath, Albert A. Schinzel, William Reardon, Eva Seemanova, and Wolfgang Engel
- 446 De Novo Alu-Element Insertions in FGFR2 Identify a Distinct Pathological Basis for Apert Syndrome**
Michael Oldridge, Elaine H. Zackai, Donna M. McDonald-McGinn, Sachiko Iseki, Gillian M. Morriss-Kay, Stephen R. F. Twigg, David Johnson, Steven A. Wall, Wen Jiang, Christiane Theda, Ethylin Wang Jabs, and Andrew O. M. Wilkie
- 462 Identification and Characterization of a Mutation, in the Human UDP-Galactose-4-Epimerase Gene, Associated with Generalized Epimerase-Deficiency Galactosemia**
Travis M. Wohlers, Nicole C. Christacos, Michelle T. Harreman, and Judith L. Fridovich-Keil
- 471 DNA Rearrangements on Both Homologues of Chromosome 17 in a Mildly Delayed Individual with a Family History of Autosomal Dominant Carpal Tunnel Syndrome**
Lorraine Potocki, Ken-Shiung Chen, Thearith Koeuth, James Killian, Susan T. Iannaccone, Stuart K. Shapira, Catherine D. Kashork, Aimee S. Spikes, Lisa G. Shaffer, and James R. Lupski
- 479 Clear Correlation of Genotype with Disease Phenotype in Very-Long-Chain Acyl-CoA Dehydrogenase Deficiency**
Brage Storstein Andresen, Simon Olpin, Ben J. H. M. Poorthuis, Hans R. Scholte, Christine Vianey-Saban, Ronald Wanders, Lodewijk Ijlst, Andrew Morris, Morteza Pourfarzam, Kim Bartlett, E. Regula Baumgartner, Johannis B. C. deKlerk, Lisbeth Dahl Schroeder, Thomas J. Corydon, Hans Lund, Vibeke Winter, Peter Bross, Lars Bolund, and Niels Gregersen
- 495 Prevalence and Phenotype Consequence of FRAXA and FRAXE Alleles in a Large, Ethnically Diverse, Special Education-Needs Population**
Dana C. Crawford, Kellen L. Meadows, James L. Newman, Lisa F. Taft, Dorothy L. Pettay, Laura B. Gold, S. Jane Hersey, Elizabeth F. Hinkle, Mary L. Stanfield, Patricia Holmgreen, Marshalyn Yeargin-Allsopp, Coleen Boyle, and Stephanie L. Sherman
- 508 DNA Variation in a 5-Mb Region of the X Chromosome and Estimates of Sex-Specific/Type-Specific Mutation Rates**
Theodore Anagnostopoulos, Peter M. Green, Gabriella Rowley, Cathryn M. Lewis, and Francesco Giannelli
- 518 Hyperparathyroidism-Jaw Tumor Syndrome: The HRPT2 Locus Is within a 0.7-cM Region on Chromosome 1q**
Maurine R. Hobbs, Ann R. Pole, Gregory N. Pidwirny, Irving B. Rosen, Richard J. Zarbo, Hilary Coon, Hunter Heath III, Mark Leppert, and Charles E. Jackson
- 526 A Gene for Autosomal Recessive Symmetrical Spastic Cerebral Palsy Maps to Chromosome 2q24-25**
D. P. McHale, S. Mitchell, S. Bunday, L. Moynihan, D. A. Campbell, C. G. Woods, N. J. Lench, R. F. Mueller, and A. F. Markham

- 533 Mapping of a Familial Moyamoya Disease Gene to Chromosome 3p24.2-p26**
Hidetoshi Ikeda, Toru Sasaki, Takashi Yoshimoto, Masashi Fukui, and Tadao Arinami
- 538 Limb Mammary Syndrome: A New Genetic Disorder with Mammary Hypoplasia, Ectrodactyly, and Other Hand/Foot Anomalies Maps to Human Chromosome 3q27**
Hans van Bokhoven, Martin Jung, Arie P. T. Smits, Sylvia van Beersum, Franz Rüschenhoff, Maurice van Steensel, Monique Veenstra, Joep H. A. M. Tuerlings, Edwin C. M. Mariman, Han G. Brunner, Thomas F. Wienker, Andre Reis, Hans-Hilger Ropers, and Ben C. J. Hamel
- 547 Mapping of Primary Congenital Lymphedema to the 5q35.3 Region**
Alison L. Evans, Glen Brice, Vihra Sotirova, Peter Mortimer, Joseph Beninson, Kevin Burnand, Jane Rosbotham, Anne Child, and Mansoor Sarfarazi
- 556 Identification of a New Autosomal Dominant Limb-Girdle Muscular Dystrophy Locus on Chromosome 7**
Marcy C. Speer, Jeffery M. Vance, Janet M. Grubber, Felicia Lennon Graham, Jeffrey M. Stajich, Kristi D. Viles, Allison Rogala, Robert McMichael, Jerry Chutkow, Claire Goldsmith, Richard W. Tim, and Margaret A. Pericak-Vance
- 563 Novel Locus for Autosomal Dominant Hereditary Spastic Paraplegia, on Chromosome 8q**
Peter Hedera, Shirley Rainier, David Alvarado, Xinping Zhao, Jeffery Williamson, Brith Otterud, Mark Leppert, and John K. Fink
- 570 Brachydactyly Type B: Clinical Description, Genetic Mapping to Chromosome 9q, and Evidence for a Shared Ancestral Mutation**
Yaoqin Gong, David Chitayat, Bronwyn Kerr, Taiping Chen, Riyana Babul-Hirji, Adatiya Pal, Michael Reiss, and Matthew L. Warman
- 578 Brachydactyly Type B: Linkage to Chromosome 9q22 and Evidence for Genetic Heterogeneity**
Michael Oldridge, I. Karen Temple, Heloisa G. Santos, Richard J. Gibbons, Zehra Mustafa, Kay E. Chapman, John Loughlin, and Andrew O. M. Wilkie
- 586 Genetic Mapping to 10q23.3-q24.2, in a Large Italian Pedigree, of a New Syndrome Showing Bilateral Cataracts, Gastroesophageal Reflux, and Spastic Paraparesis with Amyotrophy**
Marco Seri, Roberto Cusano, Paola Forabosco, Roberta Cinti, Francesco Caroli, Paolo Picco, Rita Bini, Vincenzo Brescia Morra, Giuseppe De Michele, Margherita Lerone, Margherita Silengo, Ivana Pela, Carla Borrone, Giovanni Romeo, and Marcella Devoto
- 594 Mapping of a New Autosomal Dominant Spinocerebellar Ataxia to Chromosome 22**
Lan Zu, Karla P. Figueroa, Raji Grewal, and Stefan-M. Pulst
- 600 Congenital Motor Nystagmus Linked to Xq26-q27**
John B. Kerrison, M. Reza Vagefi, M. Michael Barmada, and Irene H. Maumenee
- 608 Linkage of Low-Density Lipoprotein Size to the Lipoprotein Lipase Gene in Heterozygous Lipoprotein Lipase Deficiency**
John E. Hokanson, John D. Brunzell, Gail P. Jarvik, Ellen M. Wijsman, and Melissa A. Austin
- 619 The Central Siberian Origin for Native American Y Chromosomes**
Fabrício R. Santos, Arpita Pandya, Chris Tyler-Smith, Sérgio D. J. Pena, Moses Schanfield, William R. Leonard, Ludmila Osipova, Michael H. Crawford, and R. John Mitchell
- 629 Comparison of the Power and Accuracy of Biallelic and Microsatellite Markers in Population-Based Gene-Mapping Methods**
Momiao Xiong and Li Jin
- 641 Power of Association and Linkage Tests When the Disease Alleles Are Unobserved**
I-Ping Tu and Alice S. Whittemore

Letters to the Editor

- 651 Both Recessive and Dominant Forms of Anhidrotic/Hypohidrotic Ectodermal Dysplasia Map to Chromosome 2q11-q13**
L. Baala, S. Hadj Rabia, J. Zlotogora, K. Kabbaj, H. Chhoul, A. Munnich, S. Lyonnet, and A. Sefiani
- 653 Mosaicism and Sporadic Familial Adenomatous Polyposis**
Susan M. Farrington and Malcolm G. Dunlop
- 658 *HPS* Gene Mutations in Hermansky-Pudlak Syndrome**
Richard A. Spritz and Jangsuk Oh
- 659 A Novel 22q11.2 Microdeletion in DiGeorge Syndrome**
Anita Rauch, Rudolf A. Pfeiffer, Georg Leipold, Helmut Singer, Monika Tigges, and Michael Hofbeck
- 667 *RB1* Gene Mutations in Peripheral Blood DNA of Patients with Isolated Unilateral Retinoblastoma**
Martina Klutz, Bernhard Horsthemke, and Dietmar R. Lohmann
- 668 TDT Clarification**
Richard S. Spielman and Warren J. Ewens

Announcements

- 670 Employment and Fellowship Opportunities; Cell Lines; Meetings; Course**

Information for Contributors

March 1999

i This Month in the *Journal*

John Ashkenas

The Cardiovascular System '99

- 673 Nitric Oxide in Endothelial Dysfunction and Vascular Remodeling: Clinical Correlates and Experimental Links**
Radu D. Rudic and William C. Sessa
- 678 The Molecular Basis of Vascular Disorders**
Jeffrey A. Towbin, Brett Casey, and John Belmont
- 685 Stress-Response Proteins in Cardiovascular Disease**
XianZhong Xiao and Ivor J. Benjamin

Insights from Model Systems

- 691 Specificity in Transforming Growth Factor- β Signaling Pathways**
C. J. Ring and K. W. Y. Cho
- 692 Technical Sidebar: Getting Organized**

Original Articles

- 698 Human Molybdopterin Synthase Gene: Identification of a Bicistronic Transcript with Overlapping Reading Frames**
B. Stallmeyer, G. Drugeon, J. Reiss, A.L. Haenni, and R.R. Mendel
- 706 Human Molybdopterin Synthase Gene: Genomic Structure and Mutations in Molybdenum Cofactor Deficiency Type B**
J. Reiss, C. Dorche, B. Stallmeyer, R. R. Mendel, N. Cohen, and M. T. Zobot
- 712 Characterization and Mutation Analysis of Human *LEFTY A* and *LEFTY B*, Homologues of Murine Genes Implicated in Left-Right Axis Development**
K. Kosaki, M. T. Bassi, R. Kosaki, M. Lewin, J. Belmont, G. Schauer, and B. Casey
- 722 A Novel Skeletal Dysplasia with Developmental Delay and Acanthosis Nigricans Is Caused by a *Lys650Met* Mutation in the Fibroblast Growth Factor Receptor 3 Gene**
Patricia L. Tavormina, Gary A. Bellus, Melanie K. Webster, Michael J. Bamshad, Alexander E. Fraley, Iain McIntosh, Jinny Szabo, Wen Jiang, Ethylin W. Jabs, William R. Wilcox, John J. Wasmuth, Daniel J. Donoghue, Leslie M. Thompson, and Clair A. Francomano
- 732 Cyclic Ichthyosis with Epidermolytic Hyperkeratosis: A Phenotype Conferred by Mutations in the 2B Domain of Keratin K1**
Virginia P. Sybert, Julie S. Francis, Laura D. Corden, Lynne T. Smith, Molly Weaver, Karen Stephens, and W. H. Irwin McLean
- 739 Genomic Structure of the Canalicular Multispecific Organic Anion–Transporter Gene (*MRP2/cMOAT*) and Mutations in the ATP-Binding–Cassette Region in Dubin-Johnson Syndrome**
Satoshi Toh, Morimasa Wada, Takeshi Uchiumi, Akihiko Inokuchi, Yoshinari Makino, Yutaka Horie, Yukihiro Adachi, Shotaro Sakisaka, and Michihiko Kuwano
- 747 Der(22) Syndrome and Velo-Cardio-Facial Syndrome/DiGeorge Syndrome Share a 1.5-Mb Region of Overlap on Chromosome 22q11**
B. Funke, L. Edelmann, N. McCain, R. K. Pandita, J. Ferreira, S. Merscher, M. Zohouri, L. Cannizzaro, A. Shanske, and B. E. Morrow
- 759 Evidence That Mutations in the X-linked *DDP* Gene Cause Incompletely Penetrant and Variable Skewed X Inactivation**
Robert M. Plenge, Lisbeth Tranebjaerg, Peter K. A. Jensen, Charles Schwartz, and Huntington F. Willard
- 768 Location Score and Haplotype Analyses of the Locus for Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay, in Chromosome Region 13q11**
Andrea Richter, John D. Rioux, Jean-Pierre Bouchard, Jocelyne Mercier, Jean Mathieu, Bing Ge, Josée Poirier, Dominique Julien, Gabor Gyapay, Jean Weissenbach, Thomas J. Hudson, Serge B. Melançon, and Kenneth Morgan
- 776 Evidence for a Rare Prostate Cancer–Susceptibility Locus at Chromosome 1p36**
Mark Gibbs, Janet L. Stanford, Richard A. McIndoe, Gail P. Jarvik, Suzanne Kolb, Ellen L. Goode, Lisa Chakrabarti, Eugene F. Schuster, Valerie A. Buckley, Elizabeth L. Miller, Susan Brandzel, Sarah Li, Leroy Hood, and Elaine A. Ostrander
- 788 Autosomal Dominant Myopathy with Proximal Weakness and Early Respiratory Muscle Involvement Maps to Chromosome 2q**
Piero Nicolao, Fengqing Xiang, Lars-Gunnar Gunnarsson, Bruno Giometto, Lars Edström, Maria Anvret, and Zhiping Zhang

793 The Predisposition to Type 1 Diabetes Linked to the Human Leukocyte Antigen Complex Includes at Least One Non–Class II Gene

Benedicte A. Lie, John A. Todd, Flemming Pociot, Jørn Nerup, Hanne E. Akselsen, Geir Joner, Knut Dahl-Jørgensen, Kjersti S. Rønningen, Erik Thorsby, and Dag E. Undlien

801 Diaphyseal Medullary Stenosis with Malignant Fibrous Histiocytoma: a Hereditary Bone Dysplasia/Cancer Syndrome Maps to 9p21-22

John A. Martignetti, Robert J. Desnick, Elias Aliprandis, Karen I. Norton, Philip Hardcastle, Sydney Nade, and Bruce D. Gelb

808 A Genomewide Analysis Provides Evidence for Novel Linkages in Inflammatory Bowel Disease in a Large European Cohort

Jochen Hampe, Stefan Schreiber, Sarah H. Shaw, Kit F. Lau, Stephen Bridger, Andrew J. S. Macpherson, Lon R. Cardon, Hakan Sakul, Timothy J. R. Harris, Alan Buckler, Jeff Hall, Pieter Stokkers, Sander J. H. van Deventer, Peter Nürnberg, Mudassar M. Mirza, John C. W. Lee, John E. Lennard-Jones, Chris G. Mathew, and Mark E. Curran

817 Ancestral Asian Source(s) of New World Y-Chromosome Founder Haplotypes

T. M. Karafet, S. L. Zegura, O. Posukh, L. Osipova, A. Bergen, J. Long, D. Goldman, W. Klitz, S. Harihara, P. de Knijff, V. Wiebe, R. C. Griffiths, A. R. Templeton, and M. F. Hammer

832 Identifying Families with Likely Genetic Protective Factors against Alzheimer Disease

Jeremy M. Silverman, Christopher J. Smith, Deborah B. Marin, Sandra Birstein, Marlene Mare, Richard C. Mohs, and Kenneth L. Davis

839 Multipoint Oligogenic Analysis of Age-at-Onset Data with Applications to Alzheimer Disease Pedigrees

E. Warwick Daw, Simon C. Heath, and Ellen M. Wijsman

852 The Duty to Recontact: Attitudes of Genetics Service Providers

Jennifer L. Fitzpatrick, Cecil Hahn, Teresa Costa, and Marlene J. Huggins

861 The Transmission/Disequilibrium Test and Parental-Genotype Reconstruction: The Reconstruction-Combined Transmission/Disequilibrium Test

Michael Knapp

871 Analysis of Affected Sib Pairs, with Covariates—With and Without Constraints

Celia M. T. Greenwood and Shelley B. Bull

886 A Parametric Copula Model for Analysis of Familial Binary Data

David-Alexandre Trégouët, Pierre Ducimetière, Valéry Bocquet, Sophie Visvikis, Florent Soubrier, and Laurence Tiret

Letters to the Editor

895 Psoriasis Linkage in the HLA Region

Richard O. Leder and Susan E. Hodge

896 Reply to Leder and Hodge

James Elder, Rajan Nair, Philip Stuart, John Voorhees, Sun-Wei Guo, Stefan Jenisch, Eckhard Westphal, Martin Krönke, Tilo Henseler, and Enno Christophers

897 Protein-Truncation Mutations in the *RP2* Gene in a North American Cohort of Families with X-Linked Retinitis Pigmentosa

Alan J. Mears, Linn Gieser, Denise Yan, Cynthia Chen, Stacey Fahrner, Suja Hiriyanna, Ricardo Fujita, Samuel G. Jacobson, Paul A. Sieving, and Anand Swaroop

900 A Fifth Locus for Bardet-Biedl Syndrome Maps to Chromosome 2q31

Terry-Lynn Young, Lynette Penney, Michael O. Woods, Patrick S. Parfrey, Jane S. Green, Donna Hefferton, and William S. Davidson

904 Autosomal Dominant (Beukes) Premature Degenerative Osteoarthropathy of the Hip Joint Maps to an 11-cM Region on Chromosome 4q35

Philip Roby, Stephen Eyre, Jane Worthington, Rajkumar Ramesar, Hendrik Cilliers, Peter Beighton, Michael Grant, and Gillian Wallis

908 Common Fragile Sites: G-Band Characteristics within an R-Band

Dan Mishmar, Yael Mandel-Gutfreund, Hanah Margalit, Ayelet Rahat, and Batsheva Kerem

910 Finite-Sample Properties of Family-Based Association Tests

J. C. Whittaker and D. J. Thompson

Announcements**916 Employment and Fellowship Opportunities; Course****Erratum****918 The Emerging Tree of West Eurasian mtDNAs: A Synthesis of Control-Region Sequences and RFLPs**

Macaulay et al. (January 1999 [64:232–249]).

Information for Contributors

April 1999

i This Month in the *Journal*

John Ashkenas

Sex Chromosome Genetics '99**921 Gonadoblastoma, Testicular and Prostate Cancers, and the *TSPY* Gene**

Yun-Fai Chris Lau

928 Male Infertility and the Y Chromosome

Ken McElreavey and Csilla Krausz

934 The X Chromosome and Recurrent Spontaneous Abortion: The Significance of Transmanifesting Carriers

Mark C. Lanasa, W. Allen Hogge, and Eric P. Hoffman

Invited Editorial**939 The Genetic Basis for Periodic Fever**

John C. Mulley

943 *BRCA1* and *BRCA2* Testing: Weighing the Demand against the Benefits

P. Devilee

Original Articles

- 949 Mutation and Haplotype Studies of Familial Mediterranean Fever Reveal New Ancestral Relationships and Evidence for a High Carrier Frequency with Reduced Penetrance in the Ashkenazi Jewish Population**
Ivona Aksentijevich, Yelizaveta Torosyan, Jonathan Samuels, Michael Centola, Elon Pras, Jae Jin Chae, Carole Oddoux, Geryl Wood, Maria Pia Azzaro, Giuseppe Palumbo, Rosario Giustolisi, Mordechai Pras, Harry Ostrer, and Daniel L. Kastner
- 963 The Prevalence of Common *BRCA1* and *BRCA2* Mutations among Ashkenazi Jews**
Patricia Hartge, Jeffery P. Struewing, Sholom Wacholder, Lawrence C. Brody, and Margaret A. Tucker
- 971 Retinitis Pigmentosa and Progressive Sensorineural Hearing Loss Caused by a C12258A Mutation in the Mitochondrial *MTTS2* Gene**
Fiona C. Mansergh, Sophia Millington-Ward, Avril Kennan, Anna-Sophia Kiang, Marian Humphries, G. Jane Farrar, Peter Humphries, and Paul F. Kenna
- 986 Germ-Line Mosaicism in Tuberous Sclerosis: How Common?**
Verna M. Rose, Kit-Sing Au, Gretchen Pollom, E. Steve Roach, Heather R. Prashner, and Hope Northrup
- 993 Recurrence of Marfan Syndrome as a Result of Parental Germ-Line Mosaicism for an *FBN1* Mutation**
Terhi Rantamäki, Ilkka Kaitila, Ann-Christine Syvänen, Matti Lukka, and Leena Peltonen
- 1002 Autoimmune Lymphoproliferative Syndrome with Defective Fas: Genotype Influences Penetrance**
Christine E. Jackson, Roxanne E. Fischer, Amy P. Hsu, Stacie M. Anderson, Youngnim Choi, Jin Wang, Janet K. Dale, Thomas A. Fleisher, Lindsay A. Middleton, Michael C. Sneller, Michael J. Lenardo, Stephen E. Straus, and Jennifer M. Puck
- 1015 Mutations in a Dominant-Negative Isoform Correlate with Phenotype in Inherited Cardiac Arrhythmias**
Raha Mohammad-Panah, Sophie Demolombe, Nathalie Neyroud, Pascale Guicheney, Florence Kyndt, Maurice van den Hoff, Isabelle Baró, and Denis Escande
- 1024 The 2588G→C Mutation in the *ABCR* Gene Is a Mild Frequent Founder Mutation in the Western European Population and Allows the Classification of *ABCR* Mutations in Patients with Stargardt Disease**
Alessandra Maugeri, Marc A. van Driel, Dorien J. R. van de Pol, B. Jeroen Klevering, Frank J. J. van Haren, Nel Tijmes, Arthur A. B. Bergen, Klaus Rohrschneider, Anita Blankenagel, Alfred J. L. G. Pinckers, Niklas Dahl, Han G. Brunner, August F. Deutman, Carel B. Hoyng, and Frans P. M. Cremers
- 1036 *COL9A3*: A Third Locus for Multiple Epiphyseal Dysplasia**
Petteri Paassilta, Jaana Lohiniva, Susanna Annunen, Jacky Bonaventure, Martine Le Merrer, Lori Pai, and Leena Ala-Kokko
- 1045 The “Thermolabile” Variant of Methylenetetrahydrofolate Reductase and Neural Tube Defects: An Evaluation of Genetic Risk and the Relative Importance of the Genotypes of the Embryo and the Mother**
Denis C. Shields, Peadar N. Kirke, James L. Mills, Dorothy Ramsbottom, Anne M. Molloy, Helen Burke, Donald G. Weir, John M. Scott, and Alexander S. Whitehead
- 1056 Multicentric Origin of Hemochromatosis Gene (*HFE*) Mutations**
J. Rochette, J. J. Pointon, C. A. Fisher, G. Perera, M. Arambepola, D. S. Kodikara Arichchi, S. De Silva, J. L. Vandwalle, J. P. Monti, J. M. Old, A. T. Merryweather-Clarke, D. J. Weatherall, and K. J. H. Robson
- 1063 Ancestral Origins and Worldwide Distribution of the *PRNP* 200K Mutation Causing Familial Creutzfeldt-Jakob Disease**
Hee Suk Lee, Nyamkhisig Sambuughin, Larisa Cervenakova, Joab Chapman, Maurizio Pocchiari, Svetlana Litvak, Hai Yan Qi, Herbert Budka, Teodoro del Ser, Hisako Furukawa, Paul Brown, D. Carleton Gajdusek, Jeffrey C. Long, Amos D. Korczyn, and Lev G. Goldfarb

- 1071 Age Estimates of Two Common Mutations Causing Factor XI Deficiency: Recent Genetic Drift Is Not Necessary for Elevated Disease Incidence among Ashkenazi Jews**
David B. Goldstein, David E. Reich, Neil Bradman, Sali Usher, Uri Seligsohn, and Hava Peretz
- 1076 Low-Copy Repeats Mediate the Common 3-Mb Deletion in Patients with Velo-cardio-facial Syndrome**
Lisa Edelmann, Raj K. Pandita, and Bernice E. Morrow
- 1087 Analysis of Chromosome 1q42.2-43 in 152 Families with High Risk of Prostate Cancer**
Mark Gibbs, Lisa Chakrabarti, Janet L. Stanford, Ellen L. Goode, Suzanne Kolb, Eugene F. Schuster, Valerie A. Buckley, Morgan Shook, Leroy Hood, Gail P. Jarvik, and Elaine A. Ostrander
- 1096 Genetic Linkage of IgA Deficiency to the Major Histocompatibility Complex: Evidence for Allele Segregation Distortion, Parent-of-Origin Penetrance Differences, and the Role of Anti-IgA Antibodies in Disease Predisposition**
Igor Vořechovský, A. David B. Webster, Alessandro Plebani, and Lennart Hammarström
- 1110 Precise Genetic Mapping and Haplotype Analysis of the Familial Dysautonomia Gene on Human Chromosome 9q31**
Anat Blumenfeld, Susan A. Slaugenhaupt, Christopher B. Liebert, Violeta Temper, Channa Maayan, Sandra Gill, Diane E. Lucente, Maria Idelson, Kathy MacCormack, Mary Anne Monahan, James Mull, Maire Leyne, Marc Mendillo, Taryn Schiripo, Esther Mishori, Xandra Breakefield, Felicia B. Axelrod, and James F. Gusella
- 1119 Delineation of the Critical Deletion Region for Congenital Heart Defects, on Chromosome 8p23.1**
Koenraad Devriendt, Gert Matthijs, Roeland Van Dael, Marc Gewillig, Benedicte Eyskens, Helle Hjalgrim, Brigitte Dolmer, Julie McCaughran, Karen Brøndum-Nielsen, Peter Marynen, Jean-Pierre Fryns, and Joris Robert Vermeesch
- 1127 Linkage of Type 2 Diabetes Mellitus and of Age at Onset to a Genetic Location on Chromosome 10q in Mexican Americans**
Ravindranath Duggirala, John Blangero, Laura Almasy, Thomas D. Dyer, Kenneth L. Williams, Robin J. Leach, Peter O'Connell, and Michael P. Stern
- 1141 A Gene for X-Linked Idiopathic Congenital Nystagmus (NYS1) Maps to Chromosome Xp11.4-p11.3**
Annick Cabot, Jean-Michel Rozet, Sylvie Gerber, Isabelle Perrault, Dominique Ducroq, Asmae Smahi, Eric Souied, Arnold Munnich, and Josseline Kaplan
- 1147 Linkage Disequilibrium at the ADH2 and ADH3 Loci and Risk of Alcoholism**
Michael Osier, Andrew J. Pakstis, Judith R. Kidd, Jia-Fu Lee, Shih-Jiun Yin, Huei-Chen Ko, Howard J. Edenberg, Ru-Band Lu, and Kenneth K. Kidd
- 1158 Relaxed Replication of mtDNA: A Model with Implications for the Expression of Disease**
Patrick F. Chinnery and David C. Samuels
- 1166 mtDNA Analysis of Nile River Valley Populations: A Genetic Corridor or a Barrier to Migration?**
Matthias Krings, Abd-el Halim Salem, Karin Bauer, Helga Geisert, Adel K. Malek, Louis Chaix, Christian Simon, Derek Welsby, Anna Di Rienzo, Gerd Utermann, Antti Sajantila, Svante Pääbo, and Mark Stoneking
- 1177 A Note on Power Approximations for the Transmission/Disequilibrium Test**
Michael Knapp
- 1186 Allowing for Missing Parents in Genetic Studies of Case-Parent Triads**
C. R. Weinberg
- 1194 Comparison of Linkage-Disequilibrium Methods for Localization of Genes Influencing Quantitative Traits in Humans**
Grier P. Page and Christopher I. Amos

Letters to the Editor

- 1207 A Novel NTRK1 Mutation Associated with Congenital Insensitivity to Pain with Anhidrosis**
Angela Greco, Riccardo Villa, Barbara Tubino, Luca Romano, Donata Penso, and Marco A. Pierotti
- 1210 Mutations in the *RP2* Gene Cause Disease in 10% of Families with Familial X-Linked Retinitis Pigmentosa Assessed in This Study**
Alison J. Hardcastle, Dawn L. Thiselton, Lionel Van Maldergem, Bratin K. Saha, Marcelle Jay, Catherine Plant, Rachel Taylor, Alan C. Bird, and Shomi Bhattacharya
- 1216 Double Heterozygosity for a *RET* Substitution Interfering with Splicing and an *EDNRB* Missense Mutation in Hirschsprung Disease**
Alberto Auricchio, Paola Griseri, Maria Luisa Carpentieri, Nicola Betsos, Annamaria Staiano, Arturo Tozzi, Manuela Priolo, Helen Thompson, Renata Bocciardi, Giovanni Romeo, Andrea Ballabio, and Isabella Ceccherini
- 1221 A Mutation (2314delG) in the Usher Syndrome Type IIA Gene: High Prevalence and Phenotypic Variation**
Xue-Zhong Liu, Carolyn Hope, Chuan Yu Liang, Jiu Mu Zou, Li Rong Xu, T. Cole, Robert F. Mueller, Sarah Bunday, Walter Nance, Karen P. Steel, and Steve D.M. Brown
- 1225 Different Functional Outcome of *RetGC1* and *RPE65* Gene Mutations in Leber Congenital Amaurosis**
Isabelle Perrault, Jean-Michel Rozet, Imad Ghazi, Corinne Leowski, Michèle Bonnemaïson, Sylvie Gerber, Dominique Ducroq, Annick Cabot, Eric Souied, Jean-Louis Dufier, Arnold Munnich, and Josseline Kaplan
- 1228 The *APC* I1307K Allele and *BRCA*-Associated Ovarian Cancer Risk**
Diane L. Maresco, Patricia H. Arnold, Yukio Sonoda, Mark G. Federici, Faina Bogomolny, Esther Rhei, and Jeff Boyd
- 1230 Germ-Line *NF2* Mutations and Disease Severity in Neurofibromatosis Type 2 Patients with Retinal Abnormalities**
Michael E. Baser, Lan Kluwe, and Victor-F. Mautner
- 1233 Gaucher Disease: The N370S Mutation in Ashkenazi Jewish and Spanish Patients has a Common Origin and Arose Several Thousand Years Ago**
Anna Díaz, Magda Montfort, Bru Cormand, Baijin Zeng, Gregory M. Pastores, Amparo Chabás, Lluïsa Vilageliu, and Daniel Grinberg
- 1238 Deafness Locus *DFNB16* Is Located on Chromosome 15q13-q21 within a 5-cM Interval Flanked by Markers *D15S994* and *D15S132***
Manuela Villamar, Ignacio del Castillo, Noelia Valle, Lourdes Romero, and Felipe Moreno
- 1241 Prevalence of Bloom Syndrome Heterozygotes among Ashkenazi Jews**
Carole Oddoux, Carlos Mark Clayton, Holly Reid Nelson, and Harry Ostrer
- 1243 Optimal Ascertainment Strategies to Detect Linkage to Common Disease Alleles**
Miron Baron
- 1246 Reply to Baron**
Judith A. Badner, Elliot S. Gershon, and Lynn R. Goldin
- 1248 Down-Weighting of Multiple Affected Sib Pairs Leads to Biased Likelihood-Ratio Tests, under the Assumption of No Linkage**
Celia M. T. Greenwood and Shelley B. Bull

Obituary

- 1253 Phyllis J. McAlpine, Ph.D., 1941–98: In Memoriam**
Diane W. Cox, Susan Povey, and Thomas B. Shows

Announcements

- 1255 Employment and Fellowship Opportunities; Meetings; Panels; Call for Patients**

Errata

- 1257 Location Score and Haplotype Analyses for Autosomal Recessive Spastic Ataxia of Charlevoix-Saugenay, in Chromosome Region 13q11**
Richter et al. (March 1999 [64:768-775]).
- 1257 Common Fragile Sites: G-Band Characteristics within an R-Band**
Mishmar et al. (March 1999 [64:908-910]).

Information for Contributors

May 1999

i This Month in the *Journal*

John Ashkenas

DNA Repair '99

- 1259 Transcription-Coupled Repair of DNA Damage: Unanticipated Players, Unexpected Complexities**
Steven A. Leadon
- 1264 The Mammalian Mre11-Rad50-Nbs1 Protein Complex: Integration of Functions in the Cellular DNA-Damage Response**
John H. J. Petrini
- 1270 Immunoglobulin Class Switch Recombination: Will Genetics Provide New Clues to Mechanism?**
Nancy Maizels
- 1276 Repair of mtDNA in Vertebrates**
Daniel F. Bogenhagen
- 1282 Poly(ADP-Ribose) Polymerase in the Cellular Response to DNA Damage, Apoptosis, and Disease**
F. Javier Oliver, Josiane Menissier-de Murcia, and Gilbert de Murcia

Invited Editorial

- 1289 Outrageous Fortune: The Risk of Suicide in Genetic Testing for Huntington Disease**
Thomas D. Bird

Original Articles

- 1293 A Worldwide Assessment of the Frequency of Suicide, Suicide Attempts, or Psychiatric Hospitalization after Predictive Testing for Huntington Disease**
Elisabeth W. Almqvist, Maurice Bloch, Ryan Brinkman, David Craufurd, and Michael R. Hayden
- 1305 Comprehensive Mutation Analysis of *TSC1* and *TSC2*—and Phenotypic Correlations in 150 Families with Tuberous Sclerosis**
Alistair C. Jones, Magitha M. Shyamsundar, Meinir W. Thomas, Julie Maynard, Shelley Idziaszczyk, Susan Tomkins, Julian R. Sampson, and Jeremy P. Cheadle
- 1316 Analysis of Alkaptonuria (AKU) Mutations and Polymorphisms Reveals that the CCC Sequence Motif Is a Mutational Hot Spot in the Homogentisate 1,2 Dioxygenase Gene (*HGO*)**
D. Beltrán-Valero de Bernabé, F. J. Jimenez, R. Aquaron, and S. Rodríguez de Córdoba
- 1323 Identification of a Genetic Defect in the Hairless Gene in Atrichia with Papular Lesions: Evidence for Phenotypic Heterogeneity among Inherited Atrichias**
Eli Sprecher, Reuven Bergman, Raymonde Szargel, Rachel Friedman-Birnbaum, and Nadine Cohen
- 1330 An mtDNA Mutation in the Initiation Codon of the Cytochrome C Oxidase Subunit II Gene Results in Lower Levels of the Protein and a Mitochondrial Encephalomyopathy**
Kim M. Clark, Robert W. Taylor, Margaret A. Johnson, Patrick F. Chinnery, Zofia M.A. Chrzanowska-Lightowlers, Richard M. Andrews, Isobel P. Nelson, Nicholas W. Wood, Phillipa J. Lamont, Michael G. Hanna, Robert N. Lightowlers, and Douglass M. Turnbull
- 1340 Quantitative Analysis of Survival Motor Neuron Copies: Identification of Subtle *SMN1* Mutations in Patients with Spinal Muscular Atrophy, Genotype-Phenotype Correlation, and Implications for Genetic Counseling**
Brunhilde Wirth, M. Herz, A. Wetter, S. Moskau, E. Hahnen, S. Rudnik-Schöneborn, T. Wienker, and K. Zerres
- 1357 Connexin46 Mutations in Autosomal Dominant Congenital Cataract**
Donna Mackay, Alexander Ionides, Zoha Kibar, Guy Rouleau, Vanita Berry, Anthony Moore, Alan Shiels, and Shomi Bhattacharya
- 1365 The Promoters of the Survival Motor Neuron Gene (*SMN*) and Its Copy (*SMNc*) Share Common Regulatory Elements**
Andoni Echaniz-Laguna, Pierre Miniou, Deborah Bartholdi, and Judith Melki
- 1371 Modification of *BRCA1*-Associated Breast Cancer Risk by the Polymorphic Androgen-Receptor CAG Repeat**
Timothy R. Rebbeck, Philip W. Kantoff, Krishna Krithivas, Susan Neuhausen, M. Anne Blackwood, Andrew K. Godwin, Mary B. Daly, Steven A. Narod, Judy E. Garber, Henry T. Lynch, Barbara L. Weber, and Myles Brown
- 1378 A Third Major Locus for Autosomal Dominant Hypercholesterolemia Maps to 1p34.1-p32**
Mathilde Varret, Jean-Pierre Rabès, Bruno Saint-Jore, Ana Cenarro, Jean-Christophe Marinoni, Fernando Civeira, Martine Devillers, Michel Krempf, Monique Coulon, Rochelle Thiant, Maritha J. Kotze, Helena Schmidt, Jean-Claude Buzzi, Gert M. Kostner, Stephano Bertolini, Miguel Pocovi, Alberto Rosa, Michel Farnier, Maria Martinez, Claudine Junien, and Catherine Boileau
- 1388 Juvenile Hemochromatosis Locus Maps to Chromosome 1q**
A. Roetto, A. Totaro, M. Cazzola, M. Cicilano, S. Bosio, G. D'Ascola, M. Carella, L. Zelante, A. L. Kelly, T. M. Cox, P. Gasparini, and C. Camaschella
- 1394 A New Locus for Autosomal Dominant Stargardt-Like Disease Maps to Chromosome 4**
Marina Kniazeva, Michael F. Chiang, Basil Morgan, Alfred L. Anduze, Donald J. Zack, Min Han, and Kang Zhang

- 1400 The Fanconi Anemia Group E Gene, *FANCE*, Maps to Chromosome 6p**
 Quinten Waisfisz, Kathrin Saar, Neil V. Morgan, Cigdem Altay, Peter A. Leegwater, Johan P. de Winter, Kenshi Komatsu, Gareth R. Evans, Rolf-Dieter Wegner, André Reis, Hans Joenje, Fré Arwert, Christopher G. Mathew, Jan C. Pronk, and Martin Digweed
- 1406 The Critical Region for Behçet Disease in the Human Major Histocompatibility Complex Is Reduced to a 46-kb Segment Centromeric of HLA-B, by Association Analysis Using Refined Microsatellite Mapping**
 Masao Ota, Nobuhisa Mizuki, Yoshihiko Katsuyama, Gen Tamiya, Takashi Shiina, Akira Oka, Hitoshi Ando, Minoru Kimura, Kaori Goto, Shigeaki Ohno, and Hidetoshi Inoko
- 1411 Evidence for Linkage of Adolescent-Onset Idiopathic Generalized Epilepsies to Chromosome 8—and Genetic Heterogeneity**
 Martina Durner, Guillan Zhou, Dingyi Fu, Paula Abreu, Shlomo Shinnar, Stanley R. Resor, Solomon L. Moshe, David Rosenbaum, Jeffrey Cohen, Cynthia Harden, Harriet Kang, Sibylle Wallace, Daniel Luciano, Karen Ballaban-Gil, Irene Klotz, Elisa Dicker, and David A. Greenberg
- 1420 Dominant Hereditary Inclusion-Body Myopathy Gene (*IBM3*) Maps to Chromosome Region 17p13.1**
 Tommy Martinsson, Niklas Darin, Mårten Kyllerman, Anders Oldfors, Birgitta Hallberg, and Jan Wahlström
- 1427 Evidence for Effective Suppression of Recombination in the Chromosome 17q21 Segment Spanning *RNU2–BRCA1***
 Xudong Liu and David F. Barker
- 1440 Transmission of a Fully Functional Human Neocentromere through Three Generations**
 Chris Tyler-Smith, Giorgio Gimelli, Sabrina Giglio, Giovanna Florida, Arpita Pandya, Gianluigi Terzoli, Peter E. Warburton, William C. Earnshaw, and Orsetta Zuffardi
- 1445 Heterogeneous X Inactivation in Trophoblastic Cells of Human Full-Term Female Placentas**
 Leendert H. J. Looijenga, Ad J. M. Gillis, Annemieke J. M. H. Verkerk, Wim L. J. van Putten, and J. Wolter Oosterhuis
- 1453 Genomewide Scan for Familial Combined Hyperlipidemia Genes in Finnish Families, Suggesting Multiple Susceptibility Loci Influencing Triglyceride, Cholesterol, and Apolipoprotein B Levels**
 Päivi Pajukanta, Joseph D. Terwilliger, Markus Perola, Tero Hiekkalinna, Ilpo Nuotio, Pekka Ellonen, Maija Parkkonen, Jaana Hartiala, Kati Ylitalo, Jussi Pihlajamäki, Kimmo Porkka, Markku Laakso, Jorma Viikari, Christian Ehnholm, Marja-Riitta Taskinen, and Leena Peltonen
- 1464 Relationship Estimation by Markov-Process Models in a Sib-Pair Linkage Study**
 Jane M. Olson

Letters to the Editor

- 1473 Mutation Rate in Human Microsatellites**
 Jürgen Henke and Lotte Henke
- 1473 Reply to Henke and Henke**
 B. Rolf and B. Brinkmann
- 1475 Recurrent Williams-Beuren Syndrome in a Sibship Suggestive of Maternal Germ-Line Mosaicism**
 Ali Kara-Mostefa, Odile Raoul, Stanislas Lyonnet, Jeanne Amiel, Arnold Munnich, Michel Vekemans, Suzel Magnier, Batool Ossareh, and Jean-Paul Bonnefont
- 1478 Localization of a Gene for Bitter-Taste Perception to Human Chromosome 5p15**
 Danielle R. Reed, Elizabeth Nanthakumar, Michael North, Callum Bell, Linda M. Bartoshuk, and R. Arlen Price

1480 Sperm Chromosome Analysis in a Man Heterozygous for a Paracentric Inversion of Chromosome 14 (q24.1q32.1)

R. H. Martin

1484 A Program for the Monte Carlo Evaluation of Significance of the Extended Transmission/Disequilibrium Test

Jing Hua Zhao, Pak Chung Sham, and David Curtis

1485 Genomewide Transmission/Disequilibrium Testing: A Correction

Nicola J. Camp

Book Review**1488 *DNA Transfer to Cultured Cells*. Edited by Katya Ravid and R. Ian Freshney. New York: Wiley, 1998. Pp. 296. \$69.95.**

Beverly L. Davidson

Announcements**1489 Employment and Fellowship Opportunities; Meetings; Conference****Errata****1491 Multicentric Origin of Hemochromatosis Gene (*HFE*) Mutations**

Rochette et al. (April 1999 [64:1056-1062]).

1491 Molecular Analysis of Mutations in the *CSB* (*ERCC6*) Gene in Patients with Cockayne Syndrome

Mallery et al. (January 1999 [62:77-85]).

Information for Contributors

June 1999

i This Month in the *Journal*

John Ashkenas

Protein Biosynthesis '99**1493 From the ER to the Golgi: Insights from the Study of Combined Factors V and VIII Deficiency**

William C. Nichols and David Ginsburg

1499 Cystic Fibrosis as a Disease of Misprocessing of the Cystic Fibrosis Transmembrane Conductance Regulator Glycoprotein

John R. Riordan

1505 Human Mitochondrial Complex I in Health and Disease

Jan Smeitink and Lambert van den Heuvel

Original Articles

- 1511 Mutational Analysis of the Defective Protease in Classic Late-Infantile Neuronal Ceroid Lipofuscinosis, a Neurodegenerative Lysosomal Storage Disorder**
David E. Sleat, Rosalie M. Gin, Istvan Sohar, Krystyna Wisniewski, Susan Sklower-Brooks, Raju K. Pullarkat, David N. Palmer, Terry J. Lerner, Rose-Mary Boustany, Peter Uldall, Aristotle N. Siakotos, Robert J. Donnelly, and Peter Lobel
- 1524 Calpainopathy—A Survey of Mutations and Polymorphisms**
I. Richard, C. Roudaut, A. Saenz, R. Pogue, J. E. M. A. Grimbergen, L. V. B. Anderson, C. Beley, A-M Cobo, C. de Diego, B. Eymard, P. Gallano, H. B. Ginjaar, A. Lasa, C. Pollitt, H. Topaloglu, J. A. Urtizberea, M. de Visser, A. van der Kooi, K. Bushby, E. Bakker, A. Lopez de Munain, M. Fardeau, and J. S. Beckmann
- 1541 Complete Genomic Structure and Mutational Spectrum of PHKA2 in Patients with X-Linked Liver Glycogenosis Type I and II**
Jan Hendrickx, Philip Lee, James P. Keating, Dietbrand Carton, Imdadali B. Sardharwalla, Mendel Tuchman, Christiane Baussan, and Patrick J. Willems
- 1550 The Spectrum of Mutations in *TBX3*: Genotype/Phenotype Relationship in Ulnar-Mammary Syndrome**
M. Bamshad, T. Le, W. S. Watkins, M. E. Dixon, B. E. Kramer, A. D. Roeder, J. C. Carey, S. Root, A. Schinzel, L. Van Maldergem, R. J. M. Gardner, R. C. Lin, C. E. Seidman, J. G. Seidman, R. Wallerstein, E. Moran, R. Sutphen, C. E. Campbell, and L. B. Jorde
- 1563 Mutations in the Human UDP-N-Acetylglucosamine 2-Epimerase Gene Define the Disease Sialuria and the Allosteric Site of the Enzyme**
Raili Seppala, Veli-Pekka Lehto, and William A. Gahl
- 1570 Congenital Insensitivity to Pain with Anhidrosis: Novel Mutations in the *TRKA (NTRK1)* Gene Encoding A High-Affinity Receptor for Nerve Growth Factor**
Sek Mardy, Yuichi Miura, Fumio Endo, Ichiro Matsuda, László Sztriha, Philippe Frossard, Allie Moosa, Essam A.R. Ismail, Alfons Macaya, Generoso Andria, Ennio Toscano, William Gibson, Gail E. Graham, and Yasuhiro Indo
- 1580 A Unique Point Mutation in the *PMP22* Gene Is Associated with Charcot-Marie-Tooth Disease and Deafness**
Margaret J. Kovach, Jing-Ping Lin, Simeon Boyadjiev, Kathleen Campbell, Larry Mazzeo, Kristin Herman, Lisa A. Rimer, William Frank, Barbara Llewellyn, Ethylin Wang Jabs, David Gelber, and Virginia E. Kimonis
- 1594 Molecular and Clinical Study of 18 Families with ADCA Type II: Evidence for Genetic Heterogeneity and De Novo Mutation**
P. Giunti, G. Stevanin, P. F. Worth, G. David, A. Brice, and N. W. Wood
- 1604 X-Linked Late-Onset Sensorineural Deafness Caused by a Deletion Involving *OA1* and a Novel Gene Containing WD-40 Repeats**
Maria T. Bassi, Rajkumar S. Ramesar, Barbara Caciotti, Ingrid M. Winship, Alessandro De Grandi, Mirko Riboni, Philip L. Townes, Peter Beighton, Andrea Ballabio, and Giuseppe Borsani
- 1617 Splicing Defects in the Ataxia-Telangiectasia Gene, *ATM*: Underlying Mutations and Consequences**
Sharon N. Teraoka, Milhan Telatar, Sara Becker-Catania, Teresa Liang, Suna Önençüt, Asli Tolun, Luciana Chessa, Özden Sanal, Eva Bernatowska, Richard A. Gatti, and Patrick Concannon
- 1632 High Rate of Mosaicism in Tuberous Sclerosis Complex**
Senno Verhoef, Lida Bakker, Anita M. P. Tempelaars, Arjenne L. W. Hesselting-Janssen, Tadeusz Mazurczak, Sergiusz Jozwiak, Alberto Fois, Gabriella Bartalini, Bernard A. Zonnenberg, Anthonie J. van Essen, Dick Lindhout, Dicky J. J. Halley, and Ans M. W. van den Ouweland

- 1638 Germ-Cell Nondisjunction in Testes Biopsies of Men With Idiopathic Infertility**
William J. Huang, Dolores J. Lamb, Edward D. Kim, Jocelyn de Lara, William W. Lin, Larry I. Lipshultz, and Farideh Z. Bischoff
- 1646 Fine Mapping of the Split-Hand/Split-Foot Locus (*SHFM3*) at 10q24: Evidence for Anticipation and Segregation Distortion**
Rýdvan S. Özen, Bora E. Baysal, Bernie Devlin, Joan E. Farr, Michael Gorry, Garth D. Ehrlich, and Charles W. Richard
- 1655 Identification of a New Locus for Medullary Cystic Disease, on Chromosome 16p12**
Francesco Scolari, Daniela Puzzer, Antonio Amoroso, Gianluca Caridi, Gian Marco Ghiggeri, Rosario Maiorca, Paolo Aridon, Maurizio De Fusco, Andrea Ballabio, and Giorgio Casari
- 1661 Localization of the Gene for Sclerosteosis to the van Buchem Disease–Gene Region on Chromosome 17q12–q21**
Wendy Balemans, Jenneke Van Den Ende, Auristela Freire Paes-Alves, Frederik G. Dikkers, Patrick J. Willems, Filip Vanhoenacker, Neli de Almeida-Melo, Cristiane Freire Alves, Constantine A. Stratakis, Suvimol C. Hill, and Wim Van Hul
- 1670 Assessing the Feasibility of Linkage Disequilibrium Methods for Mapping Complex Traits: An Initial Screen for Bipolar Disorder Loci on Chromosome 18**
Michael A. Escamilla, L. Alison McInnes, Mitzi Spesny, Victor I. Reus, Susan K. Service, Norito Shimayoshi, David J. Tyler, Sandra Silva, Julio Molina, Alvaro Gallegos, Luis Meza, Maria L. Cruz, Steven Batki, Sophia Vinogradov, Thomas Neylan, Jasmine B. Nguyen, Eduardo Fournier, Carmen Araya, Samuel H. Barondes, Pedro Leon, Lodewijk A. Sandkuijl, and Nelson B. Freimer
- 1679 Homozygosity Mapping of the Achromatopsia Locus in the Pingelapese**
Jeffrey D. Winick, Maude L. Blundell, Brandi L. Galke, Ambar A. Salam, Suzanne M. Leal, and Maria Karayiorgou
- 1686 Human Pedigree-Based Quantitative-Trait–Locus Mapping: Localization of Two Genes Influencing HDL-Cholesterol Metabolism**
Laura Almasy, James E. Hixson, David L. Rainwater, Shelley Cole, Jeff T. Williams, Michael C. Mahaney, John L. VandeBerg, Michael P. Stern, Jean W. MacCluer, and John Blangero
- 1694 An Extreme-Sib-Pair Genome Scan for Genes Regulating Blood Pressure**
Xiping Xu, John J. Rogus, Henry A. Terwedow, Jianhua Yang, Zhaoxi Wang, Changzhong Chen, Tianhua Niu, Binyan Wang, Hengqiu Xu, Scott Weiss, Nicholas J. Schork, and Zhian Fang
- 1702 A Chromosomal Duplication Map of Malformations: Regions of Suspected Haplo- and Triplolethality—and Tolerance of Segmental Aneuploidy—in Humans**
Carole Brewer, Susan Holloway, Paul Zawalynski, Albert Schinzel, and David FitzPatrick
- 1709 Tracing the Origin of HLA-DRB1 Alleles by Microsatellite Polymorphism**
Tomas F. Bergström, Hans Engkvist, Rikard Erlandsson, Agnetha Josefsson, Steven J. Mack, Henry A. Erlich, and Ulf Gyllensten
- 1719 The Role of Community Review in Evaluating the Risks of Human Genetic Variation Research**
Morris W. Foster, Richard R. Sharp, William L. Freeman, Michelle Chino, Deborah Bernsten, and Thomas H. Carter
- 1728 Linkage-Disequilibrium Mapping of Disease Genes by Reconstruction of Ancestral Haplotypes in Founder Populations**
S. K. Service, D. W. Temple Lang, N. B. Freimer, and L. A. Sandkuijl
- 1739 On the Assessment of Statistical Significance in Disease-Gene Discovery**
Lue Ping Zhao, Ross Prentice, Fumin Shen, and Li Hsu

1754 Sibling-Based Tests of Linkage and Association for Quantitative Traits

David B. Allison, Moonseong Heo, Norman Kaplan, and Eden R. Martin

1765 Disequilibrium Mapping of a Quantitative-Trait Locus in an Expanding Population

Montgomery Slatkin

Letters to the Editor**1775 Mutations of the *TIGR/MYOC* Gene in Primary Open-Angle Glaucoma in Korea**

Sung-Joo Kim Yoon, Hae-Suk Kim, Joung-Il Moon, Jung Min Lim, and Choun-Ki Joo

1778 Evidence for the Genetic Heterogeneity of Nephropathic Phenotypes Associated with Denys-Drash and Frasier Syndromes

A. B. Koziell, R. Grundy, T. M. Barratt, and P. Scambler

1781 Rett Syndrome in a Boy with a 47,XXY Karyotype

José Salomão Schwartzman, Mayana Zatz, Luciana dos Reis Vasquez, Raquel Ribeiro Gomes, Célia P. Koiffmann, Cintia Fridman, and Priscilla Guimarães Otto

1785 Combining the Sibling Disequilibrium Test and Transmission/Disequilibrium Test for Multiallelic Markers

David Curtis, Michael B. Miller, and Pak C. Sham

Book Reviews**1787 *Mathematical and Statistical Methods for Genetic Analysis*. By Kenneth Lange**

Reviewed by Daniel Schaid

1788 *Biology of Aging: Observations and Principles*, 2d ed. By Robert Arking

Reviewed by Caleb E. Finch

Announcements**1789 Employment Opportunity; Symposia; Cell Repository; Call for Submissions****Errata****1791 A Gene on Chromosome 11q23 Coding for a Putative Glucose- 6-Phosphate Translocase Is Mutated in Glycogen-Storage Disease Types Ib and Ic**

Veiga-da-Cunha et al. (October 1998 [63: 976-983]).

1791 Gaucher Disease: The N370S Mutation in Ashkenazi Jewish and Spanish Patients Has a Common Origin and Arose Several Thousand Years Ago

Díaz et al. (April 1999 [64: 1233-1238]).

1792 Author Index for Volume 64**1802 Subject Index for Volume 64****1811 Contents of Volume 64****Information for Contributors**