

Supplementary References

- S1. Aitman TJ, Dong R, Vyse TJ, Norsworthy PJ, Johnson MD, et al. 2006. Copy number polymorphism in *Fcgr3* predisposes to glomerulonephritis in rats and humans. *Nature* 439: 851-5
- S2. Antonarakis SE, Kazazian HH, Tuddenham EG. 1995. Molecular etiology of factor VIII deficiency in hemophilia A. *Hum. Mutat.* 5: 1-22
- S3. Bauters M, Van Esch H, Friez MJ, Boespflug-Tanguy O, Zenker M, et al. 2008. Nonrecurrent *MECP2* duplications mediated by genomic architecture-driven DNA breaks and break-induced replication repair. *Genome Res.* 18: 847-58
- S4. Bayes M, Magano LF, Rivera N, Flores R, Perez Jurado LA. 2003. Mutational mechanisms of Williams-Beuren syndrome deletions. *Am. J. Hum. Genet.* 73: 131-51
- S5. Beutler E, Gelbart T. 1994. Erroneous assignment of Gaucher disease genotype as a consequence of a complete gene deletion. *Hum. Mutat.* 4: 212-6
- S6. Bi W, Sapir T, Shchelochkov OA, Zhang F, Withers MA, et al. 2009. Increased LIS1 expression affects human and mouse brain development. *Nat. Genet.* (in press)
- S7. Bien-Willner GA, Stankiewicz P, Lupski JR. 2007. SOX9cre1, a *cis*-acting regulatory element located 1.1 Mb upstream of *SOX9*, mediates its enhancement through the SHH pathway. *Hum. Mol. Genet.* 16: 1143-56
- S8. Bondeson ML, Dahl N, Malmgren H, Kleijer WJ, Tonnesen T, et al. 1995. Inversion of the *IDS* gene resulting from recombination with *IDS*-related sequences is a common cause of the Hunter syndrome. *Hum. Mol. Genet.* 4: 615-21
- S9. Braga S, Phillips JA, 3rd, Joss E, Schwarz H, Zuppinger K. 1986. Familial growth hormone deficiency resulting from a 7.6 kb deletion within the growth hormone gene cluster. *Am. J. Med. Genet.* 25: 443-52
- S10. Cardoso C, Leventer RJ, Ward HL, Toyo-Oka K, Chung J, et al. 2003. Refinement of a 400-kb critical region allows genotypic differentiation between isolated lissencephaly, Miller-Dieker syndrome, and other phenotypes secondary to deletions of 17p13.3. *Am. J. Hum. Genet.* 72: 918-30
- S11. Chance PF, Alderson MK, Leppig KA, Lensch MW, Matsunami N, et al. 1993. DNA deletion associated with hereditary neuropathy with liability to pressure palsies. *Cell* 72: 143-51
- S12. Chartier-Harlin MC, Kachergus J, Roumier C, Mouroux V, Douay X, et al. 2004. Alpha-synuclein locus duplication as a cause of familial Parkinson's disease. *Lancet* 364: 1167-9
- S13. Chen KS, Manian P, Koeuth T, Potocki L, Zhao Q, et al. 1997. Homologous recombination of a flanking repeat gene cluster is a mechanism for a common contiguous gene deletion syndrome. *Nat. Genet.* 17: 154-63

- S14. Combes P, Bonnet-Dupeyron MN, Gauthier-Barichard F, Schiffmann R, Bertini E, et al. 2006. *PLP1* and *GPM6B* intragenic copy number analysis by MAPH in 262 patients with hypomyelinating leukodystrophies: Identification of one partial triplication and two partial deletions of *PLP1*. *Neurogenetics* 7: 31-7
- S15. del Gaudio D, Fang P, Scaglia F, Ward PA, Craigen WJ, et al. 2006. Increased *MECP2* gene copy number as the result of genomic duplication in neurodevelopmentally delayed males. *Genet. Med.* 8: 784-92
- S16. Edelmann L, Pandita RK, Spiteri E, Funke B, Goldberg R, et al. 1999. A common molecular basis for rearrangement disorders on chromosome 22q11. *Hum. Mol. Genet.* 8: 1157-67
- S17. Ensenauer RE, Adeyinka A, Flynn HC, Michels VV, Lindor NM, et al. 2003. Microduplication 22q11.2, an emerging syndrome: clinical, cytogenetic, and molecular analysis of thirteen patients. *Am. J. Hum. Genet.* 73: 1027-40
- S18. Fanciulli M, Norsworthy PJ, Petretto E, Dong R, Harper L, et al. 2007. *FCGR3B* copy number variation is associated with susceptibility to systemic, but not organ-specific, autoimmunity. *Nat. Genet.* 39: 721-3
- S19. Farrer M, Kachergus J, Forno L, Lincoln S, Wang DS, et al. 2004. Comparison of kindreds with parkinsonism and alpha-synuclein genomic multiplications. *Ann. Neurol.* 55: 174-9
- S20. Fellermann K, Stange DE, Schaeffeler E, Schmalzl H, Wehkamp J, et al. 2006. A chromosome 8 gene-cluster polymorphism with low human beta-defensin 2 gene copy number predisposes to Crohn disease of the colon. *Am. J. Hum. Genet.* 79: 439-48
- S21. Froyen G, Corbett M, Vandewalle J, Jarvela I, Lawrence O, et al. 2008. Submicroscopic duplications of the hydroxysteroid dehydrogenase *HSD17B10* and the E3 ubiquitin ligase *HUWE1* are associated with mental retardation. *Am. J. Hum. Genet.* 82: 432-43
- S22. Fuchs J, Nilsson C, Kachergus J, Munz M, Larsson EM, et al. 2007. Phenotypic variation in a large Swedish pedigree due to *SNCA* duplication and triplication. *Neurology* 68: 916-22
- S23. Gonzalez E, Kulkarni H, Bolivar H, Mangano A, Sanchez R, et al. 2005. The influence of *CCL3L1* gene-containing segmental duplications on HIV-1/AIDS susceptibility. *Science* 307: 1434-40
- S24. Goossens M, Brauner R, Czernichow P, Duquesnoy P, Rappaport R. 1986. Isolated growth hormone (GH) deficiency type 1A associated with a double deletion in the human *GH* gene cluster. *J. Clin. Endocrinol. Metab.* 62: 712-6
- S25. Higgs DR, Pressley L, Old JM, Hunt DM, Clegg JB, et al. 1979. Negro alpha-thalassaemia is caused by deletion of a single alpha-globin gene. *Lancet* 2: 272-6
- S26. Hollox EJ, Huffmeier U, Zeeuwen PL, Palla R, Lascorz J, et al. 2008. Psoriasis is associated with increased beta-defensin genomic copy number. *Nat. Genet.* 40:

- 23-5
- S27. Ibanez P, Bonnet AM, Debarges B, Lohmann E, Tison F, et al. 2004. Causal relation between alpha-synuclein gene duplication and familial Parkinson's disease. *Lancet* 364: 1169-71
- S28. Inoue K, Osaka H, Thurston VC, Clarke JT, Yoneyama A, et al. 2002. Genomic rearrangements resulting in *PLP1* deletion occur by nonhomologous end joining and cause different dysmyelinating phenotypes in males and females. *Am. J. Hum. Genet.* 71: 838-53
- S29. Kan YW, Golbus MS, Trecartin R. 1975. Prenatal diagnosis of homozygous beta-thalassaemia. *Lancet* 2: 790-1
- S30. Knight MA, Hernandez D, Diede SJ, Dauwerse HG, Rafferty I, et al. 2008. A duplication at chromosome 11q12.2-11q12.3 is associated with spinocerebellar ataxia type 20. *Hum. Mol. Genet.* 17: 3847-53
- S31. Konrad M, Saunier S, Heidet L, Silbermann F, Benessy F, et al. 1996. Large homozygous deletions of the 2q13 region are a major cause of juvenile nephronophthisis. *Hum. Mol. Genet.* 5: 367-71
- S32. Koolen DA, Vissers LE, Pfundt R, de Leeuw N, Knight SJ, et al. 2006. A new chromosome 17q21.31 microdeletion syndrome associated with a common inversion polymorphism. *Nat. Genet.* 38: 999-1001
- S33. Kuhn L, Schramm DB, Donninger S, Meddows-Taylor S, Coovadia AH, et al. 2007. African infants' *CCL3* gene copies influence perinatal HIV transmission in the absence of maternal nevirapine. *AIDS* 21: 1753-61
- S34. Kumar RA, KaraMohamed S, Sudi J, Conrad DF, Brune C, et al. 2008. Recurrent 16p11.2 microdeletions in autism. *Hum. Mol. Genet.* 17: 628-38
- S35. Kurotaki N, Shen JJ, Touyama M, Kondoh T, Visser R, et al. 2005. Phenotypic consequences of genetic variation at hemizygous alleles: Sotos syndrome is a contiguous gene syndrome incorporating coagulation factor twelve (*FXII*) deficiency. *Genet. Med.* 7: 479-83
- S36. Le Marechal C, Masson E, Chen JM, Morel F, Ruszniewski P, et al. 2006. Hereditary pancreatitis caused by triplication of the trypsinogen locus. *Nat. Genet.* 38: 1372-4
- S37. Lee JA, Carvalho CM, Lupski JR. 2007. A DNA replication mechanism for generating nonrecurrent rearrangements associated with genomic disorders. *Cell* 131: 1235-47
- S38. Lee JA, Inoue K, Cheung SW, Shaw CA, Stankiewicz P, Lupski JR. 2006. Role of genomic architecture in *PLP1* duplication causing Pelizaeus-Merzbacher disease. *Hum. Mol. Genet.* 15: 2250-65
- S39. Lifton RP, Dluhy RG, Powers M, Rich GM, Cook S, et al. 1992. A chimaeric 11 beta-hydroxylase/aldosterone synthase gene causes glucocorticoid-remediable aldosteronism and human hypertension. *Nature* 355: 262-5
- S40. Lupski JR, Chance, P.F. 2005. Hereditary motor and sensory neuropathies

- involving altered dosage or mutation of *PMP22*: The CMT1A duplication and HNPP deletion. In *Peripheral Neuropathy*, ed. PJ Dyck, Thomas, P.K., pp. 1659-80. Philadelphia: Elsevier Science
- S41. Lupski JR, de Oca-Luna RM, Slaugenhaupt S, Pentao L, Guzzetta V, et al. 1991. DNA duplication associated with Charcot-Marie-Tooth disease type 1A. *Cell* 66: 219-32
- S42. Marshall CR, Noor A, Vincent JB, Lionel AC, Feuk L, et al. 2008. Structural variation of chromosomes in autism spectrum disorder. *Am. J. Hum. Genet.* 82: 477-88
- S43. Matthijs G, Schollen E, Legius E, Devriendt K, Goemans N, et al. 1996. Unusual molecular findings in autosomal recessive spinal muscular atrophy. *J. Med. Genet.* 33: 469-74
- S44. McCarroll SA, Huett A, Kuballa P, Chilewski SD, Landry A, et al. 2008. Deletion polymorphism upstream of *IRGM* associated with altered *IRGM* expression and Crohn's disease. *Nat. Genet.* 40: 1107-12
- S45. Morrow EM, Yoo SY, Flavell SW, Kim TK, Lin Y, et al. 2008. Identifying autism loci and genes by tracing recent shared ancestry. *Science* 321: 218-23
- S46. Nathans J, Piantanida TP, Eddy RL, Shows TB, Hogness DS. 1986. Molecular genetics of inherited variation in human color vision. *Science* 232: 203-10
- S47. Ou Z, Berg JS, Yonath H, Enciso VB, Miller DT, et al. 2008. Microduplications of 22q11.2 are frequently inherited and are associated with variable phenotypes. *Genet. Med.* 10: 267-77
- S48. Padiath QS, Saigoh K, Schiffmann R, Asahara H, Yamada T, et al. 2006. Lamin B1 duplications cause autosomal dominant leukodystrophy. *Nat. Genet.* 38: 1114-23
- S49. Potocki L, Bi W, Treadwell-Deering D, Carvalho CM, Eifert A, et al. 2007. Characterization of Potocki-Lupski syndrome (dup(17)(p11.2p11.2)) and delineation of a dosage-sensitive critical interval that can convey an autism phenotype. *Am. J. Hum. Genet.* 80: 633-49
- S50. Reiner O, Carrozzo R, Shen Y, Wehnert M, Faustinella F, et al. 1993. Isolation of a Miller-Dieker lissencephaly gene containing G protein beta-subunit-like repeats. *Nature* 364: 717-21
- S51. Rodrigues NR, Owen N, Talbot K, Ignatius J, Dubowitz V, Davies KE. 1995. Deletions in the survival motor neuron gene on 5q13 in autosomal recessive spinal muscular atrophy. *Hum. Mol. Genet.* 4: 631-4
- S52. Rovelet-Lecrux A, Hannequin D, Raux G, Le Meur N, Laquerriere A, et al. 2006. APP locus duplication causes autosomal dominant early-onset Alzheimer disease with cerebral amyloid angiopathy. *Nat. Genet.* 38: 24-6
- S53. Saunier S, Calado J, Benessy F, Silbermann F, Heilig R, et al. 2000. Characterization of the *NPHP1* locus: mutational mechanism involved in deletions in familial juvenile nephronophthisis. *Am. J. Hum. Genet.* 66: 778-89

- S54. Sebat J, Lakshmi B, Malhotra D, Troge J, Lese-Martin C, et al. 2007. Strong association of de novo copy number mutations with autism. *Science* 316: 445-9
- S55. Shaikh TH, Kurahashi H, Saitta SC, O'Hare AM, Hu P, et al. 2000. Chromosome 22-specific low copy repeats and the 22q11.2 deletion syndrome: genomic organization and deletion endpoint analysis. *Hum. Mol. Genet.* 9: 489-501
- S56. Shapiro LJ, Yen P, Pomerantz D, Martin E, Rolewic L, Mohandas T. 1989. Molecular studies of deletions at the human steroid sulfatase locus. *Proc. Natl. Acad. Sci. USA* 86: 8477-81
- S57. Sharp AJ, Hansen S, Selzer RR, Cheng Z, Regan R, et al. 2006. Discovery of previously unidentified genomic disorders from the duplication architecture of the human genome. *Nat. Genet.* 38: 1038-42
- S58. Sharp AJ, Mefford HC, Li K, Baker C, Skinner C, et al. 2008. A recurrent 15q13.3 microdeletion syndrome associated with mental retardation and seizures. *Nat. Genet.* 40: 322-8
- S59. Shaw-Smith C, Pittman AM, Willatt L, Martin H, Rickman L, et al. 2006. Microdeletion encompassing *MAPT* at chromosome 17q21.3 is associated with developmental delay and learning disability. *Nat. Genet.* 38: 1032-7
- S60. Shy ME, Scavina MT, Clark A, Krajewski KM, Li J, et al. 2006. T118M *PMP22* mutation causes partial loss of function and HNPP-like neuropathy. *Ann. Neurol.* 59: 358-64
- S61. Singleton AB, Farrer M, Johnson J, Singleton A, Hague S, et al. 2003. alpha-Synuclein locus triplication causes Parkinson's disease. *Science* 302: 841
- S62. Somerville MJ, Mervis CB, Young EJ, Seo EJ, del Campo M, et al. 2005. Severe expressive-language delay related to duplication of the Williams-Beuren locus. *N. Engl. J. Med.* 353: 1694-701
- S63. Stefansson H, Rujescu D, Cichon S, Pietilainen OP, Ingason A, et al. 2008. Large recurrent microdeletions associated with schizophrenia. *Nature* 455: 232-6
- S64. The International Schizophrenia Consortium. 2008. Rare chromosomal deletions and duplications increase risk of schizophrenia. *Nature* 455: 237-41
- S65. Van Esch H, Bauters M, Ignatius J, Jansen M, Raynaud M, et al. 2005. Duplication of the *MECP2* region is a frequent cause of severe mental retardation and progressive neurological symptoms in males. *Am. J. Hum. Genet.* 77: 442-53
- S66. Velagaleti GV, Bien-Willner GA, Northup JK, Lockhart LH, Hawkins JC, et al. 2005. Position effects due to chromosome breakpoints that map approximately 900 Kb upstream and approximately 1.3 Mb downstream of *SOX9* in two patients with campomelic dysplasia. *Am. J. Hum. Genet.* 76: 652-62
- S67. Walsh T, McClellan JM, McCarthy SE, Addington AM, Pierce SB, et al. 2008. Rare structural variants disrupt multiple genes in neurodevelopmental pathways in schizophrenia. *Science* 320: 539-43
- S68. Weiss LA, Shen Y, Korn JM, Arking DE, Miller DT, et al. 2008. Association between microdeletion and microduplication at 16p11.2 and autism. *N. Engl. J.*

- Med.* 358: 667-75
- S69. Willcocks LC, Lyons PA, Clatworthy MR, Robinson JI, Yang W, et al. 2008. Copy number of *FCGR3B*, which is associated with systemic lupus erythematosus, correlates with protein expression and immune complex uptake. *J. Exp. Med.* 205: 1573-82
- S70. Wilson PJ, Suthers GK, Callen DF, Baker E, Nelson PV, et al. 1991. Frequent deletions at Xq28 indicate genetic heterogeneity in Hunter syndrome. *Hum. Genet.* 86: 505-8
- S71. Wolf NI, Sistermans EA, Cundall M, Hobson GM, Davis-Williams AP, et al. 2005. Three or more copies of the proteolipid protein gene *PLPI* cause severe Pelizaeus-Merzbacher disease. *Brain* 128: 743-51
- S72. Wraith JE, Cooper A, Thornley M, Wilson PJ, Nelson PV, et al. 1991. The clinical phenotype of two patients with a complete deletion of the iduronate-2-sulphatase gene (mucopolysaccharidosis II--Hunter syndrome). *Hum. Genet.* 87: 205-6
- S73. Yan J, Bi W, Lupski JR. 2007. Penetrance of craniofacial anomalies in mouse models of Smith-Magenis syndrome is modified by genomic sequence surrounding *Rai1*: not all null alleles are alike. *Am. J. Hum. Genet.* 80: 518-25
- S74. Yang Y, Chung EK, Wu YL, Savelli SL, Nagaraja HN, et al. 2007. Gene copy-number variation and associated polymorphisms of complement component C4 in human systemic lupus erythematosus (SLE): low copy number is a risk factor for and high copy number is a protective factor against SLE susceptibility in European Americans. *Am. J. Hum. Genet.* 80: 1037-54
- S75. Yu S, Cox K, Friend K, Smith S, Buchheim R, et al. 2008. Familial 22q11.2 duplication: a three-generation family with a 3-Mb duplication and a familial 1.5-Mb duplication. *Clin. Genet.* 73: 160-4