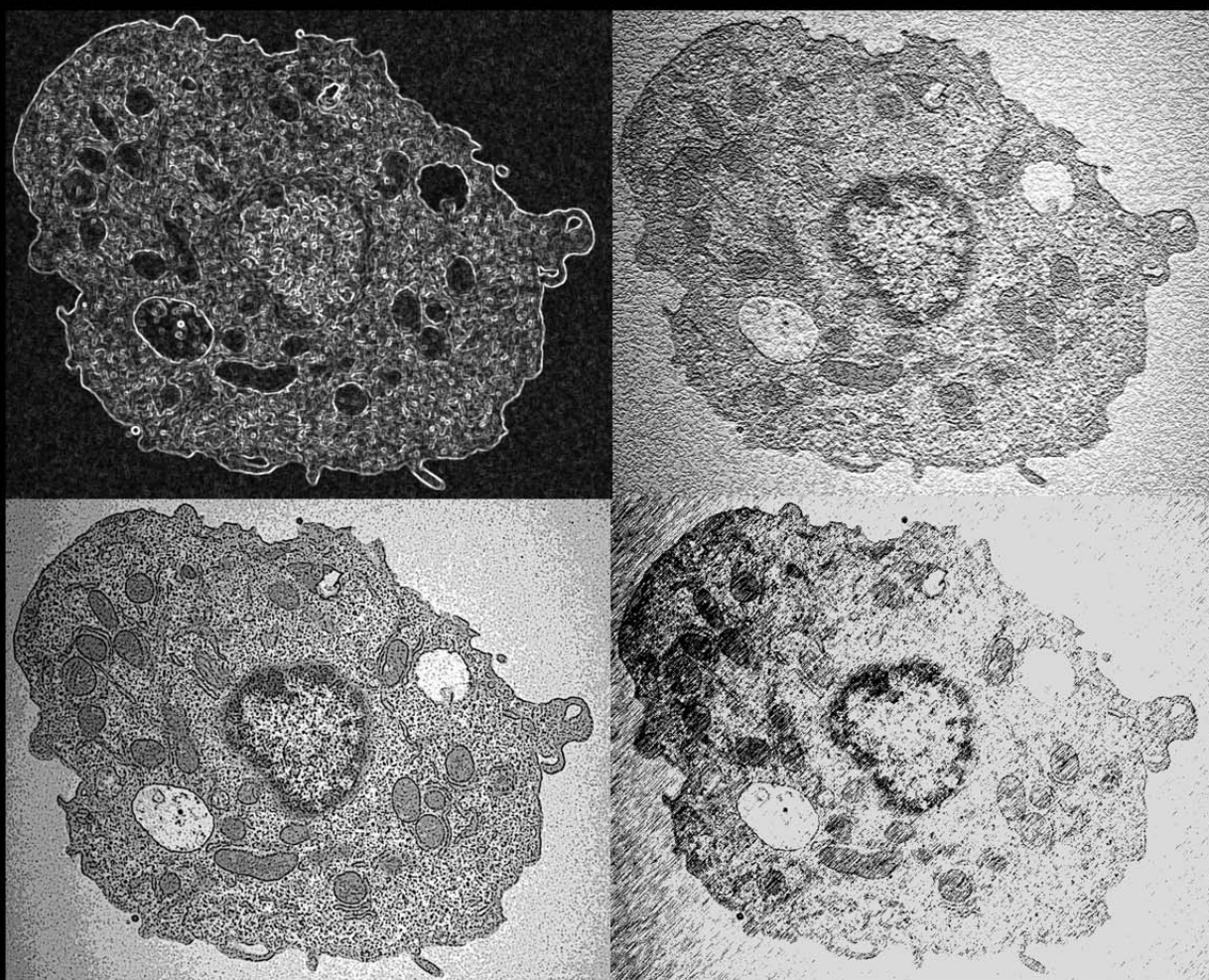


Caracterització de mutacions causants de la malaltia de Gaucher. Aproximació a una teràpia gènica.



Anna Diaz Font
2006

Bibliografia

A

- Abrahamov, A., Elstein, D., Gross-Tsur, V., Farber, B., Glaser, Y., Hadas-Halpern, I., Ronen, S., Tafakjdi, M., Horowitz, M., and Zimran, A., 1995, Gaucher's disease variant characterised by progressive calcification of heart valves and unique genotype, *Lancet* **346**(8981):1000-3.
- Aerts, J. M., Hollak, C., Boot, R., and Groener, A., 2003, Biochemistry of glycosphingolipid storage disorders: implications for therapeutic intervention, *Philos Trans R Soc Lond B Biol Sci* **358**(1433):905-14.
- Amaral, O., Marcao, A., Pinto, E., Zimran, A., and Miranda, M. C., 1997, Distinct haplotype in non-Ashkenazi Gaucher patients with N370S mutation, *Blood Cells Mol Dis* **23**(3):415-6.
- Amaral, O., Pinto, E., Fortuna, M., Lacerda, L., and Sa Miranda, M. C., 1996, Type 1 Gaucher disease: identification of N396T and prevalence of glucocerebrosidase mutations in the Portuguese, *Hum Mutat* **8**(3):280-1.
- Amsallem, D., Rodriguez, D., Vanier, M., Khayat, N., Millat, G., Campello, M., Guillaume, C., and Billette De Villemeur, T., 2005, Third case of Gaucher disease with SAP-C deficiency and evaluation of twelve months therapy by miglustat, *J Inherit Metab Dis* **28**(Suppl 1).
- Armstrong, L. C., Komiya, T., Bergman, B. E., Mihara, K., and Bornstein, P., 1997, Metaxin is a component of a preprotein import complex in the outer membrane of the mammalian mitochondrion, *J Biol Chem* **272**(10):6510-8.

B

- Balicki, D., and Beutler, E., 1995, Gaucher disease, *Medicine (Baltimore)* **74**(6):305-23.
- Bantounas, I., Phylactou, L. A., and Uney, J. B., 2004, RNA interference and the use of small interfering RNA to study gene function in mammalian systems, *J Mol Endocrinol* **33**(3):545-57.
- Bar-Am, I., Avivi, L., and Horowitz, M., 1996, Assignment of the human prosaposin gene (PSAP) to 10q22.1 by fluorescence in situ hybridization. Giraffidae, okapi (*Okapia johnstoni*), and giraffe (*Giraffa camelopardalis*): evidence for ancestral telomeres at the okapi polymorphic rob (4;26) fusion site, *Cytogenet Cell Genet* **72**(4):316-8.
- Barak, V., Acker, M., Nisman, B., Kalickman, I., Abrahamov, A., Zimran, A., and Yatziv, S., 1999, Cytokines in Gaucher's disease, *Eur Cytokine Netw* **10**(2):205-10.
- Baralle, M., Baralle, D., De Conti, L., Mattocks, C., Whittaker, J., Knezevich, A., Ffrench-Constant, C., and Baralle, F. E., 2003, Identification of a mutation that perturbs NF1 agene splicing using genomic DNA samples and a minigene assay, *J Med Genet* **40**(3):220-2.
- Baron, R., Neff, L., Louvard, D., and Courtoy, P. J., 1985, Cell-mediated extracellular acidification and bone resorption: evidence for a low pH in resorbing lacunae and localization of a 100-kD lysosomal membrane protein at the osteoclast ruffled border, *J Cell Biol* **101**(6):2210-22.
- Barranger, J. A., Rice, E. O., and Swaney, W. P., 1999, Gene transfer approaches to the lysosomal storage disorders, *Neurochem Res* **24**(4):601-15.
- Barranger, J. M., and Novelli, E. A., 2001, Gene therapy for lysosomal storage disorders, *Expert Opin Biol Ther* **1**(5):857-67.
- Barton, N. W., Furbish, F. S., Murray, G. J., Garfield, M., and Brady, R. O., 1990, Therapeutic response to intravenous infusions of glucocerebrosidase in a patient with Gaucher disease, *Proc Natl Acad Sci U S A* **87**(5):1913-6.
- Beetham, P. R., Kipp, P. B., Sawycky, X. L., Arntzen, C. J., and May, G. D., 1999, A tool for functional plant genomics: chimeric RNA/DNA oligonucleotides cause in vivo gene-specific mutations, *Proc Natl Acad Sci U S A* **96**(15):8774-8.
- Berent, S. L., and Radin, N. S., 1981, Mechanism of activation of glucocerebrosidase by co-beta-glucosidase (glucosidase activator protein), *Biochim Biophys Acta* **664**(3):572-82.
- Bernstein, E., Caudy, A. A., Hammond, S. M., and Hannon, G. J., 2001, Role for a bidentate ribonuclease in the initiation step of RNA interference, *Nature* **409**(6818):363-6.

- Berrobi, A., Wishnitzer, R., and Von-der-Walde, U., 1984, Gaucher's disease: unexpected diagnosis in three patients over seventy years old, *Nouv Rev Fr Hematol* **26**(3):201-3.
- Beutler, E., 1991, Bone marrow transplantation for sickle cell anemia: summarizing comments, *Semin Hematol* **28**(3):263-7.
- Beutler, E., 1992, Gaucher disease: new molecular approaches to diagnosis and treatment, *Science* **256**(5058):794-9.
- Beutler, E., Demina, A., Laubscher, K., Garver, P., Gelbart, T., Balicki, D., and Vaughan, L., 1995, The clinical course of treated and untreated Gaucher disease. A study of 45 patients, *Blood Cells Mol Dis* **21**(2):86-108.
- Beutler, E., and Gelbart, T., 1994, Erroneous assignment of Gaucher disease genotype as a consequence of a complete gene deletion, *Hum Mutat* **4**(3):212-6.
- Beutler, E., Gelbart, T., Kuhl, W., Sorge, J., and West, C., 1991, Identification of the second common Jewish Gaucher disease mutation makes possible population-based screening for the heterozygous state, *Proc Natl Acad Sci U S A* **88**(23):10544-7.
- Beutler, E., Gelbart, T., Kuhl, W., Zimran, A., and West, C., 1992a, Mutations in Jewish patients with Gaucher disease, *Blood* **79**(7):1662-6.
- Beutler, E., Gelbart, T., and Scott, C. R., 2005, Hematologically important mutations: Gaucher disease, *Blood Cells Mol Dis* **35**(3):355-64.
- Beutler, E., and Grabowski, G. A., 2001, Gaucher disease, *Scriver*.
- Beutler, E., and Kuhl, W., 1970a, Detection of the defect of Gaucher's disease and its carrier state in peripheral-blood leucocytes, *Lancet* **1**(7647):612-3.
- Beutler, E., and Kuhl, W., 1970b, The diagnosis of the adult type of Gaucher's disease and its carrier state by demonstration of deficiency of beta-glucosidase activity in peripheral blood leukocytes, *J Lab Clin Med* **76**(5):747-55.
- Beutler, E., Kuhl, W., Trinidad, F., Teplitz, R., and Nadler, H., 1971, Beta-glucosidase activity in fibroblasts from homozygotes and heterozygotes for Gaucher's disease, *Am J Hum Genet* **23**(1):62-6.
- Beutler, E., Nguyen, N. J., Henneberger, M. W., Smolec, J. M., McPherson, R. A., West, C., and Gelbart, T., 1993, Gaucher disease: gene frequencies in the Ashkenazi Jewish population, *Am J Hum Genet* **52**(1):85-8.
- Beutler, E., West, C., and Gelbart, T., 1992b, Polymorphisms in the human glucocerebrosidase gene, *Genomics* **12**(4):795-800.
- Bitton, A., Etzell, J., Grenert, J. P., and Wang, E., 2004, Erythrophagocytosis in Gaucher cells, *Arch Pathol Lab Med* **128**(10):1191-2.
- Bodennec, J., Pelled, D., Riebeling, C., Trajkovic, S., and Futerman, A. H., 2002, Phosphatidylcholine synthesis is elevated in neuronal models of Gaucher disease due to direct activation of CTP:phosphocholine cytidyltransferase by glucosylceramide, *Faseb J* **16**(13):1814-6.
- Bohlega, S., Kambouris, M., Shahid, M., Al Homsy, M., and Al Sous, W., 2000, Gaucher disease with oculomotor apraxia and cardiovascular calcification (Gaucher type IIIC), *Neurology* **54**(1):261-3.
- Boot, R. G., Verhoek, M., de Fost, M., Hollak, C. E., Maas, M., Bleijlevens, B., van Breemen, M. J., van Meurs, M., Boven, L. A., Laman, J. D., Moran, M. T., Cox, T. M., and Aerts, J. M., 2004, Marked elevation of the chemokine CCL18/PARC in Gaucher disease: a novel surrogate marker for assessing therapeutic intervention, *Blood* **103**(1):33-9.
- Boven, L. A., van Meurs, M., Boot, R. G., Mehta, A., Boon, L., Aerts, J. M., and Laman, J. D., 2004, Gaucher cells demonstrate a distinct macrophage phenotype and resemble alternatively activated macrophages, *Am J Clin Pathol* **122**(3):359-69.
- Brady, R. O., 2005, Enzyme Replacement for Lysosomal Diseases, *Annu Rev Med*.
- Brady, R. O., Kanfer, J. N., and Shapiro, D., 1965, Metabolism Of Glucocerebrosides. Ii. Evidence Of An Enzymatic Deficiency In Gaucher's Disease, *Biochem Biophys Res Commun* **18**:221-5.
- Brady, R. O., Murray, G. J., Moore, D. F., and Schiffmann, R., 2001, Enzyme replacement therapy in Fabry disease, *J Inherit Metab Dis* **24 Suppl 2**:18-24; discussion 11-2.
-

- Brady, R. O., Pentchev, P. G., Gal, A. E., Hibbert, S. R., and Dekaban, A. S., 1974, Replacement therapy for inherited enzyme deficiency. Use of purified glucocerebrosidase in Gaucher's disease, *N Engl J Med* **291**(19):989-93.
- Brill, N., Mandelbaum, F., and Libman, E., 1905, Primary splenomegaly-Gaucher type. Report on one of few cases occurring in a single generation of one family., *Am J Med Sci* **129**(491).
- Brummelkamp, T. R., Bernards, R., and Agami, R., 2002, A system for stable expression of short interfering RNAs in mammalian cells, *Science* **296**(5567):550-3.
- Burger, K. N., van der Bijl, P., and van Meer, G., 1996, Topology of sphingolipid galactosyltransferases in ER and Golgi: transbilayer movement of monohexosyl sphingolipids is required for higher glycosphingolipid biosynthesis, *J Cell Biol* **133**(1):15-28.
- Burns, G. F., Cawley, J. C., Flemans, R. J., Higgy, K. E., Worman, C. P., Barker, C. R., Roberts, B. E., and Hayhoe, F. G., 1977, Surface marker and other characteristics of Gaucher's cells, *J Clin Pathol* **30**(10):981-8.

C

- Cantz, M., and Kresse, H., 1974, Sandhoff disease: defective glycosaminoglycan catabolism in cultured fibroblasts and its correction by beta-N-acetylhexosaminidase, *Eur J Biochem* **47**(3):581-90.
- Chabas, A., Cormand, B., Balcells, S., Gonzalez-Duarte, R., Casanova, C., Colomer, J., Vilageliu, L., and Grinberg, D., 1996, Neuronopathic and non-neuronopathic presentation of Gaucher disease in patients with the third most common mutation (D409H) in Spain, *J Inherit Metab Dis* **19**(6):798-800.
- Chabas, A., Cormand, B., Grinberg, D., Burguera, J. M., Balcells, S., Merino, J. L., Mate, I., Sobrino, J. A., Gonzalez-Duarte, R., and Vilageliu, L., 1995, Unusual expression of Gaucher's disease: cardiovascular calcifications in three sibs homozygous for the D409H mutation, *J Med Genet* **32**(9):740-2.
- Chabas, A., Gort, L., Diaz-Font, A., Montfort, M., Santamaria, R., Cidras, M., Grinberg, D., and Vilageliu, L., 2005, Perinatal lethal phenotype with generalized ichthyosis in a type 2 Gaucher disease patient with the [L444P;E326K]/P182L genotype: effect of the E326K change in neonatal and classic forms of the disease, *Blood Cells Mol Dis* **35**(2):253-8.
- Charrow, J., Andersson, H. C., Kaplan, P., Kolodny, E. H., Mistry, P., Pastores, G., Rosenbloom, B. E., Scott, C. R., Wappner, R. S., Weinreb, N. J., and Zimran, A., 2000, The Gaucher registry: demographics and disease characteristics of 1698 patients with Gaucher disease, *Arch Intern Med* **160**(18):2835-43.
- Check, E., 2005, A crucial test, *Nat Med* **11**(3):243-4.
- Chiavegatto, S., Sun, J., Nelson, R. J., and Schnaar, R. L., 2000, A functional role for complex gangliosides: motor deficits in GM2/GD2 synthase knockout mice, *Exp Neurol* **166**(2):227-34.
- Cohen, T., Ravid, L., Altman, N., Madar-Shapiro, L., Fein, A., Weil, M., and Horowitz, M., 2004, Conservation of expression and alternative splicing in the prosaposin gene, *Brain Res Mol Brain Res* **129**(1-2):8-19.
- Cole-Strauss, A., Gamper, H., Holloman, W. K., Munoz, M., Cheng, N., and Kmiec, E. B., 1999, Targeted gene repair directed by the chimeric RNA/DNA oligonucleotide in a mammalian cell-free extract, *Nucleic Acids Res* **27**(5):1323-30.
- Cole-Strauss, A., Yoon, K., Xiang, Y., Byrne, B. C., Rice, M. C., Gryn, J., Holloman, W. K., and Kmiec, E. B., 1996, Correction of the mutation responsible for sickle cell anemia by an RNA-DNA oligonucleotide, *Science* **273**(5280):1386-9.
- Conzelmann, E., and Sandhoff, K., 1983, Partial enzyme deficiencies: residual activities and the development of neurological disorders, *Dev Neurosci* **6**(1):58-71.
- Cormand, B., Diaz, A., Grinberg, D., Chabas, A., and Vilageliu, L., 2000, A new gene-pseudogene fusion allele due to a recombination in intron 2 of the glucocerebrosidase gene causes Gaucher disease, *Blood Cells Mol Dis* **26**(5):409-16.

- Cormand, B., Grinberg, D., Gort, L., Chabas, A., and Vilageliu, L., 1998a, Molecular analysis and clinical findings in the Spanish Gaucher disease population: putative haplotype of the N370S ancestral chromosome, *Hum Mutat* **11**(4):295-305.
- Cormand, B., Grinberg, D., Gort, L., Fiumara, A., Barone, R., Vilageliu, L., and Chabas, A., 1997a, Two new mild homozygous mutations in Gaucher disease patients: clinical signs and biochemical analyses, *Am J Med Genet* **70**(4):437-43.
- Cormand, B., Harboe, T. L., Gort, L., Campoy, C., Blanco, M., Chamoles, N., Chabas, A., Vilageliu, L., and Grinberg, D., 1998b, Mutation analysis of Gaucher disease patients from Argentina: high prevalence of the RecNcil mutation, *Am J Med Genet* **80**(4):343-51.
- Cormand, B., Montfort, M., Chabas, A., Vilageliu, L., and Grinberg, D., 1997b, Genetic fine localization of the beta-glucocerebrosidase (GBA) and prosaposin (PSAP) genes: implications for Gaucher disease, *Hum Genet* **100**(1):75-9.
- Cormand, B., Vilageliu, L., Burguera, J. M., Balcells, S., Gonzalez-Duarte, R., Grinberg, D., and Chabas, A., 1995, Gaucher disease in Spanish patients: analysis of eight mutations, *Hum Mutat* **5**(4):303-9.
- Coste, H., Martel, M. B., and Got, R., 1986, Topology of glucosylceramide synthesis in Golgi membranes from porcine submaxillary glands, *Biochim Biophys Acta* **858**(1):6-12.

D

- Dahl, N., Lagerstrom, M., Erikson, A., and Pettersson, U., 1990, Gaucher disease type III (Norrbottnian type) is caused by a single mutation in exon 10 of the glucocerebrosidase gene, *Am J Hum Genet* **47**(2):275-8.
- Danckwardt, S., Neu-Yilik, G., Thermann, R., Frede, U., Hentze, M. W., and Kulozik, A. E., 2002, Abnormally spliced beta-globin mRNAs: a single point mutation generates transcripts sensitive and insensitive to nonsense-mediated mRNA decay, *Blood* **99**(5):1811-6.
- de Alba, E., Weiler, S., and Tjandra, N., 2003, Solution structure of human saposin C: pH-dependent interaction with phospholipid vesicles, *Biochemistry* **42**(50):14729-40.
- De Duve, C., Pressman, B. C., Gianetto, R., Wattiaux, R., and Appelmans, F., 1955, Tissue fractionation studies. 6. Intracellular distribution patterns of enzymes in rat-liver tissue, *Biochem J* **60**(4):604-17.
- Deguchi, H., Fernandez, J. A., Pabinger, I., Heit, J. A., and Griffin, J. H., 2001, Plasma glucosylceramide deficiency as potential risk factor for venous thrombosis and modulator of anticoagulant protein C pathway, *Blood* **97**(7):1907-14.
- Dell'Angelica, E. C., Mullins, C., Caplan, S., and Bonifacino, J. S., 2000, Lysosome-related organelles, *Faseb J* **14**(10):1265-78.
- Den Tandt, W. R., and Van Hoof, F., 1996, Plasma methylumbelliferyl-tetra-N-acetyl-beta-D-chitotetraoside hydrolase as a parameter during treatment of gaucher patients, *Biochem Mol Med* **57**(1):71-2.
- Desnick, R. J., Dean, K. J., Grabowski, G., Bishop, D. F., and Sweeley, C. C., 1979, Enzyme therapy in Fabry disease: differential in vivo plasma clearance and metabolic effectiveness of plasma and splenic alpha-galactosidase A isozymes, *Proc Natl Acad Sci U S A* **76**(10):5326-30.
- Diamond, J. M., 1994, Human genetics. Jewish lysosomes, *Nature* **368**(6469):291-2.
- Diaz-Font, A., Santamaria, R., Cozar, M., Blanco, M., Chamoles, N., Coll, M. J., Chabas, A., Vilageliu, L., and Grinberg, D., 2005, Clinical and mutational characterization of three patients with multiple sulfatase deficiency: report of a new splicing mutation, *Mol Genet Metab* **86**(1-2):206-11.
- Diaz, A., Montfort, M., Cormand, B., Zeng, B., Pastores, G. M., Chabas, A., Vilageliu, L., and Grinberg, D., 1999, Gaucher disease: the N370S mutation in Ashkenazi Jewish and Spanish patients has a common origin and arose several thousand years ago, *Am J Hum Genet* **64**(4):1233-8.
- Diaz, G. A., Gelb, B. D., Risch, N., Nygaard, T. G., Frisch, A., Cohen, I. J., Miranda, C. S., Amaral, O., Maire, I., Poenaru, L., Caillaud, C., Weizberg, M., Mistry, P., and Desnick, R. J., 2000, Gaucher disease: the origins of the Ashkenazi Jewish N370S and 84GG acid beta-glucosidase mutations, *Am J Hum Genet* **66**(6):1821-32.

- Dickson, R. C., and Lester, R. L., 1999, Yeast sphingolipids, *Biochim Biophys Acta* **1426**(2):347-57.
- Doebber, T. W., Wu, M. S., Bugianesi, R. L., Ponpipom, M. M., Furbish, F. S., Barranger, J. A., Brady, R. O., and Shen, T. Y., 1982, Enhanced macrophage uptake of synthetically glycosylated human placental beta-glucocerebrosidase, *J Biol Chem* **257**(5):2193-9.
- Dunbar, C. E., Kohn, D. B., Schiffmann, R., Barton, N. W., Nolte, J. A., Esplin, J. A., Pensiero, M., Long, Z., Lockey, C., Emmons, R. V., Csik, S., Leitman, S., Krebs, C. B., Carter, C., Brady, R. O., and Karlsson, S., 1998, Retroviral transfer of the glucocerebrosidase gene into CD34+ cells from patients with Gaucher disease: in vivo detection of transduced cells without myeloablation, *Hum Gene Ther* **9**(17):2629-40.
- Dvir, H., Harel, M., McCarthy, A. A., Toker, L., Silman, I., Futerman, A. H., and Sussman, J. L., 2003, X-ray structure of human acid-beta-glucosidase, the defective enzyme in Gaucher disease, *EMBO Rep* **4**(7):704-9.
- Dwek, R. A., Butters, T. D., Platt, F. M., and Zitzmann, N., 2002, Targeting glycosylation as a therapeutic approach, *Nat Rev Drug Discov* **1**(1):65-75.

E

- Elbashir, S. M., Harborth, J., Lendeckel, W., Yalcin, A., Weber, K., and Tuschl, T., 2001, Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells, *Nature* **411**(6836):494-8.
- Elbashir, S. M., Harborth, J., Weber, K., and Tuschl, T., 2002, Analysis of gene function in somatic mammalian cells using small interfering RNAs, *Methods* **26**(2):199-213.
- Ellis, H. M., Yu, D., DiTizio, T., and Court, D. L., 2001, High efficiency mutagenesis, repair, and engineering of chromosomal DNA using single-stranded oligonucleotides, *Proc Natl Acad Sci U S A* **98**(12):6742-6.
- Elstein, D., Hollak, C., Aerts, J. M., van Weely, S., Maas, M., Cox, T. M., Lachmann, R. H., Hrebicek, M., Platt, F. M., Butters, T. D., Dwek, R. A., and Zimran, A., 2004, Sustained therapeutic effects of oral miglustat (Zavesca, N-butyldeoxynojirimycin, OGT 918) in type I Gaucher disease, *J Inherit Metab Dis* **27**(6):757-66.
- Enderlin, C., Vogel, R., and Conaway, P., 2003, Gaucher disease, *Am J Nurs* **103**(12):50-60; quiz 61.
- Erickson, A. H., Ginns, E. I., and Barranger, J. A., 1985, Biosynthesis of the lysosomal enzyme glucocerebrosidase, *J Biol Chem* **260**(26):14319-24.
- Erikson, A., 1986, Gaucher disease--Norrbottnian type (III). Neuropaediatric and neurobiological aspects of clinical patterns and treatment, *Acta Paediatr Scand Suppl* **326**:1-42.
- Eyal, N., Wilder, S., and Horowitz, M., 1990, Prevalent and rare mutations among Gaucher patients, *Gene* **96**(2):277-83.

F

- Fenderson, B. A., Ostrander, G. K., Hausken, Z., Radin, N. S., and Hakomori, S., 1992, A ceramide analogue (PDMP) inhibits glycolipid synthesis in fish embryos, *Exp Cell Res* **198**(2):362-6.
- Filocamo, M., Bonuccelli, G., Mazzotti, R., Giona, F., and Gatti, R., 2000, Identification of a novel recombinant allele in three unrelated Italian Gaucher patients: implications for prognosis and genetic counseling, *Blood Cells Mol Dis* **26**(4):307-11.
- Fire, A., Xu, S., Montgomery, M. K., Kostas, S. A., Driver, S. E., and Mello, C. C., 1998, Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*, *Nature* **391**(6669):806-11.
- Fleshner, P. R., Aufses, A. H., Jr., Grabowski, G. A., and Elias, R., 1991, A 27-year experience with splenectomy for Gaucher's disease, *Am J Surg* **161**(1):69-75.
- Fried, K., 1973, Population study of chronic Gaucher's disease, *Isr J Med Sci* **9**(9):1396-8.

- Fujita, N., Suzuki, K., Vanier, M. T., Popko, B., Maeda, N., Klein, A., Henseler, M., Sandhoff, K., Nakayasu, H., and Suzuki, K., 1996, Targeted disruption of the mouse sphingolipid activator protein gene: a complex phenotype, including severe leukodystrophy and wide-spread storage of multiple sphingolipids, *Hum Mol Genet* **5**(6):711-25.
- Furbish, F. S., Blair, H. E., Shiloach, J., Pentchev, P. G., and Brady, R. O., 1977, Enzyme replacement therapy in Gaucher's disease: large-scale purification of glucocerebrosidase suitable for human administration, *Proc Natl Acad Sci U S A* **74**(8):3560-3.
- Furbish, F. S., Steer, C. J., Krett, N. L., and Barranger, J. A., 1981, Uptake and distribution of placental glucocerebrosidase in rat hepatic cells and effects of sequential deglycosylation, *Biochim Biophys Acta* **673**(4):425-34.
- Furst, W., Machleidt, W., and Sandhoff, K., 1988, The precursor of sulfatide activator protein is processed to three different proteins, *Biol Chem Hoppe Seyler* **369**(5):317-28.
- Futerman, A. H., and van Meer, G., 2004, The cell biology of lysosomal storage disorders, *Nat Rev Mol Cell Biol* **5**(7):554-65.

G

- Gamper, H. B., Jr., Cole-Strauss, A., Metz, R., Parekh, H., Kumar, R., and Kmiec, E. B., 2000, A plausible mechanism for gene correction by chimeric oligonucleotides, *Biochemistry* **39**(19):5808-16.
- George, R., McMahon, J., Lytle, B., Clark, B., and Lichtin, A., 2001, Severe valvular and aortic arch calcification in a patient with Gaucher's disease homozygous for the D409H mutation, *Clin Genet* **59**(5):360-3.
- Germain, D. P., Puech, J. P., Caillaud, C., Kahn, A., and Poenaru, L., 1998, Exhaustive screening of the acid beta-glucosidase gene, by fluorescence-assisted mismatch analysis using universal primers: mutation profile and genotype/phenotype correlations in Gaucher disease, *Am J Hum Genet* **63**(2):415-27.
- Gillard, B. K., Clement, R. G., and Marcus, D. M., 1998, Variations among cell lines in the synthesis of sphingolipids in de novo and recycling pathways, *Glycobiology* **8**(9):885-90.
- Ginns, E. I., Choudary, P. V., Tsuji, S., Martin, B., Stubblefield, B., Sawyer, J., Hozier, J., and Barranger, J. A., 1985, Gene mapping and leader polypeptide sequence of human glucocerebrosidase: implications for Gaucher disease, *Proc Natl Acad Sci U S A* **82**(20):7101-5.
- Ginzburg, L., Kacher, Y., and Futerman, A. H., 2004, The pathogenesis of glycosphingolipid storage disorders, *Semin Cell Dev Biol* **15**(4):417-31.
- Goker-Alpan, O., Hruska, K. S., Orvisky, E., Kishnani, P. S., Stubblefield, B. K., Schiffmann, R., and Sidransky, E., 2005, Divergent phenotypes in Gaucher disease implicate the role of modifiers, *J Med Genet* **42**(6):e37.
- Goker-Alpan, O., Schiffmann, R., LaMarca, M. E., Nussbaum, R. L., McInerney-Leo, A., and Sidransky, E., 2004, Parkinsonism among Gaucher disease carriers, *J Med Genet* **41**(12):937-40.
- Goldblatt, J., Sacks, S., Dall, D., and Beighton, P., 1988, Total hip arthroplasty in Gaucher's disease. Long-term prognosis, *Clin Orthop Relat Res* (228):94-8.
- Grabowski, G. A., Gatt, S., and Horowitz, M., 1990, Acid beta-glucosidase: enzymology and molecular biology of Gaucher disease, *Crit Rev Biochem Mol Biol* **25**(6):385-414.
- Grabowski, G. A., Saal, H. M., Wenstrup, R. J., and Barton, N. W., 1996, Gaucher disease: a prototype for molecular medicine, *Crit Rev Oncol Hematol* **23**(1):25-55.
- Graham, I. R., and Dickson, G., 2002, Gene repair and mutagenesis mediated by chimeric RNA-DNA oligonucleotides: chimeraplasty for gene therapy and conversion of single nucleotide polymorphisms (SNPs), *Biochim Biophys Acta* **1587**(1):1-6.
- Groen, J., 1948, The hereditary mechanism of Gauchers disease, *Blood* **3**:1238-49.

H

- Hacein-Bey-Abina, S., Von Kalle, C., Schmidt, M., McCormack, M. P., Wulffraat, N., Leboulch, P., Lim, A., Osborne, C. S., Pawliuk, R., Morillon, E., Sorensen, R., Forster, A., Fraser, P., Cohen, J. I., de Saint Basile, G., Alexander, I., Wintergerst, U., Frebourg, T., Aurias, A., Stoppa-Lyonnet, D., Romana, S., Radford-Weiss, I., Gross, F., Valensi, F., Delabesse, E., Macintyre, E., Sigaux, F., Soulier, J., Leiva, L. E., Wissler, M., Prinz, C., Rabbitts, T. H., Le Deist, F., Fischer, A., and Cavazzana-Calvo, M., 2003, LMO2-associated clonal T cell proliferation in two patients after gene therapy for SCID-X1, *Science* **302**(5644):415-9.
- Hakomori, S., 1981, Glycosphingolipids in cellular interaction, differentiation, and oncogenesis, *Annu Rev Biochem* **50**:733-64.
- Hammond, S. M., Bernstein, E., Beach, D., and Hannon, G. J., 2000, An RNA-directed nuclease mediates post-transcriptional gene silencing in *Drosophila* cells, *Nature* **404**(6775):293-6.
- Hannun, Y. A., and Bell, R. M., 1989, Functions of sphingolipids and sphingolipid breakdown products in cellular regulation, *Science* **243**(4890):500-7.
- Hannun, Y. A., and Luberto, C., 2000, Ceramide in the eukaryotic stress response, *Trends Cell Biol* **10**(2):73-80.
- Harper, S. Q., Staber, P. D., He, X., Eliason, S. L., Martins, I. H., Mao, Q., Yang, L., Kotin, R. M., Paulson, H. L., and Davidson, B. L., 2005, RNA interference improves motor and neuropathological abnormalities in a Huntington's disease mouse model, *Proc Natl Acad Sci U S A* **102**(16):5820-5.
- Hatton, C. E., Cooper, A., Whitehouse, C., and Wraith, J. E., 1997, Mutation analysis in 46 British and Irish patients with Gaucher's disease, *Arch Dis Child* **77**(1):17-22.
- Hazkani-Covo, E., Altman, N., Horowitz, M., and Graur, D., 2002, The evolutionary history of prosaposin: two successive tandem-duplication events gave rise to the four saposin domains in vertebrates, *J Mol Evol* **54**(1):30-4.
- Henseler, M., Klein, A., Glombitza, G. J., Suzuki, K., and Sandhoff, K., 1996a, Expression of the three alternative forms of the sphingolipid activator protein precursor in baby hamster kidney cells and functional assays in a cell culture system, *J Biol Chem* **271**(14):8416-23.
- Henseler, M., Klein, A., Reber, M., Vanier, M. T., Landrieu, P., and Sandhoff, K., 1996b, Analysis of a splice-site mutation in the sap-precursor gene of a patient with metachromatic leukodystrophy, *Am J Hum Genet* **58**(1):65-74.
- Hers, H. G., 1965, Inborn Lysosomal Diseases, *Gastroenterology* **48**:625-33.
- Ho, M. W., and O'Brien, J. S., 1971, Gaucher's disease: deficiency of 'acid' -glucosidase and reconstitution of enzyme activity in vitro, *Proc Natl Acad Sci U S A* **68**(11):2810-3.
- Hodanov inverted question mark, K., Hrebicek, M., Cervenkova inverted question mark, M., Mr inverted question mark, L., Veprekov inverted question mark, L., and Zemen, J., 1999, Analysis of the beta-glucocerebrosidase gene in Czech and Slovak Gaucher patients: mutation profile and description of six novel mutant alleles, *Blood Cells Mol Dis* **25**(5-6):287-98.
- Hollak, C. E., Evers, L., Aerts, J. M., and van Oers, M. H., 1997, Elevated levels of M-CSF, sCD14 and IL8 in type 1 Gaucher disease, *Blood Cells Mol Dis* **23**(2):201-12.
- Hollak, C. E., van Weely, S., van Oers, M. H., and Aerts, J. M., 1994, Marked elevation of plasma chitotriosidase activity. A novel hallmark of Gaucher disease, *J Clin Invest* **93**(3):1288-92.
- Holtschmidt, H., Sandhoff, K., Kwon, H. Y., Harzer, K., Nakano, T., and Suzuki, K., 1991, Sulfatide activator protein. Alternative splicing that generates three mRNAs and a newly found mutation responsible for a clinical disease, *J Biol Chem* **266**(12):7556-60.
- Horowitz, M., Tzuri, G., Eyal, N., Berebi, A., Kolodny, E. H., Brady, R. O., Barton, N. W., Abrahamov, A., and Zimran, A., 1993, Prevalence of nine mutations among Jewish and non-Jewish Gaucher disease patients, *Am J Hum Genet* **53**(4):921-30.
- Horowitz, M., Wilder, S., Horowitz, Z., Reiner, O., Gelbart, T., and Beutler, E., 1989, The human glucocerebrosidase gene and pseudogene: structure and evolution, *Genomics* **4**(1):87-96.
- Hulkova, H., Cervenkova, M., Ledvinova, J., Tochackova, M., Hrebicek, M., Poupetova, H., Befekadu, A., Berna, L., Paton, B. C., Harzer, K., Boor, A., Smid, F., and Elleder, M., 2001, A novel mutation in the coding region of the prosaposin gene leads to a complete deficiency of prosaposin

and saposins, and is associated with a complex sphingolipidosis dominated by lactosylceramide accumulation, *Hum Mol Genet* **10**(9):927-40.

Huwiler, A., Kolter, T., Pfeilschifter, J., and Sandhoff, K., 2000, Physiology and pathophysiology of sphingolipid metabolism and signaling, *Biochim Biophys Acta* **1485**(2-3):63-99.

I

Ichikawa, S., and Hirabayashi, Y., 1998, Glucosylceramide synthase and glycosphingolipid synthesis, *Trends Cell Biol* **8**(5):198-202.

Igoucheva, O., Alexeev, V., and Yoon, K., 2001, Targeted gene correction by small single-stranded oligonucleotides in mammalian cells, *Gene Ther* **8**(5):391-9.

Imai, K., 1985, Characterization of beta-glucosidase as a peripheral enzyme of lysosomal membranes from mouse liver and purification, *J Biochem (Tokyo)* **98**(5):1405-16.

Inokuchi, J., and Radin, N. S., 1987, Preparation of the active isomer of 1-phenyl-2-decanoylamino-3-morpholino-1-propanol, inhibitor of murine glucocerebrosidase synthetase, *J Lipid Res* **28**(5):565-71.

Inoue, M., Fujii, Y., Furukawa, K., Okada, M., Okumura, K., Hayakawa, T., Furukawa, K., and Sugiura, Y., 2002, Refractory skin injury in complex knock-out mice expressing only the GM3 ganglioside, *J Biol Chem* **277**(33):29881-8.

J

Jackson, A. L., Bartz, S. R., Schelter, J., Kobayashi, S. V., Burchard, J., Mao, M., Li, B., Cavet, G., and Linsley, P. S., 2003, Expression profiling reveals off-target gene regulation by RNAi, *Nat Biotechnol* **21**(6):635-7.

Jeyakumar, M., Butters, T. D., Cortina-Borja, M., Hunnam, V., Proia, R. L., Perry, V. H., Dwek, R. A., and Platt, F. M., 1999, Delayed symptom onset and increased life expectancy in Sandhoff disease mice treated with N-butyldeoxynojirimycin, *Proc Natl Acad Sci U S A* **96**(11):6388-93.

Jeyakumar, M., Butters, T. D., Dwek, R. A., and Platt, F. M., 2002, Glycosphingolipid lysosomal storage diseases: therapy and pathogenesis, *Neuropathol Appl Neurobiol* **28**(5):343-57.

K

Kampine, J. P., Brady, R. O., Kanfer, J. N., Feld, M., and Shapiro, D., 1967, Diagnosis of gaucher's disease and niemann-pick disease with small samples of venous blood, *Science* **155**(758):86-8.

Karlsson, K. A., 1995, Microbial recognition of target-cell glycoconjugates, *Curr Opin Struct Biol* **5**(5):622-35.

Kasahara, K., Watanabe, Y., Yamamoto, T., and Sanai, Y., 1997, Association of Src family tyrosine kinase Lyn with ganglioside GD3 in rat brain. Possible regulation of Lyn by glycosphingolipid in caveolae-like domains, *J Biol Chem* **272**(47):29947-53.

Katzmann, D. J., Odorizzi, G., and Emr, S. D., 2002, Receptor downregulation and multivesicular-body sorting, *Nat Rev Mol Cell Biol* **3**(12):893-905.

Kawai, H., Allende, M. L., Wada, R., Kono, M., Sango, K., Deng, C., Miyakawa, T., Crawley, J. N., Werth, N., Bierfreund, U., Sandhoff, K., and Proia, R. L., 2001, Mice expressing only monosialoganglioside GM3 exhibit lethal audiogenic seizures, *J Biol Chem* **276**(10):6885-8.

Kaye, E. M., 2001, Lysosomal Storage Diseases, *Curr Treat Options Neurol* **3**(3):249-256.

Kim, E. Y., Hong, Y. B., Lai, Z., Cho, Y. H., Brady, R. O., and Jung, S. C., 2005, Long-term expression of the human glucocerebrosidase gene in vivo after transplantation of bone-marrow-derived cells transformed with a lentivirus vector, *J Gene Med* **7**(7):878-87.

- Kishimoto, Y., Hiraiwa, M., and O'Brien, J. S., 1992, Saposins: structure, function, distribution, and molecular genetics, *J Lipid Res* **33**(9):1255-67.
- Klein, A., Henseler, M., Klein, C., Suzuki, K., Harzer, K., and Sandhoff, K., 1994, Sphingolipid activator protein D (sap-D) stimulates the lysosomal degradation of ceramide in vivo, *Biochem Biophys Res Commun* **200**(3):1440-8.
- Kmiec, E. B., 2003, Targeted gene repair -- in the arena, *J Clin Invest* **112**(5):632-6.
- Kolter, T., Doering, T., Wilkening, G., Werth, N., and Sandhoff, K., 1999, Recent advances in the biochemistry of glycosphingolipid metabolism, *Biochem Soc Trans* **27**(4):409-15.
- Kolter, T., Proia, R. L., and Sandhoff, K., 2002, Combinatorial ganglioside biosynthesis, *J Biol Chem* **277**(29):25859-62.
- Korkotian, E., Schwarz, A., Pelled, D., Schwarzmann, G., Segal, M., and Futerman, A. H., 1999, Elevation of intracellular glucosylceramide levels results in an increase in endoplasmic reticulum density and in functional calcium stores in cultured neurons, *J Biol Chem* **274**(31):21673-8.
- Kornfeld, S., and Mellman, I., 1989, The biogenesis of lysosomes, *Annu Rev Cell Biol* **5**:483-525.
- Kren, B. T., Bandyopadhyay, P., and Steer, C. J., 1998, In vivo site-directed mutagenesis of the factor IX gene by chimeric RNA/DNA oligonucleotides, *Nat Med* **4**(3):285-90.
- Kren, B. T., Cole-Strauss, A., Kmiec, E. B., and Steer, C. J., 1997, Targeted nucleotide exchange in the alkaline phosphatase gene of HuH-7 cells mediated by a chimeric RNA/DNA oligonucleotide, *Hepatology* **25**(6):1462-8.
- Kretz, K. A., Carson, G. S., Morimoto, S., Kishimoto, Y., Fluharty, A. L., and O'Brien, J. S., 1990, Characterization of a mutation in a family with saposin B deficiency: a glycosylation site defect, *Proc Natl Acad Sci U S A* **87**(7):2541-4.

L

- Lachmann, R. H., te Vruchte, D., Lloyd-Evans, E., Reinkensmeier, G., Sillence, D. J., Fernandez-Guillen, L., Dwek, R. A., Butters, T. D., Cox, T. M., and Platt, F. M., 2004, Treatment with miglustat reverses the lipid-trafficking defect in Niemann-Pick disease type C, *Neurobiol Dis* **16**(3):654-8.
- Lam, K. W., Li, C. Y., Yam, L. T., Smith, R. S., and Hacker, B., 1982, Comparison of prostatic and nonprostatic acid phosphatase, *Ann N Y Acad Sci* **390**:1-15.
- Landmann, L., 1988, The epidermal permeability barrier, *Anat Embryol (Berl)* **178**(1):1-13.
- Lannert, H., Bunning, C., Jeckel, D., and Wieland, F. T., 1994, Lactosylceramide is synthesized in the lumen of the Golgi apparatus, *FEBS Lett* **342**(1):91-6.
- Lannert, H., Gorgas, K., Meissner, I., Wieland, F. T., and Jeckel, D., 1998, Functional organization of the Golgi apparatus in glycosphingolipid biosynthesis. Lactosylceramide and subsequent glycosphingolipids are formed in the lumen of the late Golgi, *J Biol Chem* **273**(5):2939-46.
- Latham, T., Grabowski, G. A., Theophilus, B. D., and Smith, F. I., 1990, Complex alleles of the acid beta-glucosidase gene in Gaucher disease, *Am J Hum Genet* **47**(1):79-86.
- Latham, T. E., Theophilus, B. D., Grabowski, G. A., and Smith, F. I., 1991, Heterogeneity of mutations in the acid beta-glucosidase gene of Gaucher disease patients, *DNA Cell Biol* **10**(1):15-21.
- Lau, E. K., Tayebi, N., Ingraham, L. J., Winfield, S. L., Koprivica, V., Stone, D. L., Zimran, A., Ginns, E. I., and Sidransky, E., 1999, Two novel polymorphic sequences in the glucocerebrosidase gene region enhance mutational screening and founder effect studies of patients with Gaucher disease, *Hum Genet* **104**(4):293-300.
- le Coutre, P., Demina, A., Beutler, E., Beck, M., and Petrides, P. E., 1997, Molecular analysis of Gaucher disease: distribution of eight mutations and the complete gene deletion in 27 patients from Germany, *Hum Genet* **99**(6):816-21.
- Li, Z. H., Liu, D. P., Yin, W. X., Guo, Z. C., and Liang, C. C., 2001, Targeted correction of the point mutations of beta-thalassemia and targeted mutagenesis of the nucleotide associated with HPFH by RNA/DNA oligonucleotides: potential for beta-thalassemia gene therapy, *Blood Cells Mol Dis* **27**(2):530-8.

- Lieberman, J., and Beutler, E., 1976, Elevation of serum angiotensin-converting enzyme in Gaucher's disease, *N Engl J Med* **294**(26):1442-4.
- Linke, T., Wilkening, G., Sadeghlar, F., Mozcall, H., Bernardo, K., Schuchman, E., and Sandhoff, K., 2001, Interfacial regulation of acid ceramidase activity. Stimulation of ceramide degradation by lysosomal lipids and sphingolipid activator proteins, *J Biol Chem* **276**(8):5760-8.
- Liu, Y., Suzuki, K., Reed, J. D., Grinberg, A., Westphal, H., Hoffmann, A., Doring, T., Sandhoff, K., and Proia, R. L., 1998, Mice with type 2 and 3 Gaucher disease point mutations generated by a single insertion mutagenesis procedure, *Proc Natl Acad Sci U S A* **95**(5):2503-8.
- Liu, Y., Wada, R., Kawai, H., Sango, K., Deng, C., Tai, T., McDonald, M. P., Araujo, K., Crawley, J. N., Bierfreund, U., Sandhoff, K., Suzuki, K., and Proia, R. L., 1999, A genetic model of substrate deprivation therapy for a glycosphingolipid storage disorder, *J Clin Invest* **103**(4):497-505.
- Luther-Wyrsh, A., Costello, E., Thali, M., Buetti, E., Nissen, C., Surbek, D., Holzgreve, W., Gratwohl, A., Tichelli, A., and Wodnar-Filipowicz, A., 2001, Stable transduction with lentiviral vectors and amplification of immature hematopoietic progenitors from cord blood of preterm human fetuses, *Hum Gene Ther* **12**(4):377-89.
- Luzio, J. P., Rous, B. A., Bright, N. A., Pryor, P. R., Mullock, B. M., and Piper, R. C., 2000, Lysosome-endosome fusion and lysosome biogenesis, *J Cell Sci* **113** (Pt 9):1515-24.
- Lwin, A., Orvisky, E., Goker-Alpan, O., LaMarca, M. E., and Sidransky, E., 2004, Glucocerebrosidase mutations in subjects with parkinsonism, *Mol Genet Metab* **81**(1):70-3.
- Lynch, W. P., Sharpe, A. H., and Snyder, E. Y., 1999, Neural stem cells as engraftable packaging lines can mediate gene delivery to microglia: evidence from studying retroviral env-related neurodegeneration, *J Virol* **73**(8):6841-51.

M

- Malagarie-Cazenave, S., Andrieu-Abadie, N., Sgui, B., Gouaz, V., Tardy, C., Cuvillier, O., and Levade, T., 2002, Sphingolipid signalling: molecular basis and role in TNF-induced cell death, *Expert Rev Mol Med* **2002**:1-15.
- Mancini, G. M., Havelaar, A. C., and Verheijen, F. W., 2000, Lysosomal transport disorders, *J Inherit Metab Dis* **23**(3):278-92.
- Manzano, A., Mohri, Z., Sperber, G., Ogris, M., Graham, I., Dickson, G., and Owen, J. S., 2003, Failure to generate atheroprotective apolipoprotein AI phenotypes using synthetic RNA/DNA oligonucleotides (chimeraplasts), *J Gene Med* **5**(9):795-802.
- Marks, D. L., Wu, K., Paul, P., Kamisaka, Y., Watanabe, R., and Pagano, R. E., 1999, Oligomerization and topology of the Golgi membrane protein glucosylceramide synthase, *J Biol Chem* **274**(1):451-6.
- Markwell, M. A., Svennerholm, L., and Paulson, J. C., 1981, Specific gangliosides function as host cell receptors for Sendai virus, *Proc Natl Acad Sci U S A* **78**(9):5406-10.
- Mateu, E., Perez-Lezaun, A., Martinez-Arias, R., Andres, A., Valles, M., Bertranpetit, J., and Calafell, F., 2002, PKLR- GBA region shows almost complete linkage disequilibrium over 70 kb in a set of worldwide populations, *Hum Genet* **110**(6):532-44.
- Matsuda, J., Vanier, M. T., Saito, Y., Tohyama, J., Suzuki, K., and Suzuki, K., 2001, A mutation in the saposin A domain of the sphingolipid activator protein (prosaposin) gene results in a late-onset, chronic form of globoid cell leukodystrophy in the mouse, *Hum Mol Genet* **10**(11):1191-9.
- McNicol, A., and Israels, S. J., 1999, Platelet dense granules: structure, function and implications for haemostasis, *Thromb Res* **95**(1):1-18.
- Meikle, P. J., Hopwood, J. J., Clague, A. E., and Carey, W. F., 1999, Prevalence of lysosomal storage disorders, *Jama* **281**(3):249-54.
- Merrill, A. H., Jr., Schmelz, E. M., Dillehay, D. L., Spiegel, S., Shayman, J. A., Schroeder, J. J., Riley, R. T., Voss, K. A., and Wang, E., 1997, Sphingolipids--the enigmatic lipid class: biochemistry, physiology, and pathophysiology, *Toxicol Appl Pharmacol* **142**(1):208-25.
- Miller, V. M., Xia, H., Marrs, G. L., Gouvion, C. M., Lee, G., Davidson, B. L., and Paulson, H. L., 2003, Allele-specific silencing of dominant disease genes, *Proc Natl Acad Sci U S A* **100**(12):7195-200.

- Miocic, S., Filocamo, M., Dominissini, S., Montalvo, A. L., Vlahovicek, K., Deganuto, M., Mazzotti, R., Cariati, R., Bembi, B., and Pittis, M. G., 2005, Identification and functional characterization of five novel mutant alleles in 58 Italian patients with Gaucher disease type 1, *Hum Mutat* **25**(1):100.
- Mistry, P. K., Smith, S. J., Ali, M., Hatton, C. S., McIntyre, N., and Cox, T. M., 1992, Genetic diagnosis of Gaucher's disease, *Lancet* **339**(8798):889-92.
- Mittal, V., 2004, Improving the efficiency of RNA interference in mammals, *Nat Rev Genet* **5**(5):355-65.
- Montfort, M., Chabas, A., Vilageliu, L., and Grinberg, D., 2005, Functional analysis of 13 mutant alleles identified in Gaucher disease patients: pathogenic changes and "modifier" polymorphisms, *Hum Mutat* **26**(3):276.
- Morimoto, S., Kishimoto, Y., Tomich, J., Weiler, S., Ohashi, T., Barranger, J. A., Kretz, K. A., and O'Brien, J. S., 1990, Interaction of saposins, acidic lipids, and glucosylceramidase, *J Biol Chem* **265**(4):1933-7.
- Morton, D. L., Ravindranath, M. H., and Irie, R. F., 1994, Tumor gangliosides as targets for active specific immunotherapy of melanoma in man, *Prog Brain Res* **101**:251-75.
- Mullins, C., and Bonifacino, J. S., 2001, The molecular machinery for lysosome biogenesis, *Bioessays* **23**(4):333-43.

N

- Nagy, E., and Maquat, L. E., 1998, A rule for termination-codon position within intron-containing genes: when nonsense affects RNA abundance, *Trends Biochem Sci* **23**(6):198-9.
- Nakano, T., Sandhoff, K., Stumper, J., Christomanou, H., and Suzuki, K., 1989, Structure of full-length cDNA coding for sulfatide activator, a Co-beta-glucosidase and two other homologous proteins: two alternate forms of the sulfatide activator, *J Biochem (Tokyo)* **105**(2):152-4.
- Neufeld, E. F., 1991, Lysosomal storage diseases, *Annu Rev Biochem* **60**:257-80.
- Nilsson, O., and Svennerholm, L., 1982, Accumulation of glucosylceramide and glucosylsphingosine (psychosine) in cerebrum and cerebellum in infantile and juvenile Gaucher disease, *J Neurochem* **39**(3):709-18.
- Nozue, M., Sakiyama, H., Tsuchiya, K., Hirabayashi, Y., and Taniguchi, M., 1988, Melanoma antigen expression and metastatic ability of mutant B16 melanoma clones, *Int J Cancer* **42**(5):734-8.

O

- O'Brien, J. S., Kretz, K. A., Dewji, N., Wenger, D. A., Esch, F., and Fluharty, A. L., 1988, Coding of two sphingolipid activator proteins (SAP-1 and SAP-2) by same genetic locus, *Science* **241**(4869):1098-101.
- O'Brien, J. S., Miller, A. L., Loverde, A. W., and Veath, M. L., 1973, Sanfilippo disease type B: enzyme replacement and metabolic correction in cultured fibroblasts, *Science* **181**(101):753-5.
- Ockerman, P. A., and Kohlin, P., 1969, Acid hydrolases in plasma in Gaucher's disease, *Clin Chem* **15**(1):61-4.
- Okada, M., Itoh Mi, M., Haraguchi, M., Okajima, T., Inoue, M., Oishi, H., Matsuda, Y., Iwamoto, T., Kawano, T., Fukumoto, S., Miyazaki, H., Furukawa, K., Aizawa, S., and Furukawa, K., 2002, b-series Ganglioside deficiency exhibits no definite changes in the neurogenesis and the sensitivity to Fas-mediated apoptosis but impairs regeneration of the lesioned hypoglossal nerve, *J Biol Chem* **277**(3):1633-6.

P

- Peters, C., and von Figura, K., 1994, Biogenesis of lysosomal membranes, *FEBS Lett* **346**(1):108-14.

- Platt, F. M., and Butters, T. D., 1998, New therapeutic prospects for the glycosphingolipid lysosomal storage diseases, *Biochem Pharmacol* **56**(4):421-30.
- Platt, F. M., and Butters, T. D., 2000, Substrate deprivation: a new therapeutic approach for the glycosphingolipid lysosomal storage diseases, *Expert Rev Mol Med* **2000**:1-17.
- Platt, F. M., Neises, G. R., Dwek, R. A., and Butters, T. D., 1994a, N-butyldeoxynojirimycin is a novel inhibitor of glycolipid biosynthesis, *J Biol Chem* **269**(11):8362-5.
- Platt, F. M., Neises, G. R., Karlsson, G. B., Dwek, R. A., and Butters, T. D., 1994b, N-butyldeoxygalactonojirimycin inhibits glycolipid biosynthesis but does not affect N-linked oligosaccharide processing, *J Biol Chem* **269**(43):27108-14.
- Platt, F. M., Neises, G. R., Reinkensmeier, G., Townsend, M. J., Perry, V. H., Proia, R. L., Winchester, B., Dwek, R. A., and Butters, T. D., 1997a, Prevention of lysosomal storage in Tay-Sachs mice treated with N-butyldeoxynojirimycin, *Science* **276**(5311):428-31.
- Platt, F. M., Reinkensmeier, G., Dwek, R. A., and Butters, T. D., 1997b, Extensive glycosphingolipid depletion in the liver and lymphoid organs of mice treated with N-butyldeoxynojirimycin, *J Biol Chem* **272**(31):19365-72.
- Porter, M. T., Fluharty, A. L., and Kihara, H., 1971, Correction of abnormal cerebroside sulfate metabolism in cultured metachromatic leukodystrophy fibroblasts, *Science* **172**(989):1263-5.
- Proia, R. L., 2003, Glycosphingolipid functions: insights from engineered mouse models, *Philos Trans R Soc Lond B Biol Sci* **358**(1433):879-83.

R

- Rafi, M. A., de Gala, G., Zhang, X. L., and Wenger, D. A., 1993, Mutational analysis in a patient with a variant form of Gaucher disease caused by SAP-2 deficiency, *Somat Cell Mol Genet* **19**(1):1-7.
- Ralph, G. S., Radcliffe, P. A., Day, D. M., Carthy, J. M., Leroux, M. A., Lee, D. C., Wong, L. F., Bilsland, L. G., Greensmith, L., Kingsman, S. M., Mitrophanous, K. A., Mazarakis, N. D., and Azzouz, M., 2005, Silencing mutant SOD1 using RNAi protects against neurodegeneration and extends survival in an ALS model, *Nat Med* **11**(4):429-33.
- Rando, T. A., Disatnik, M. H., and Zhou, L. Z., 2000, Rescue of dystrophin expression in mdx mouse muscle by RNA/DNA oligonucleotides, *Proc Natl Acad Sci U S A* **97**(10):5363-8.
- Raper, S. E., 2005, Gene therapy: the good, the bad, and the ugly, *Surgery* **137**(5):487-92.
- Raper, S. E., Chirmule, N., Lee, F. S., Wivel, N. A., Bagg, A., Gao, G. P., Wilson, J. M., and Batshaw, M. L., 2003, Fatal systemic inflammatory response syndrome in a ornithine transcarbamylase deficient patient following adenoviral gene transfer, *Mol Genet Metab* **80**(1-2):148-58.
- Rapola, J., 1994, Lysosomal storage diseases in adults, *Pathol Res Pract* **190**(8):759-66.
- Regis, S., Filocamo, M., Corsolini, F., Caroli, F., Keulemans, J. L., van Diggelen, O. P., and Gatti, R., 1999, An Asn > Lys substitution in saposin B involving a conserved amino acidic residue and leading to the loss of the single N-glycosylation site in a patient with metachromatic leukodystrophy and normal arylsulphatase A activity, *Eur J Hum Genet* **7**(2):125-30.
- Reiner, O., Wigderson, M., and Horowitz, M., 1988, Structural analysis of the human glucocerebrosidase genes, *Dna* **7**(2):107-16.
- Reiner, O., Wilder, S., Givol, D., and Horowitz, M., 1987, Efficient in vitro and in vivo expression of human glucocerebrosidase cDNA, *Dna* **6**(2):101-8.
- Reissner, K., Tayebi, N., Stubblefield, B. K., Koprivica, V., Blitzer, M., Holleran, W., Cowan, T., Almashanu, S., Maddalena, A., Karson, E. M., and Sidransky, E., 1998, Type 2 Gaucher disease with hydrops fetalis in an Ashkenazi Jewish family resulting from a novel recombinant allele and a rare splice junction mutation in the glucocerebrosidase locus, *Mol Genet Metab* **63**(4):281-8.
- Ringden, O., Groth, C. G., Erikson, A., Granqvist, S., Mansson, J. E., and Sparrelid, E., 1995, Ten years' experience of bone marrow transplantation for Gaucher disease, *Transplantation* **59**(6):864-70.
- Robinson, D. B., and Glew, R. H., 1980, Acid phosphatase in Gaucher's disease, *Clin Chem* **26**(3):371-82.

- Rodriguez-Mari, A., Diaz-Font, A., Chabas, A., Pastores, G. M., Grinberg, D., and Vilageliu, L., 2001, New insights into the origin of the Gaucher disease-causing mutation N370S: extended haplotype analysis using the 5GC3.2, 5470 G/A, and ITG6.2 polymorphisms, *Blood Cells Mol Dis* **27**(5):950-9.
- Rorman, E. G., and Grabowski, G. A., 1989, Molecular cloning of a human co-beta-glucosidase cDNA: evidence that four sphingolipid hydrolase activator proteins are encoded by single genes in humans and rats, *Genomics* **5**(3):486-92.
- Rotter, J. I., and Diamond, J. M., 1987, What maintains the frequencies of human genetic diseases? *Nature* **329**(6137):289-90.
- Ruiter, R., van den Brande, I., Stals, E., Delaure, S., Cornelissen, M., and D'Halluin, K., 2003, Spontaneous mutation frequency in plants obscures the effect of chimeroplasty, *Plant Mol Biol* **53**(5):675-89.
- Ryther, R. C., Flynt, A. S., Harris, B. D., Phillips, J. A., 3rd, and Patton, J. G., 2004, GH1 splicing is regulated by multiple enhancers whose mutation produces a dominant-negative GH isoform that can be degraded by allele-specific small interfering RNA (siRNA), *Endocrinology* **145**(6):2988-96.

S

- Sandhoff, K., and Kolter, T., 2003, Biosynthesis and degradation of mammalian glycosphingolipids, *Philos Trans R Soc Lond B Biol Sci* **358**(1433):847-61.
- Sarria, A. J., Giraldo, P., Perez-Calvo, J. I., and Pocovi, M., 1999, Detection of three rare (G377S, T134P and 1451delAC), and two novel mutations (G195W and Rec[1263del55;1342G>C]) in Spanish Gaucher disease patients. Mutation in brief no. 251. Online, *Hum Mutat* **14**(1):88.
- Sawkar, A. R., Adamski-Werner, S. L., Cheng, W. C., Wong, C. H., Beutler, E., Zimmer, K. P., and Kelly, J. W., 2005, Gaucher disease-associated glucocerebrosidases show mutation-dependent chemical chaperoning profiles, *Chem Biol* **12**(11):1235-44.
- Sawkar, A. R., Cheng, W. C., Beutler, E., Wong, C. H., Balch, W. E., and Kelly, J. W., 2002, Chemical chaperones increase the cellular activity of N370S beta -glucosidase: a therapeutic strategy for Gaucher disease, *Proc Natl Acad Sci U S A* **99**(24):15428-33.
- Schiffmann, R., Kopp, J. B., Austin, H. A., 3rd, Sabnis, S., Moore, D. F., Weibel, T., Balow, J. E., and Brady, R. O., 2001, Enzyme replacement therapy in Fabry disease: a randomized controlled trial, *Jama* **285**(21):2743-9.
- Schnaar, R. L., 1991, Glycosphingolipids in cell surface recognition, *Glycobiology* **1**(5):477-85.
- Schnabel, D., Schroder, M., Furst, W., Klein, A., Hurwitz, R., Zenk, T., Weber, J., Harzer, K., Paton, B. C., Poulos, A., and et al., 1992, Simultaneous deficiency of sphingolipid activator proteins 1 and 2 is caused by a mutation in the initiation codon of their common gene, *J Biol Chem* **267**(5):3312-5.
- Schnabel, D., Schroder, M., and Sandhoff, K., 1991, Mutation in the sphingolipid activator protein 2 in a patient with a variant of Gaucher disease, *FEBS Lett* **284**(1):57-9.
- Schuening, F., Longo, W. L., Atkinson, M. E., Zaboikin, M., Kiem, H. P., Sanders, J., Scott, C. R., Storb, R., Miller, A. D., Reynolds, T., Bensinger, W., Rowley, S., Gooley, T., Darovsky, B., and Appelbaum, F., 1997, Retrovirus-mediated transfer of the cDNA for human glucocerebrosidase into peripheral blood repopulating cells of patients with Gaucher's disease, *Hum Gene Ther* **8**(17):2143-60.
- Schwarz, A., Rapaport, E., Hirschberg, K., and Futerman, A. H., 1995, A regulatory role for sphingolipids in neuronal growth. Inhibition of sphingolipid synthesis and degradation have opposite effects on axonal branching, *J Biol Chem* **270**(18):10990-8.
- Shapiro, M. B., and Senapathy, P., 1987, RNA splice junctions of different classes of eukaryotes: sequence statistics and functional implications in gene expression, *Nucleic Acids Res* **15**(17):7155-74.
- Sibille, A., Eng, C. M., Kim, S. J., Pastores, G., and Grabowski, G. A., 1993, Phenotype/genotype correlations in Gaucher disease type I: clinical and therapeutic implications, *Am J Hum Genet* **52**(6):1094-101.
- Sidransky, E., 2004, Gaucher disease: complexity in a "simple" disorder, *Mol Genet Metab* **83**(1-2):6-15.
- Sidransky, E., 2005, Gaucher disease and parkinsonism, *Mol Genet Metab* **84**(4):302-4.

- Sidransky, E., Tayebi, N., Stubblefield, B. K., Eliason, W., Klineburgess, A., Pizzolato, G. P., Cox, J. N., Porta, J., Bottani, A., and DeLozier-Blanchet, C. D., 1996, The clinical, molecular, and pathological characterisation of a family with two cases of lethal perinatal type 2 Gaucher disease, *J Med Genet* **33**(2):132-6.
- Sidransky, E., Tsuji, S., Martin, B. M., Stubblefield, B., and Ginns, E. I., 1992, DNA mutation analysis of Gaucher patients, *Am J Med Genet* **42**(3):331-6.
- Silverstein, E., and Friedland, J., 1977, Elevated serum and spleen angiotensin converting enzyme and serum lysozyme in Gaucher's disease, *Clin Chim Acta* **74**(1):21-5.
- Simons, K., and Ikonen, E., 1997, Functional rafts in cell membranes, *Nature* **387**(6633):569-72.
- Simpson, M. A., Cross, H., Proukakis, C., Priestman, D. A., Neville, D. C., Reinkensmeier, G., Wang, H., Wiznitzer, M., Gurtz, K., Verganelaki, A., Pryde, A., Patton, M. A., Dwek, R. A., Butters, T. D., Platt, F. M., and Crosby, A. H., 2004, Infantile-onset symptomatic epilepsy syndrome caused by a homozygous loss-of-function mutation of GM3 synthase, *Nat Genet* **36**(11):1225-9.
- Sinclair, G., Choy, F. Y., and Humphries, L., 1998, A novel complex allele and two new point mutations in type 2 (acute neuronopathic) Gaucher disease, *Blood Cells Mol Dis* **24**(4):420-7.
- Sly, W. S., Kaplan, A., Achord, D. T., Brot, F. E., and Bell, C. E., 1978, Receptor-mediated uptake of lysosomal enzymes, *Prog Clin Biol Res* **23**:547-51.
- Smith, D. C., Lord, J. M., Roberts, L. M., and Johannes, L., 2004, Glycosphingolipids as toxin receptors, *Semin Cell Dev Biol* **15**(4):397-408.
- Sorge, J., Gross, E., West, C., and Beutler, E., 1990, High level transcription of the glucocerebrosidase pseudogene in normal subjects and patients with Gaucher disease, *J Clin Invest* **86**(4):1137-41.
- Sorge, J., West, C., Westwood, B., and Beutler, E., 1985, Molecular cloning and nucleotide sequence of human glucocerebrosidase cDNA, *Proc Natl Acad Sci U S A* **82**(21):7289-93.
- Sorge, J. A., West, C., Kuhl, W., Treger, L., and Beutler, E., 1987, The human glucocerebrosidase gene has two functional ATG initiator codons, *Am J Hum Genet* **41**(6):1016-24.
- Spiegel, R., Bach, G., Sury, V., Mengistu, G., Meidan, B., Shalev, S., Shneor, Y., Mandel, H., and Zeigler, M., 2005, A mutation in the saposin A coding region of the prosaposin gene in an infant presenting as Krabbe disease: first report of saposin A deficiency in humans, *Mol Genet Metab* **84**(2):160-6.
- Stahl, P. D., Rodman, J. S., Miller, M. J., and Schlesinger, P. H., 1978, Evidence for receptor-mediated binding of glycoproteins, glycoconjugates, and lysosomal glycosidases by alveolar macrophages, *Proc Natl Acad Sci U S A* **75**(3):1399-403.
- Stark, G. R., Kerr, I. M., Williams, B. R., Silverman, R. H., and Schreiber, R. D., 1998, How cells respond to interferons, *Annu Rev Biochem* **67**:227-64.
- Strasberg, P. M., Skomorowski, M. A., Warren, I. B., Hilson, W. L., Callahan, J. W., and Clarke, J. T., 1994, Homozygous presence of the crossover (fusion gene) mutation identified in a type II Gaucher disease fetus: is this analogous to the Gaucher knock-out mouse model? *Biochem Med Metab Biol* **53**(1):16-21.
- Sullards, M. C., Lynch, D. V., Merrill, A. H., Jr., and Adams, J., 2000, Structure determination of soybean and wheat glucosylceramides by tandem mass spectrometry, *J Mass Spectrom* **35**(3):347-53.
- Sun, Y., Qi, X., and Grabowski, G. A., 2003, Saposin C is required for normal resistance of acid beta-glucosidase to proteolytic degradation, *J Biol Chem* **278**(34):31918-23.

T

- Tagalakis, A. D., Graham, I. R., Riddell, D. R., Dickson, J. G., and Owen, J. S., 2001, Gene correction of the apolipoprotein (Apo) E2 phenotype to wild-type ApoE3 by in situ chimeroplasty, *J Biol Chem* **276**(16):13226-30.
- Tagalakis, A. D., Owen, J. S., and Simons, J. P., 2005, Lack of RNA-DNA oligonucleotide (chimeroplast) mutagenic activity in mouse embryos, *Mol Reprod Dev* **71**(2):140-4.
- Takamiya, K., Yamamoto, A., Furukawa, K., Yamashiro, S., Shin, M., Okada, M., Fukumoto, S., Haraguchi, M., Takeda, N., Fujimura, K., Sakae, M., Kishikawa, M., Shiku, H., Furukawa, K., and Aizawa, S.,

- 1996, Mice with disrupted GM2/GD2 synthase gene lack complex gangliosides but exhibit only subtle defects in their nervous system, *Proc Natl Acad Sci U S A* **93**(20):10662-7.
- Taubes, G., 2002, Gene therapy. The strange case of chimeraplasty, *Science* **298**(5601):2116-20.
- Tayebi, N., Callahan, M., Madike, V., Stubblefield, B. K., Orvisky, E., Krasnewich, D., Fillano, J. J., and Sidransky, E., 2001, Gaucher disease and parkinsonism: a phenotypic and genotypic characterization, *Mol Genet Metab* **73**(4):313-21.
- Tayebi, N., Cushner, S., and Sidransky, E., 1996, Differentiation of the glucocerebrosidase gene from pseudogene by long-template PCR: implications for Gaucher disease, *Am J Hum Genet* **59**(3):740-1.
- Tayebi, N., Cushner, S. R., Kleijer, W., Lau, E. K., Damschroder-Williams, P. J., Stubblefield, B. K., Den Hollander, J., and Sidransky, E., 1997, Prenatal lethality of a homozygous null mutation in the human glucocerebrosidase gene, *Am J Med Genet* **73**(1):41-7.
- Tayebi, N., Park, J., Madike, V., and Sidransky, E., 2000, Gene rearrangement on 1q21 introducing a duplication of the glucocerebrosidase pseudogene and a metaxin fusion gene, *Hum Genet* **107**(4):400-3.
- Tayebi, N., Stone, D. L., and Sidransky, E., 1999, Type 2 gaucher disease: an expanding phenotype, *Mol Genet Metab* **68**(2):209-19.
- Tayebi, N., Stubblefield, B. K., Park, J. K., Orvisky, E., Walker, J. M., LaMarca, M. E., and Sidransky, E., 2003a, Reciprocal and nonreciprocal recombination at the glucocerebrosidase gene region: implications for complexity in Gaucher disease, *Am J Hum Genet* **72**(3):519-34.
- Tayebi, N., Walker, J., Stubblefield, B., Orvisky, E., LaMarca, M. E., Wong, K., Rosenbaum, H., Schiffmann, R., Bembi, B., and Sidransky, E., 2003b, Gaucher disease with parkinsonian manifestations: does glucocerebrosidase deficiency contribute to a vulnerability to parkinsonism? *Mol Genet Metab* **79**(2):104-9.
- Thakker, D.R., Hoyer, D., and Cryan, J.F., 2005, Interfering with the brain: Use of RNA interference for understanding the pathophysiology of psychiatric and neurological disorders. *Pharmacol Ther.* Epub ahead of print.
- Theophilus, B., Latham, T., Grabowski, G. A., and Smith, F. I., 1989a, Gaucher disease: molecular heterogeneity and phenotype-genotype correlations, *Am J Hum Genet* **45**(2):212-25.
- Theophilus, B. D., Latham, T., Grabowski, G. A., and Smith, F. I., 1989b, Comparison of RNase A, a chemical cleavage and GC-clamped denaturing gradient gel electrophoresis for the detection of mutations in exon 9 of the human acid beta-glucosidase gene, *Nucleic Acids Res* **17**(19):7707-22.
- Trajkovic-Bodennec, S., Bodennec, J., and Futerman, A. H., 2004, Phosphatidylcholine metabolism is altered in a monocyte-derived macrophage model of Gaucher disease but not in lymphocytes, *Blood Cells Mol Dis* **33**(1):77-82.
- Tsai, S. Y., Schillinger, K., and Ye, X., 2000, Adenovirus-mediated transfer of regulable gene expression, *Curr Opin Mol Ther* **2**(5):515-23.
- Tsuji, S., Choudary, P. V., Martin, B. M., Stubblefield, B. K., Mayor, J. A., Barranger, J. A., and Ginns, E. I., 1987, A mutation in the human glucocerebrosidase gene in neuronopathic Gaucher's disease, *N Engl J Med* **316**(10):570-5.
- Tsuji, S., Choudary, P. V., Martin, B. M., Winfield, S., Barranger, J. A., and Ginns, E. I., 1986, Nucleotide sequence of cDNA containing the complete coding sequence for human lysosomal glucocerebrosidase, *J Biol Chem* **261**(1):50-3.
- Tybulewicz, V. L., Tremblay, M. L., LaMarca, M. E., Willemsen, R., Stubblefield, B. K., Winfield, S., Zablocka, B., Sidransky, E., Martin, B. M., Huang, S. P., and et al., 1992, Animal model of Gaucher's disease from targeted disruption of the mouse glucocerebrosidase gene, *Nature* **357**(6377):407-10.

U

- Uyama, E., Uchino, M., Ida, H., Eto, Y., and Owada, M., 1997, D409H/D409H genotype in Gaucher-like disease, *J Med Genet* **34**(2):175.

V

- Vaccaro, A. M., Salvioli, R., Barca, A., Tatti, M., Ciaffoni, F., Maras, B., Siciliano, R., Zappacosta, F., Amoresano, A., and Pucci, P., 1995, Structural analysis of saposin C and B. Complete localization of disulfide bridges, *J Biol Chem* **270**(17):9953-60.
- Vaccaro, A. M., Salvioli, R., Tatti, M., and Ciaffoni, F., 1999, Saposins and their interaction with lipids, *Neurochem Res* **24**(2):307-14.
- Van De Water, N. S., Jolly, R. D., and Farrow, B. R., 1979, Canine Gaucher disease--the enzymic defect, *Aust J Exp Biol Med Sci* **57**(5):551-4.
- van Meer, G., and Lisman, Q., 2002, Sphingolipid transport: rafts and translocators, *J Biol Chem* **277**(29):25855-8.
- Varkonyi, J., Rosenbaum, H., Baumann, N., MacKenzie, J. J., Simon, Z., Aharon-Peretz, J., Walker, J. M., Tayebi, N., and Sidransky, E., 2003, Gaucher disease associated with parkinsonism: four further case reports, *Am J Med Genet A* **116**(4):348-51.
- Vellodi, A., 2005, Lysosomal storage disorders, *Br J Haematol* **128**(4):413-31.
- Vunnam, R. R., and Radin, N. S., 1980, Analogs of ceramide that inhibit glucocerebrosidase in mouse brain, *Chem Phys Lipids* **26**(3):265-78.

W

- Wafaei, J. R., and Choy, F. Y., 2005, Glucocerebrosidase recombinant allele: Molecular evolution of the glucocerebrosidase gene and pseudogene in primates, *Blood Cells Mol Dis*.
- Watts, R. W., 2003, A historical perspective of the glycosphingolipids and sphingolipidoses, *Philos Trans R Soc Lond B Biol Sci* **358**(1433):975-83.
- Weinreb, N. J., Brady, R. O., and Tappel, A. L., 1968, The lysosomal localization of sphingolipid hydrolases, *Biochim Biophys Acta* **159**(1):141-6.
- Weinthal, J., Nolta, J. A., Yu, X. J., Lilley, J., Uribe, L., and Kohn, D. B., 1991, Expression of human glucocerebrosidase following retroviral vector-mediated transduction of murine hematopoietic stem cells, *Bone Marrow Transplant* **8**(5):403-12.
- Wertz, P. W., and van den Bergh, B., 1998, The physical, chemical and functional properties of lipids in the skin and other biological barriers, *Chem Phys Lipids* **91**(2):85-96.
- Whelan, J., 2005, First clinical data on RNAi, *Drug Discov Today* **10**(15):1014-5.
- Wilda, M., Fuchs, U., Wossmann, W., and Borkhardt, A., 2002, Killing of leukemic cells with a BCR/ABL fusion gene by RNA interference (RNAi), *Oncogene* **21**(37):5716-24.
- Wilkening, G., Linke, T., and Sandhoff, K., 1998, Lysosomal degradation on vesicular membrane surfaces. Enhanced glucosylceramide degradation by lysosomal anionic lipids and activators, *J Biol Chem* **273**(46):30271-8.
- Winfield, S. L., Tayebi, N., Martin, B. M., Ginns, E. I., and Sidransky, E., 1997, Identification of three additional genes contiguous to the glucocerebrosidase locus on chromosome 1q21: implications for Gaucher disease, *Genome Res* **7**(10):1020-6.
- Wrobe, D., Henseler, M., Huettler, S., Pascual Pascual, S. I., Chabas, A., and Sandhoff, K., 2000, A non-glycosylated and functionally deficient mutant (N215H) of the sphingolipid activator protein B (SAP-B) in a novel case of metachromatic leukodystrophy (MLD), *J Inher Metab Dis* **23**(1):63-76.

X

- Xu, Y. H., Quinn, B., Witte, D., and Grabowski, G. A., 2003, Viable mouse models of acid beta-glucosidase deficiency: the defect in Gaucher disease, *Am J Pathol* **163**(5):2093-101.

Y

- Yamamoto, A., Serizawa, S., Ito, M., and Sato, Y., 1990, Fatty acid composition of sebum wax esters and urinary androgen level in normal human individuals, *J Dermatol Sci* **1**(4):269-76.
- Yamashita, T., Wada, R., and Proia, R. L., 2002, Early developmental expression of the gene encoding glucosylceramide synthase, the enzyme controlling the first committed step of glycosphingolipid synthesis, *Biochim Biophys Acta* **1573**(3):236-40.
- Yamashita, T., Wada, R., Sasaki, T., Deng, C., Bierfreund, U., Sandhoff, K., and Proia, R. L., 1999, A vital role for glycosphingolipid synthesis during development and differentiation, *Proc Natl Acad Sci U S A* **96**(16):9142-7.
- Yoon, K., Cole-Strauss, A., and Kmiec, E. B., 1996, Targeted gene correction of episomal DNA in mammalian cells mediated by a chimeric RNA-DNA oligonucleotide, *Proc Natl Acad Sci U S A* **93**(5):2071-6.

Z

- Zeller, C. B., and Marchase, R. B., 1992, Gangliosides as modulators of cell function, *Am J Physiol* **262**(6 Pt 1):C1341-55.
- Zervas, M., Somers, K. L., Thrall, M. A., and Walkley, S. U., 2001, Critical role for glycosphingolipids in Niemann-Pick disease type C, *Curr Biol* **11**(16):1283-7.
- Zhang, X. L., Rafi, M. A., DeGala, G., and Wenger, D. A., 1990, Insertion in the mRNA of a metachromatic leukodystrophy patient with sphingolipid activator protein-1 deficiency, *Proc Natl Acad Sci U S A* **87**(4):1426-30.
- Zhao, H., Keddache, M., Bailey, L., Arnold, G., and Grabowski, G., 2003, Gaucher's disease: identification of novel mutant alleles and genotype-phenotype relationships, *Clin Genet* **64**(1):57-64.
- Zhou, D., Cantu, C., 3rd, Sagiv, Y., Schrantz, N., Kulkarni, A. B., Qi, X., Mahuran, D. J., Morales, C. R., Grabowski, G. A., Benlagha, K., Savage, P., Bendelac, A., and Teyton, L., 2004, Editing of CD1d-bound lipid antigens by endosomal lipid transfer proteins, *Science* **303**(5657):523-7.
- Zhu, T., Peterson, D. J., Tagliani, L., St Clair, G., Baszczyński, C. L., and Bowen, B., 1999, Targeted manipulation of maize genes in vivo using chimeric RNA/DNA oligonucleotides, *Proc Natl Acad Sci U S A* **96**(15):8768-73.
- Zimran, A., Gelbart, T., and Beutler, E., 1990a, Linkage of the PvuII polymorphism with the common Jewish mutation for Gaucher disease, *Am J Hum Genet* **46**(5):902-5.
- Zimran, A., Gelbart, T., Westwood, B., Grabowski, G. A., and Beutler, E., 1991, High frequency of the Gaucher disease mutation at nucleotide 1226 among Ashkenazi Jews, *Am J Hum Genet* **49**(4):855-9.
- Zimran, A., Glass, C., Thorpe, V. S., and Beutler, E., 1989a, Analysis of 'color PCR' by automatic DNA sequencer, *Nucleic Acids Res* **17**(18):7538.
- Zimran, A., and Horowitz, M., 1994, RecTL: a complex allele of the glucocerebrosidase gene associated with a mild clinical course of Gaucher disease, *Am J Med Genet* **50**(1):74-8.
- Zimran, A., Sorge, J., Gross, E., Kubitz, M., West, C., and Beutler, E., 1989b, Prediction of severity of Gaucher's disease by identification of mutations at DNA level, *Lancet* **2**(8659):349-52.
- Zimran, A., Sorge, J., Gross, E., Kubitz, M., West, C., and Beutler, E., 1990b, A glucocerebrosidase fusion gene in Gaucher disease. Implications for the molecular anatomy, pathogenesis, and diagnosis of this disorder, *J Clin Invest* **85**(1):219-22.