

REFERENCES

- Abd-Elsalam KA (2003). Bioinformatic tools and guideline for PCR primer design. *Afr J Biotechnol.* 2 (5):91-95.
- Adzhubei IA, Schmidt S, Peshkin L, Ramensky VE, Gerasimova A, Bork P, et al (2010). A method and server for predicting damaging missense mutations, *Nat Methods.* 7 (4):248-249.
- Ainsworth PJ, Coulter-Mackie MB (1992). A double mutation in exon 6 of the beta-hexosaminidase alpha subunit in a patient with the B1 variant of Tay-Sachs disease. *Am J Hum Genet.* 51(4):802-809.
- Akalin N, Shi HP, Vavouglis G, Hechtman P, Lo W, Scriver CR, Mahuran D, et al (1992). Novel Tay-Sachs disease mutations from China. *Hum Mutat.* 1(1):40-46.
- Akerman BR, Natowicz MR, Kaback MM, Loyer M, Campeau E, Gravel RA (1997). Novel mutations and DNA-based screening in non-Jewish carriers of Tay-Sachs disease. *Am J Hum Genet.* 60(5):1099-1106.
- Akli S, Chelly J, Mezard C, Gandy S, Kahn A, Poenaru L (1990). A "G" to "A" mutation at position -1 of a 5' splice site in a late infantile form of Tay-Sachs disease. *J Biol Chem.* 265(13):7324-7330.
- Akli S, Chelly J, Lacorte JM, Poenaru L, Kahn A (1991). Seven novel Tay-Sachs mutations detected by chemical mismatch cleavage of PCR-amplified cDNA fragments. *Genomics.* 11(1):124-134.
- Akli S, Boue J, Sandhoff K, Kleijer W, Vamos E, Young E, et al (1993a). Collaborative study of the molecular epidemiology of Tay-Sachs disease in Europe. *Eur J Hum Genet.* 1(3):229-238.
- Akli S, Chomel JC, Lacorte JM, Bachner L, Kahn A, Poenaru L (1993b). Ten novel mutations in the HEXA gene in non-Jewish Tay-Sachs patients. *Hum Mol Genet.* 2(1):61-67.
- Altschul SF, Madden TL, Schaffer AA, Zhang J, Zhang Z, Miller W, et al (1997). Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. *Nucleic Acids Res.* 25(17):3389-3402.
- Alvarez-Rodríguez A, Triggs-Raine B, Barros-Núñez P, Lozano CM (2001). A novel HEXA mutation [1393G>A (D465N)] in a Mexican Tay-Sachs disease patient. *Hum Mutat.* 17(5):437.
- Ando S, Chang NC, Yu RK (1978). High-performance thin-layer chromatography and densitometric determination of brain ganglioside compositions of several species. *Anal Biochem.* 89:437-450.
- Arpaia E, Dumbrille-Ross A, Maler T, Neote K, Tropak M, Troxel C, et al (1988). Identification of an altered splice site in Ashkenazi Tay-Sachs disease. *Nature.* 333:85-86.
- Aydin K, Bakir B, Tatli B, Terzbasioglu E, Ozmen M (2005). Proton MR spectroscopy in three children with Tay-Sachs disease. *Pediatr Radiol.* 35:1081-1085.

- Barnes D, Misra VP, Young EP, Thomas PK, Harding AE (1991). An adult onset hexosaminidase A deficiency syndrome with sensory neuropathy and internuclear ophthalmoplegia. *J Neurol Neurosurg Psychiatry*. 54:1112-1113.
- Bernheimer H, Seitlberger F (1968). Über das Verhalten der Ganglioside im Gehirn bei fallen von 2 fallen von spätaufgetretener amaurotischer. *Wienerklinische Wochenschrift* 80:163
- Beutler E, Kuhl W, Comings O (1975). Hexosaminidase isozyme in Type-O GM2 gangliosidosis (Sandhoff-Jatzkewitz disease). *Am J Hum Genet*. 27:628-638.
- Boedecker HJ, Mellman WJ, Tedesco TA, Croce CM (1975). Assignment of the human gene for Hex B to chromosome 5. *Exp Cell Res*. 93:468.
- Boles DJ, Proia RL (1995). The molecular basis of HEXA mRNA deficiency caused by the most common Tay-Sachs disease mutation. *Am J Hum Genet*. 56(3):716-724.
- Boutsany RM, Tanaka A, Nishimoto J, Suzuki K (1991). Genetic cause of a juvenile form of Tay-Sachs disease in a Lebanese child. *Ann Neurol*. 29:104-107.
- Boyd RB, Lee G, Rybczynski P, Benjamin ER, Khanna R, Wustman BA, et al (2013). Pharmacological Chaperones as Therapeutics for Lysosomal Storage Diseases. *J Med Chem*. 56 (7):2705-2725
- Brett EM, Ellis RB, Haas L, Ikonne JU, Lake BD, Patrick AD, et al (1973). Late onset GM2-gangliosidosis. Clinical, pathological and biochemical studies on 8 patients. *Arch Dis Child*. 48:775-785.
- Brismer J, Brismer G, Coates R, Gascon G, Ozand P (1990). Increased density of the thalamus on CT scan in patient with GM2 gangliosidosis. *Am J Neuroradiol*. 11:125-130.
- Brown CA, Neote N, Leung A, Gravel RA, Mahuran DJ (1989). Introduction of the α -subunit mutation associated with the B1 variant of Tay-Sachs disease into the β -subunit produces a β -hexosaminidase B without catalytic activity. *J Biol Chem*. 264:21705-21710.
- Brown DH, Triggs-Raine BL, McGinniss MJ, Kaback MM (1995). A novel mutation at the invariant acceptor splice site of intron 9 in the HEXA gene [IVS9-1 G-->T] detected by a PCR-based diagnostic test. *Hum Mutat*. 5(2):173-4.
- Brown CA, Mahuran DJ (1993). β -Hexosaminidase isozymes from cells co-transfected with a and b cDNA constructs: analysis of a subunit missense mutation associated with the adult form of Tay-Sachs disease. *Am J Hum Genet*. 53:497-508.
- Cachon-Gonzalez MB, Wang SZ, Lynch A, Ziegler R, Cheng SH, Cox TM (2006). Effective gene therapy in an authentic model of Tay-Sachs-related diseases. *Proc Natl Acad Sci*. 103:10373-10378.
- Cao Z, Natowicz MR, Kaback MM, Lim-Steele JS, Prengle EM, Brown D, et al (1993). A second mutation associated with apparent beta-hexosaminidase A pseudodeficiency: identification and frequency estimation. *Am J Hum Genet*. 53:1198-1205.

- Cao Z, Petroulakis E, Salo T, Triggs-Raine B (1997). Benign HEXA mutations, C739T (R247W) and C745T (R249W), cause beta-hexosaminidase A pseudodeficiency by reducing the alpha-subunit protein levels. *J Biol Chem.* 272:14975-14982.
- Carmody PJ, Rattazzi MC (1974). Conversion of human hexosaminidase B by crude vibrio cholerae neuraminidase preparations: Merthiolate is the active factor. *Biochem Biophys Acta* 371: 117.
- Chavany C, Jendoubi M (1998). Biology and potential strategies for the treatment of GM2 gangliosidoses. *Mol Med Today.* 4(4):158-65.
- Chen B, Rigat B, Curry C, Mahuran DJ (1999). Structure of the GM2A gene: identification of an exon 2 nonsense mutation and a naturally occurring transcript with an in-frame deletion of exon 2. *Am J Hum Genet.* 65:77-87.
- Chern J, Beutler E, Kuhl W, Gilbert F, Mellman WJ, Croce CM (1976). Characterization of heteropolymeric hexosaminidase A in human X mouse hybrid cells. *Proc Natl Acad Sci.* 73:3637.
- Clarke JT, Mahuran DJ, Sathe S, Kolodny EH, Rigat BA, Raiman JA, et al (2011). An open-label Phase I/II clinical trial of pyrimethamine for the treatment of patients Affected with chronic GM2 gangliosidosis (Tay-Sachs or Sandhoff variants). *Mol Genet Metab.* 102:6-12.
- Colombaioni L, Garcia-Gil M (2004). Sphingolipid metabolites in neural signaling and function. *Brain Res Brain Res Rev.* 46:328-355.
- Conzelmann E, Sandhoff K (1978). AB variant of infantile GM2 gangliosidosis. Deficiency of a factor necessary for stimulation of hexosaminidase A-catalyzed degradation of ganglioside GM2 and glycolipid GA2. *Proc Natl Acad Sci.* 75:3979-3983.
- Cooper DN, Yousoufian H (1988) The CpG dinucleotide and human genetic disease. *Hum Genet.* 78:151-155.
- Coutinho MF, Alves S (2016). From rare to common and back again: 60 years of lysosomal dysfunction. *Mol Genet Metab.* 117(2):53-65.
- D'azzo A, Proia RL, Kolodny EH, Kaback MM, Neufeld EF (1984). Faulty association of alpha- and beta-subunits in some forms of beta-hexosaminidase A deficiency. *J Biol Chem.* 259, 11070-11074.
- Dalal A, Bhavani GSLB, Togarrati PP, Bierhals T, Nandineni MR, Danda S, et al (2012). Analysis of the WISP3 gene in Indian families with progressive pseudorheumatoid dysplasia. *Am J Med Genet. Part A.* 158A (11):2820-2828.
- De Braekeleer M, Hechtma P, Andermann E, Kaplan F (1992). The French Canadian Tay-Sachs disease deletion mutation: identification of probable founders. *Hum Genet.* 89:83-87, 1992.
- De Duve, Pressman BC, Gianetto R, Wattiaux R, Appelmans F (1955). Tissue fractionation studies: intracellular distribution patterns of enzymes in rat liver tissue. *Biochem J.*

60:604-617.

- De Gasperi R, Gama Sosa MA, Battistini S, Yeretsian J, Raghvan S, Zelnik N, et al (1996). Late-onset GM2 gangliosidosis: Ashkenazi Jewish family with an exon 5 mutation (Tyr180→His) in the Hex A alpha-chain gene. *Neurology*. 47:547-552
- Dingle JT, Fell HB. eds. (1969-1975). Lysosomes in biology and pathology vol. I, II, III, IV, *North Holland Publ. Co.* Amsterdam.
- Dionisi-Vici C, Rizzo C, Burlina AB, Caruso U, Sabetta G, Uziel G, et al (2002). Inborn errors of metabolism in the Italian pediatric population: a national retrospective survey. *J Pediatr*. 140(3):321-332
- dos Santos MR, Tanaka A, sa Miranda MC, Ribeiro MG, Maia M, Suzuki K (1991). GM2-gangliosidosis B1 variant: Analysis of beta-hexosaminidase alpha gene mutation in 11 patients from a defined region in Portugal. *Am J Hum Genet*. 49: 886-890.
- Drory VE, Birnbaum M, Peleg L, Goldman B, Korczyn AD (2003). Hexosaminidase A deficiency in an uncommon cause of a syndrome mimicking amyotrophic lateral sclerosis. *Muscle Nerve*. 28(1):109-112.
- Drucker L, Proia RL, Navon R (1992). Identification and rapid detection of three Tay-Sachs mutations in the Moroccan Jewish population. *Am J Hum Genet*. 51:371-377.
- Drucker L, Golan A, Boles DJ, el Bedour K, Proia RL, Navon R (1997a). Novel HEXA mutation in a Bedouin Tay-Sachs patient associated with exon skipping and reduced transcript level. *Hum Mutat*. 9(3):260-264.
- Drucker L, Hemli JA, Navon R (1997b). Two mutated HEXA alleles in a Druze patient with late-infantile Tay-Sachs disease. *Hum Mutat*. 10(6):451-457.
- D'Souza G, McCann CL, Hedrick J, et al (2000). Tay-Sachs disease carrier screening: a 21-year experience. *Genet Test*. 4(3):257-263.
- Fabry J (1898). Ein Beitrag zur Kenntnis der Purpura haemorrhagia nodu~lari.s (Purpura populo sa haemorrhagica nodular is). *Arch Dermat Syph*. 43:187.
- Federico A (1987). GM2 gangliosidosis with motor neuron disease phenotypes: Clinical heterogeneity of hexosaminidase deficiency disease. *Adv Exp Med Biol*. 209:19-23.
- Felderhoff-Mueser U, Sprener J, Konstanzcak P, Navon R, Weschke B (2001). Phosphorus magnetic resonance spectroscopy in late-onset Tay-Sachs disease. *J Child Neurol*. 16:377-380.
- Fernandes Filho JA, Shapiro BE (2004). Tay-sachs disease. *Arch Neurol* 61:1466–1468.
- Fernandes M, Kaplan F, Boulay B, Scriver CR, De Braekeleer M, Andermann E, et al (1991). Two novel Tay-Sachs disease mutations in French Canadians. Abstract. 8th International Congress of Human Genetics, Washington DC, October 6-11,
- Fernandes M, Kaplan F, Natowicz M, Prence E, Kolodny E, et al (1992). A new Tay-Sachs disease B1 allele in exon 7 in two compound heterozygotes each with a second novel

- mutation. *Hum Mol Genet.* 1(9):759-761.
- Fernandes MJ, Hechtman P, Boulay B, Kaplan F (1997). A chronic GM2 gangliosidosis variant with a HEXA splicing defect: quantitation of HEXA mRNAs in normal and mutant fibroblasts. *Eur J Hum Genet.* 5(3):129-136.
- Fishman PH, Brady RO (1976). Biosynthesis and function of gangliosides. *Science* 194: 906-915.
- Foster A, Heuss D, Claus D (1999). Hexosaminidase A deficiency as differential spinocerebellar disease. *Nervenarzt.* 70:162-166.
- Frey LC, Ringel SP, Filley CM (2005). The natural history of cognitive dysfunction in late-onset GM2 gangliosidosis. *Arch Neurol.* 62:989-994.
- Fukumizu M, Yoshikawa H, Takashima S, Sakuragawa N, Kurokawa T (1992). Tay-Sachs disease: Progression of changes on neuroimaging in four cases. *Neuroradiology.* 34:483-486
- Fuller M, Meikle PJ, Hopwood JJ (2006). Epidemiology of lysosomal storage diseases: an overview. Oxford: Oxford Pharma Genesis; Chapter 2
- Furukawa K, Ohmi Y, Ohkawa Y (2011). Regulatory mechanisms of nervous systems with glycosphingolipids. *Neurochem Res.* 36:1578–1586.
- Galjaard H (1980). In Genetic metabolic diseases: early diagnosis and prenatal analysis, Amsterdam, Elsevier North Holland, pp. 790-828.
- Gatti R, Lombardo C, Filocamo M, Borrone C, Porro E (1985). Comparative study of 15 lysosomal enzymes in chorionic villi and cultured amniotic fluid cells. Early prenatal diagnosis in seven pregnancies at risk for lysosomal storage diseases. *Prenat Diagn.* 5(5):329–336.
- Gaucher P (1882). De l'epithelioma primitif de la rate. These de Paris
- Geiger B, Arnon R, Sandhoff K (1977). Immunochemical and biochemical investigation of hexosaminidase S. *Am J Hum Genet.* 29:508–522.
- Georgiou T, Christopoulos G, Anastasiadou V, Hadjiloizou S, Cregeen D, Jackson M, et al (2014). The first family with Tay-Sachs disease in Cyprus: Genetic analysis reveals a nonsense (c.78G>A) and a silent (c.1305C>T) mutation and allows preimplantation genetic diagnosis. *Meta Gene* 2:200–205.
- Giraud C, Dussau J, Azouguene E, Feillet F, Puech JP, Caillaud C (2010). Rapid identification of HEXA mutations in Tay-Sachs patients. *Biochem Biophys Res Commun.* 392(4):599-602.
- Gordon BA, Gordon KE, Hinton GG, Cadera W, Feleki V, Bayleran J, et al (1988). Pediatr Neurol. 4:54-57.
- Gort L, De Olano N, Macías-Vidal J, Coll MA (2012). Spanish GM2 Working Group, GM2 gangliosidoses in Spain: analysis of the HEXA and HEXB genes in 34 Tay-Sachs and 14 Sandhoff patients, *Gene* 506 (1):25–30.

- Gravel RA, Clarke JTR, Kaback MM, Mahuran D, Sandhoff K, Suzuki K (1995). In The Metabolic and molecular bases of inherited disease 7th ed.; Scriver, C. R., Ed.; McGraw-Hill, Health Professions Division: New York: p.2839-2879.
- Gravel RA, Kaback MM, Proia RL, Sandhoff K, Suzuki K (2001). The GM2 gangliosidoses. In: Scriver CR, Beaudet AL, Sly WS, Valle D, eds. The Metabolic and Molecular Bases of Inherited Diseases. 8 ed. Vol 3, McGraw-Hill New York, 3827-77.
- Grosso S, Farnetani MA, Berardi R, Margollicci M, Galluzzi P, Bivarelli R, et al (2003). GM2 gangliosidosis in variant B1, neuroradiological findings. *J Neurol.* 250:17-21.
- Guidotti JE, Mignon A, Hasse G, Caillaud C, McDonell N, Khan A, et al (1998). Adenoviral gene therapy of the TSD on hexominadase Adeficient knockout mice. *Hum Mol Genet.* 8:831-837.
- Harding AE, Young EP, Schon F (1987). Adult onset supranuclear ophthalmoplegia, cerebellar atxia, and neurological proximal weakness in a brother and sister: another hexoasminidase A deficiency syndrome. *J Neurol Neurosurg Psychiatry.* 50:687-690.
- Harmon DL, Gardner-Medwin D, Stirling JL (1993). Two new mutations in a late infantile Tay-Sachs patient are both in exon 1 of the beta-hexosaminidase alpha subunit gene. *J Med Genet.* 30(2):123-128.
- Hasilik A, Neufeld EF (1980). Biosynthesis of lysosomal enzymes in fibroblasts. Synthesis as precursors of higher molecular weight. *J Biol Chem.* 25:4937-4945.
- Hechtman P, Le Blanc (1977). Purification and properties of the hexosaminidase-A activating protein from human liver. *Biochem J.* 167:693-670.
- Hechtman P, Boulay B, Bayleran J, Andermann E (1989). *Clin Genet.* 35:364-375.
- Hechtman P, Kaplan F, Bayleran J, Boulay B, Andermann E, De Braekeleer M, et al (1990). More than one mutation causes infantile Tay-Sachs disease in French Canadians. *Am J Hum Genet.* 47:815-822.
- Hechtman P, Boulay B, De Braekeleer M, Andermann E, Melançon S, Larochelle J, et al (1992). The intron 7 donor splice site transition: a second Tay-Sachs disease mutation in French Canada. *Hum Genet.* 90(4):402-6.
- Henderson B, Nair SP, Coates ARM (1996). Molecular Chaperones and Diseases. *Inflamm Res.* 45(4):155-158.
- Hepbildikler ST, Sandhoff R, Kölzer M, Proia RL, Sandhoff K (2002). Physiological substrates for human lysosomal O-hexosaminidase- S. *J Biol Chem.* 277:2562-2572.
- Herbert C, Phipps P, Strane R (1974). In Methods in microbiology. New York, Academic Press, 5, 209.
- Hers HG (1963). alpha-Glucosidase deficiency in generalized glycogenstorage disease (Pompe's disease). *Biochem J.* 86:11-16.
- Hoogerbrugge PM, Brouwer OF, Bordigoni P (1995). Allogeneic bone marrow transplantation

- for lysosomal storage diseases. The European Group for Bone Marrow Transplantation. *Lancet.* 345:1398–1402.
- Hou Y, Tse R, Mahuran DJ (1996). The direct determination of the substrate specificity of the α -active site in heterodimeric β -hexosaminidase A. *Biochemistry* 35:3963–3969.
- Hund E, Grau A, Fogel W, Forsting M, Cantz M, Kustermann-Kuhn B, et al (1997). Progressive cerebral ataxia, proximal neurogenic weakness and ocular motor disturbances: hexaosaminidas A deficiency with late clinical onset in four siblings. *J Neurol Sci.* 145:25–31.
- Hwu WL, Chien YH, Lee NC, Chiang SC, Dobrovolny R, Huang A, et al (2009). Newborn Screening for Fabry Disease in Taiwan Reveals a High Incidence of the Later-Onset Mutation c.936+919G>A (IVS4+919G>A). *Hum Mutat.* 30(10):1397–1405.
- Inglese M, Nusbaum AO, Pastores GM, Gianutsos J, Kolodny EH, Gonon O (2005). MR imaging and proton spectroscopy of neuronal injury in late-onset GM2 gangliosidosis. *Am J Neuroradiol.* 26:2037–2042.
- Jamali S, Eskandari N, Aryani O, Salehpour S, Zaman T, Kamalidehghan B, et al (2014). Three Novel Mutations in Iranian Patients with Tay-Sachs Disease. *Iran Biomed J.* 18:114–119.
- Jeyakumar M, Butters TD, Cortina-Borja M, Hunnam V, Proia RL, Perry VH, et al (1999). Delayed symptom onset and increased life expectancy in Sandhoff disease mice treated with Nbutyldeoxynojirimycin. *Proc Natl Acad Sci. U S A.* 96:6388–6393.
- Johnson WG, Cohen CS, Miranda AF, Waran SP, Chutorian AM (1980). Alpha-locus hexosaminidase genetic compound with juvenile gangliosidosis phenotypes: Clinical, genetic, and biochemical studies. *Am J Hum Genet.* 32:508–518.
- Kaback MM, Zeiger RS, Reynolds LW, Sonneborn M (1974). Approaches to the control and prevention of Tay-Sachs disease. *Prog Med Genet.* 10:103–134.
- Kaback M, Lim Steele J, Dabholkar D, Brown D, Levy N (1993). Tay-sachs disease carrier screening, prenatal diagnosis and the molecular era. An international perspective, 1970–1993. The International TSD data collection Network. *JAMA* 270:2307–15.
- Kaback MM. (2000) Population-based genetic screening for reproductive counseling: the Tay-Sachs disease model. *Eur J Pediatr.* 159 (3):S192–195.
- Kaback MM, Desnick RJ (1999). Hexosaminidase A Deficiency. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2015. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK1218/>. [Updated 2011 Aug 11].
- Kaida K, Ariga T, Yu RK (2009). Antiganglioside antibodies and their pathophysiological effects on Guillain-Barre syndrome and related disorders—a review. *Glycobiology.* 19:676–692.
- Kaplan F, Bouly B, Baylearn J, Hectman P (1991). Allele-specific amplification of genomic DNA for detection of deletion mutations: Identification of a French-Canadian Tay-sachs

- mutation. *J Inher Metab Dis.* 14:707–714.
- Karpati M, Peleg L, Gazit E, Akstein E, Goldman B (2000). A novel mutation in the HEXA gene specific to Tay- Sachs disease carriers of Jewish Iraqi origin. *Clin Genet.* 57(5):398-400.
- Karpati M, Gazit E, Goldman B, Frisch A, Colombo R, Peleg L (2004). Specific mutations in the HEXA gene among Iraqi Jewish Tay-Sachs disease carriers: dating of founder ancestor. *Neurogenetics.* 5(1):35-40. Epub 2003 Nov 27.
- Karimzadeh P, Jafari N, Nejad Biglari H, Jabbeh Dari S, Ahmad Abadi F, Alaee MR, et al (2014). GM2-Gangliosidosis (Sandhoff and Tay-Sachs disease): Diagnosis and Neuroimaging Findings (An Iranian Pediatric Case Series) *Iran J Child Neurol.* 8(3):55–60.
- Kaufman M, Grinshpun-Cohen J, Karpati M, Peleg L, Goldman B, Akstein E, et al (1997). Tay- Sachs disease and *HEXA* mutations among Moroccan Jews. *Hum Mutat.* 10(4):295-300.
- Kaya N, Al- Owain M, Abu Dheim N, Al-Zahrani J, Colak D, Al-Sayed M, et al (2011). GM2 gangliosidosis in Saudi Arabia: multiple mutations and considerations for future carrier screening. *Am J Hum Genet.* A:1–4.
- Klenk EZ (1942). Gangliosides a new group of sugar containing brain lipoids. *Physiol Chem.* 273:76.
- Kodama T, Togawa T, Tsukimura T, Kawashima I, Matsuoka K, Kitkaze K, et al (2011). Lyso-GM2 Ganglioside: A Possible Biomarker of Tay-Sachs disease and Sandhoff disease. *PLoS ONE* 6(12): e29074.
- Kolodny E, Sathe S, Zeng BJ, Torres P, Alroy J, Pastores G (2008). A novel GM2-activator deficiency mutation as a cause of AB variant GM2-Gangliosidosis. *Mol Genet and Metab.* 93(2):27-28.
- Kolter T, Sandhoff K (2006). Sphingolipid metabolism diseases. *Biochim Biophys Acta.* 1758(12):2057-2079.
- Kolter T, Sandhoff K (2010). Lysosomal degradation of membrane lipids. *FEBS Lett.* 584(9):1700–1712.
- Kolter T (2012). Ganglioside biochemistry. ISRN Biochem.:1–36.
- Kornfeld S (1985). Trafficking of lysosomal enzymes in normal and disease states. *J Clin Invest.* 77:1-6.
- Kracun I, Rosner H, Drnovsek V, Heffer-Lauc M, Cosovic C, Lauc G (1991). Human brain gangliosides in development, aging and disease. *Int J Devel Biol.* 35:289–295.
- Kresse H, Fuchs W, Glossl J (1981). Liberation of N-acetylglucosamine- 6-sulfate by human

- beta-N-acetylhexosaminidase A. *J Biol Chemistr.* 256:12926–12932.
- Kumar P, Henikoff S, Ng PC (2009). Predicting the effects of coding non-synonymous variants on protein function using the SIFT algorithm. *Nat Protoc.* 4(7):1073–1081.
- Kytzia HJ, Hinrichs U, Maire I, Suzuki K, Sandhoff K (1983). Variants of GM2 gangliosidosis with hexosaminidase A having a severely changes substrate specificity. *EMBO J.* 2:1201.
- Kytzia HJ, Sandhoff K (1985). Evidence for two different active sites on human beta-hexosaminidase A. Interaction of GM2 activator protein with beta-hexosaminidase A. *J Biol Chem.* 260(12):7568–7572.
- Lalley PA, Rattazzi MC, Shows TB (1974). Human β -D-N-acetylhexoasaminidase A and B: Expression and linkage relationship in somatic cell hybrids. *Proc Natl Acad Sci.* 71:1659
- Lake B, Young E, Winchester B (1998). Prenatal diagnosis of lysosomal storage diseases. *Brain Pathol.* 8(1):133–149.
- Landels EC, Green PM, Ellis IH, Fensom AH, Bobrow M (1992). Beta-hexosaminidase splice site mutation has a high frequency among non-Jewish Tay-Sachs disease carriers from the British Isles. *J Med Genet.* 29: 563-567.
- Landels EC, Green PM, Ellis IH, Fensom AH, Kaback MM, Lim-Steele J, et al (1993). Further investigation of the HEXA gene intron 9 donor splice site mutation frequently found in non-Jewish Tay-Sachs disease patients from the British Isles. *J Med Genet.* 30:479-481.
- Lau MM, Neufeld EF (1989). A frameshift mutation in a patient with Tay-Sachs disease causes premature termination and defective intracellular transport of the alpha-subunit of beta-hexosaminidase. *J Biol Chem.* 264(35):21376-21380.
- Ledeen R, Salsman K (1965). Structure of the Tay-Sachs ganglioside. *Biochemistry* 4: 2225-2232
- Ledeen R, Wu G (2008). Nuclear sphingolipids: metabolism and signaling. *J Lipid Res.* 49:1176–1186.
- Lemieux MJ, Mark BL, Cherney MM (2006). Crystallographic structure of human beta-hexosaminidase A: interpretation of Tay-Sachs mutations and loss of GM2 ganglioside hydrolysis. *J Mol Biol.* 359:913–929.
- Levit A, Nutman D, Osher E, Kamhi E, Navon R (2010). Two novel exonic point mutations in HEXA identified in a juvenile Tay-Sachs patient: role of alternative splicing and nonsense-mediated mRNA decay. *Mol Genet Metab.* 100(2):176-183.
- Li SC, Hirabayashi Y, Li YT (1981). A new variant of type-AB GM2-gangliosidosis. *Biochem Biophys Res.* 101:479.
- Li YT, Hirabayashi Y, Li SC (1983). Diffrenetiation of two variants of type-AB GM2-gangliosidosis using chromogenic substrates. *Am J Hum Genet.* 71:196.
- Lowden JA, Skomorowski MA, Henderson F, Kaback M (1973). Automated assay of hexosaminidases in serum. *Clin Chem.* 19:1345-1349.

- Lowry OH, Rosenbrough NJ, Farr AL, Randall (1951). Protein measurement with the folin phenol reagent. *J Biol Chem.* 193:265-275.
- Magalhaes J, Sa Miranda MC, Pinto R, Lemos M, Poenaru L (1984b). Sodium taurocholate effect on p-glucosidase activity: a new approach for identification of Gaucher disease using the synthetic substrate and leucocytes. *Clin Chim Acta.* 141:111-118.
- Monaghan KG, Feldman GL, Palomaki GE, Spector EB (2008). Ashkenazi Jewish Reproductive Screening Working Group, Molecular Subcommittee of the ACMG Laboratory Quality Assurance Committee. Technical standards and guidelines for reproductive screening in the Ashkenazi Jewish population. *Genet Med.* 10(1):57-72.
- Mahuran DJ (1999). Biochemical consequences of mutations causing the GM2 gangliosidoses. *Biochim Biophys Acta.* 1455:105-138.
- Maia M, Alves D, Ribeiro G, Pinto R, Sa Miranda MC (1990). Juvenile GM2 gangliosidosis variant B1: Clinical and biochemical study in seven patients. *Neuropediatrics.* 21:18-23.
- Mandon E, Ehses I, Rother J, van Echten G, Sandhoff K (1992). Subcellular localization and membrane topology of serine palmitoyltransferase, 3-oxo-sphinganine reductase and sphinganine N-acyltransferase in mouse liver. *J Biol Chem.* 267: 11144.
- Martino S, Emiliani C, Tancini B, Severini GM, Chigorno V, Bordignon C, et al (2002) Absence of metabolic cross-correction in Tay-Sachs cells: implications for gene therapy. *J Biol Chem.* 277:20177-20184.
- Martino S, Marconi P, Tancini B, Dolcetta D, De Angelis MG, Montanucci P, et al (2005) A direct gene transfer strategy via brain internal capsule reverses the biochemical defect in Tay-Sachs disease. *Hum Mol Genet.* 14:2113-2123.
- Mark BL, Mahuran DJ, Cherney MM (2003). Crystal structure of human beta-hexosaminidase B: understanding the molecular basis of Sandhoff and Tay-Sachs disease. *J Mol Biol.* 327:1093-1109.
- Marsden D, Levy H (2010). Newborn screening of lysosomal storage disorders. *Clin Chem.* 56(7):1071-1079.
- Matsuzaki K, Kato K, Yanagisawa K (2010). A β polymerization through interaction with membrane gangliosides. *Biochim Biophys Acta.* 1801:868-877.
- Mc Dowel GA, Schultz RA, Schwartz S, Blitzer MG (1989). Presence of both Ashkenazi Tay-Sachs mutations in a non-Jewish inbred population. *Am J Hum Genet.* 45 [Suppl]: A9
- Meikle PJ, Hopwood JJ, Clague AE, Carey WF (1999). Prevalence of lysosomal storage disorders. *JAMA* 281(3):249-254.
- Mikata A, Taniguchi N (1985) Glycosphingolipid. In H. Weigandt eds. *Glycolipids*. New York: Elsevier, pp.59-82.
- Miller SA, Dykes DD, Polesky HF (1998). A simple salting out procedure for extracting DNA from human nucleated cells. *Nucleic Acids Res.* 16(3):1215.

- Mistri M, Tamhankar PM, Sheth F, Sanghavi D, Kondurkar P, Patil S, *et al* (2012). Identification of Novel Mutations in HEXA Gene in Children Affected with Tay Sachs Disease from India. *PLoS ONE* 7, e39122.
- Montalvo AL, Filocamo M, Vlahovicek K, Dardis A, Lualdi S, *et al* (2005). Molecular analysis of the HEXA gene in Italian patients with infantile and late onset Tay-Sachs disease: detection of fourteen novel alleles. *Hum Mutat.* 26(3):282.
- Moriwaki S, Takashima S, Yoshida H, Kawano N, Goto M (1977). Histological observation of the brain of Tay-Sachs disease with seizures and chronic DPH intoxication-Report of an autopsy case. *Acta Pathol Jpn.* 27:387-407.
- Mules EH, Dowling CE, Petersen MB, Kazazian HH, Thomas GH (1991). A novel mutation in the invariant AG of the acceptor splice site of intron 4 of the beta-hexosaminidase alpha-subunit gene in two unrelated American black GM2-gangliosidosis (Tay-Sachs disease) patients. *Am J Hum Genet.* 48(6):1181-1185.
- Mules EH, Hayflick S, Miller CS, Reynolds LW, Thomas GH (1992). Six novel deleterious and three neutral mutations in the gene encoding the alpha-subunit of hexosaminidase A in non-Jewish individuals. *Am J Hum Genet.* 50(4):834-841.
- Myerowitz R, Proia RL. (1984). cDNA clone for the alpha-chain of human beta-hexosaminidase: deficiency of alpha-chain mRNA in Ashkenazi Tay-Sachs fibroblasts. *Proc Natl Acad Sci* 81(17):5394–5398.
- Myerowitz R, R Piekarz, Neufeld EF, Shows TB, Suzuki K (1985). Human beta-hexosaminidase alpha chain: coding sequence and homology with the beta chain. *Proc Natl Acad Sci.* 82(23):7830–7834.
- Myerowitz R, Hogikyan ND (1986). Different mutations in Ashkenazi Jewish and non-Jewish French Canadians with Tay-Sachs disease. *Science* 232 (4758):1646–1648.
- Myerowitz R, Hogikyan ND (1987). A deletion involving *Alu* sequences in the B-hexosaminidase a-chain gene of French Canadians with Tay-Sachs disease. *J Biol Chem.* 262: 15396-15399.
- Myerowitz R, Costigan FC (1988). The major defect in Ashkenazi Jews with Tay-sachs disease is an insertion in the gene for alpha-chain of beta-hexosaminidase. *J Biol Chem* 263:18587–18589.
- Myerowitz R (1997). Tay-Sachs Disease-Causing Mutations and Neutral Polymorphisms in the Hex A Gene. *Hum Mutat.* 9:195-208.
- Nagarajan S, Chen HC, Li SC, Li YT, Lockyer JM (1992). Evidence for two cDNA clones encoding human GM2-activator protein. *Biochem J.* 282 (3):807-813.
- Najmabadi H, Hu H, Garshasbi M, Zemojtel T, Abedini SS, Chen W (2011). Deep sequencing reveals 50 novel genes for recessive cognitive disorders. *Nature.* 478(7367):57-63.
- Nakano T, Muscillo M, Ohno K, Hoffman AJ, Suzuki K (1988). A point mutation in the coding sequence of the beta-hexosaminidase alpha gene results in defective processing of the

- enzyme protein in an unusual GM2-gangliosidosis variant. *J Neurochem.* 51(3):984-987.
- Nakano T, Nanba E, Tanaka A, Ohno K, Suzuki Y, Suzuki K (1990). A new point mutation within exon 5 of beta-hexosaminidase alpha gene in a Japanese infant with Tay-Sachs disease. *Ann Neurol.* 27(5):465-473.
- Nakaya-Onishi M, Suzuki A, Okamoto N, et al (2000). Observations on time course changes of the cherry red spot in a patient with Tay-Sachs disease. *Br J Ophthalmol.* 84:1320-1321.
- Nalini A, Christopher R (2004). Cerebral Glycolipidoses: Clinical Characteristics of 41 Pediatric Patients. *J Child Neurol.* 19(6):447-452.
- Navon R, Padeh B (1971). Prenatal Diagnosis of Tay-Sachs Genotypes. *BMJ.* 4:17.
- Navon R, Khosravi R, Melki J, Drucker L, Fontaine B, Trupin JC, et al (1977). Juvenile-onset spinal muscular atrophy caused by compound heterozygosity for mutation in HEXA gene. *Ann Neurol.* 41:631-638.
- Navon R, Proia RL (1989). The mutations in Ashkenazi Jews with adult GM2 gangliosidosis. the adult form of Tay-Sachs disease. *Science* 243:1471-1474
- Navon R, Kolodny EH, Mitsumoto H, Thomas GH, Proia RL (1990). Ashkenazi Jewish and non-Jewish adult GM2 gangliosidosis patients share a common genetic defect. *Am J Hum Genet.* 46:817-821.
- Navon R, Khosravi R, Korczyn T, Masson M, Sonnino S, et al (1995). A new mutation in the HEXA gene associated with a spinal muscular atrophy phenotype. *Neurology.* 45(3 Pt 1):539-543.
- Navon R, Khosravi R, Melki J, Drucker L, Fontaine B, Turpin JC, et al (1997). Juvenile-onset spinal muscular atrophy caused by compound heterozygosity for mutations in the HEXA gene. *Ann Neurol.* 41(5):631-638.
- Nelson D, Cox MM (2005). "Lipids". Lehninger Principles of Biochemistry, 4th edition. W H Freeman & Co. p. 357. ISBN 9780716743392.
- Neudorfer O, Pastores GM, Zeng BJ, Gianutsos J, Zaroff CM, Kolodny EH (2005). Late-onset Tay-Sachs disease: Phenotypic characterization and genotypic correlation in 21 affected patients. *Genet Med.* 7:119-123.
- Novikoff AB (1961). Lysosomes and related particles, In: J. Brachet and A.E. Mirsky, eds. The cell, vol. 2. Acad, Press New York and London, pp 423-488.
- O'dowd BF, Mahuran D, Cumming D, Lowden JA (1985). Characterization by nuclear magnetic resonance of the concanavalin A binding oligosaccharide on the beta b chain of placental beta-hexosaminidase B: lectin binding to the separated polypeptide chains of hexosaminidases A and B. *Can J Biochem Cell Biol.* 63:723-729.
- O'dowd BF, Klavins MM, Willard HF, Gravel R, Lowden JA, Mahuran DJ (1986). Molecular heterogeneity in the infantile and juvenile form of Sandhoff disease. (O-Variant GM2 Gangliosidosis). *J Biol Chem.* 261:12680-12685

- Ohno K, Suzuki K (1988). Mutation in GM2-gangliosidosis B1 variant. *J Neurochem.* 50(1):316-318.
- Ohno K, Suzuki K (1988a). A splicing defect due to an exon-intron junctional mutation results in abnormal β -hexosaminidase α -chain mRNAs in Ashkenazi Jewish patients with Tay-Sachs disease. *Biochem Biophys Res.* 153:463-469.
- Ohno K, Saito S, Sugawara K, Sakuraba H (2008). Structural consequences of amino acid substitutions causing Tay-sachs disease. *Mol Genet Metab.* 94:462-468.
- Okada S, O'Brien JS (1969). Tay-Sachs disease: Generalized absence of a beta-D-N-acetylhexosaminidase component. *Science.* 165:698-700.
- Ozkara HA, Navon R (1998). At least six different mutations in HEXA gene cause Tay-Sachs disease among the Turkish population. *Mol Genet Metab.* 65(3):250-253.
- Ozkara HA, Akerman BR, Ciliv G, Topçu M, Renda Y, Gravel RA (1995). Donor splice site mutation in intron 5 of the HEXA gene in a Turkish infant with Tay-Sachs disease. *Hum Mutat.* 5(2):186-187.
- Ozkara HA, Sandhoff K (2003). A new point mutation (G412 to A) at the last nucleotide of exon 3 of hexosaminidase alpha-subunit gene affects splicing. *Brain Dev.* 25 (3):203-206.
- Paciorkowski AR, Sathe S, Zeng BJ, Torres P, Rosengren SS, Kolodny E (2008). Juvenile-onset GM2 gangliosidosis in an African-American child with nystagmus. *Pediatr Neurol.* 38(4):284-286.
- Park NJ, Morgan C, Sharma R, Li Y, Lobo RM, Redman JB, et al (2010). Improving accuracy of Tay Sachs carrier screening of the non-Jewish population: analysis of 34 carriers and six late-onset patients with HEXA enzyme and DNA sequence analysis. *Pediatr Res.* 67(2):217-220.
- Parkinson-Lawrence EJ, Shandala T, Prodoehl M, Plew R, Borlace GN, Brooks DA (2010). Lysosomal Storage Disease: Revealing Lysosomal Function and Physiology. *Physiology* 25(2):102-115.
- Paw BH, Kaback MM, Neufeld EF (1989). Molecular basis of adult onset and chronic GM2 gangliosidosis in patients of Ashkenazi Jewish origin: Substitution of Serine for glycine at position 269 of the alpha-subunit of beta-hexosaminidase. *Proc Natl Acad Sci.* 86:2413-2417.
- Paw BH, Moskowitz SM, Uhrhammer N, Wright N, Kaback MM, Neufeld EF (1990). Juvenile GM2 gangliosidosis caused by substitution of histidine for arginine at position 499 or 504 of the alpha-subunit of beta-hexosaminidase. *J Biol Chem.* 265(16):9452-9457.
- Peleg L, Meltzer F, Karpati M, Goldman B (1995). GM2 gangliosidosis B1 variant: biochemical and molecular characterization of hexosaminidase A. *Biochem Mol Med.* 54(2):126-132.
- Perlman SL (2002). Late-onset Tay-Sachs disease as a Friedrich ataxia phenocopy. *Arch Neurol.* 59:1832.
- Petroulakis E, Cao Z, Clarke JT, Mahuran DJ, Lee G, Triggs-Raine B (1998). W474C amino acid

- substitution affects early processing of the alpha-subunit of beta-hexosaminidase A and is associated with subacute (GM2) gangliosidosis. *Hum Mutat.* 11(6):432-442.
- Pierson TM, Torres PA, Zeng BJ, Glanzman AM, Adams D, Finkel RS, et al (2013). Juvenile-onset motor neuron disease caused by novel mutations in β -hexosaminidase. *Mol Genet Metab.* 108:65-69.
- Pinto R, Caseiro C, Lemos M, et al (2004). Prevalence of lysosomal storage diseases in Portugal. *Eur J Hum Genet* 12(2):87-92.
- Platt FM, Neises GR, Reinkensmeier G, Townsend MJ, Perry VH, Proia RL, et al (1997). Prevention of lysosomal storage in Tay-Sachs mice treated with N-butyl deoxynojirimycin. *Science.* 276:428-431.
- Poenaru L, Akli S (1994). Molecular epidemiology of Tay-Sachs disease in Europe. *Biomed Pharmacother.* 48(8-9):341-346.
- Pons T, Olmea O, Chinea G et al. (1998) Structural model for family 32 of glycosyl-hydrolase enzymes. *Proteins.* 33:383-395.
- Poorthuis BJ, Wevers RA, Kleijer WJ, Groener JE, de Jong JG, van Weely S, et al (1999). The frequency of lysosomal storage diseases in The Netherlands. *Hum Genet.* 105(1-2):151-156.
- Poupětová H, Ledvinova J, Berna L (2010). The birth prevalence of lysosomal storage disorders in the Czech Republic: comparison with data in different populations. *J Inherit Metab Dis* 33(4):387-396.
- Proia RL, D'Azzo A, Neufeld EF (1984). Association of α - and β -subunits during the biosynthesis of B-hexosaminidase in cultured human fibroblasts. *J Biol Chem.* 259:3350-3354
- Proia RL, Navon R (1992). Identification and rapid detection of three Tay-Sachs mutations in the Moroccan Jewish population. *Am J Hum Genet.* 51(2):371-377.
- Rahmann H (1995). Brain gangliosides and memory formation. Behav. *Brain Res.* 66: 105-116.
- Renaud D, Brodsky M (2015). GM2-Gangliosidosis, AB Variant: Clinical, Ophthalmological, MRI, and Molecular Findings. *JIMD Rep.* [Epub ahead of print]
- Ribeiro MG, Sonin T, Pinto RA, Fontes A, Ribeiro H, Pinto E, et al (1996). Clinical, enzymatic, and molecular characterization of a portuguese family with a chronic form of GM-2 gangliosidosis B1 variant. *J Med Genet.* 33:341-343.
- Ribeiro MG, Pinto R, Miranda MC, Suzuki K (1995). Tay-Sachs disease: intron 7 splice junction mutation in two Portuguese patients. *Biochim Biophys Acta.* 1270(1):44-51.
- Ribeiro MG, Pinto RA, Suzuki K, Sá Miranda MC (1997). Two novel (1334delC and 1363G to A, G455R) mutations in exon 12 of the beta-hexosaminidase alpha-chain gene in two Portuguese patients. *Hum Mutat.* 10(5):359-360.
- Richard MM, Erenberg G, Triggs-Raine BL (1995). An A-to-G mutation at the +3 position of

- intron 8 of the HEXA gene is associated with exon 8 skipping and Tay-Sachs disease. *Biochem Mol Med.* 55(1):74-76.
- Robinson D, Stirling JL (1968). N-acetyl-B-D-glucosaminidases in human spleen. *Biochem J.* 107:321-327
- Roseman S (1985). Studies on specific intracellular adhesion. *J Biochem.* 97:709.
- Rountree JS, Butters TD, Wormald MR, Boomkamp SD, Dwek RA, Asano N, et al (2009). Design, synthesis, and biological evaluation of enantiomeric beta-N-acetylhexosaminidase inhibitors LABNAc and DABNAc as potential agents against Tay-Sachs and Sandhoff disease. *Chem Med Chem.* 4(3):378-392.
- Rubin M, Karpati G, Wolfe LS, Carpenter S, Klavins MH, Mahuran DJ (1988). Adult onset motor neuronopathy in the juvenile type of hexosaminidase A and B deficiency. *J Neurol Sci.* 87:103-119.
- Rucker JC, Shapiro BE, Han YH, Kumar AN, Garbutt S, Keller EL, et al (2004). Neuro-ophthalmology of late-onset Tay-Sachs disease (LOTS). *Neurology.* 63:1918-1926.
- Rutishauser J, Spiess M. (2002). Endoplasmic reticulum storage diseases. *Swiss Med Wkly.* 132(17-18):211-222.
- Sachs B (1887). On arrested cerebral development with special reference to its cortical pathology. *J Nerv Ment Dis.* 14:541-553.
- Sachs B (1896). A family form of idiocy, generally fatal associated with early blindness. *J Nerv Ment Dis.* 21:475-479.
- Saftig P, Klumperman J (2009). Lysosome biogenesis and lysosomal membrane proteins: trafficking meets function. *Nat Rev Mol Cell Biol.* 10(9):623-635.
- Salih MA, Seidahmed MZ, El Khashab HY, Hamad MH, Bosley TM, Burn S, et al (2015). Mutation in GM2A Leads to a Progressive Chorea-dementia Syndrome. *Tremor Other Hyperkinet Mov.* 5:306.
- Salman MS, Clarke JT, Midroni G, Waxman MB (2001). Peripheral and autonomic nervous system involvement in chronic GM-2 gangliosidosis. *J Inherit Metab Dis.* 24:65-71.
- Sambrook J, Fritsch EF, Maniatis T (1989). Molecular Cloning: A laboratory Manual.
- Sandhoff K, Andreae U, Jatzkewitz H (1968). Deficient hexosaminidase activity in an exceptional case of Tay-Sachs disease with additional storage of kidney globoside in visceral organs. *Pathol Eur.* 3:278.
- Sandhoff K (1969). Variation of beta-N-acetylhexosaminidase-pattern in Tay-Sachs disease. *FEBS Lett.* 4:351.
- Sandhoff K, Harzer K, Wassle W, Jatzkewitz H (1971). Enzyme alteration and lipid storage in three variants of Tay-Sachs disease. *J Neurochem.* 18:2469.
- Sandhof K, Conzelmann E, Neufeld EF, Kaback MM, Suzuki K, in: C.R. Scriver, A.L. Beaudet,

- W.S. Sly, D.Valle (Eds.), The Metabolic and Molecular Bases of Inherited Disease, Vol. 2, 6 edn., McGraw-Hill, New York, 1989,pp. 1807-1839
- Sandhoff K (2001). The GM2-gangliosidoses and the elucidation of the O-hexosaminidase system. *Adv Genet.* 44: 67–91.
- Sandhoff K (2012). My journey into the world of sphingolipids and sphingolipidoses. *Proc Jpn Acad Ser B Phys Biol Sci.* 88(10): 554–582.
- Sandhoff K, Harzer K (2013). Gangliosides and gangliosidoses: principles of molecular and metabolic pathogenesis. *J Neurosci.* 33(25):10195-10208.
- Sanger F, Nicklen S, Coulson AR (1977). DNA sequencing with chain-terminating inhibitors. *Proc Natl Acad Sci.* 74(12):5463–5467.
- Schepers U, Glombitza G, Lemm T, Hoffmann A, Chabas A, Ozand P, et al (1996). Molecular analysis of a GM2-activator deficiency in two patients with GM2-gangliosidosis AB variant. *Am J of Hum Genet.* 59(5):1048–1056.
- Schiffmann R, van der Knaap MS (2009). Invited article: an MRI-based approach to the diagnosis of white matter disorders. *Neurology.* 72:750-759.
- Schnaar RL, Gerardy-Schahn R, Hildebrandt H (2014). Sialic acid in the brain: Gangliosides and polysialic acid in nervous system development, stability, disease, and regeneration. *Physiol Rev.* 94:461–518.
- Schneider A, Nakagawa S, Keep R, et al (2009). Population-based Tay-Sachs screening among Ashkenazi Jewish young adults in the 21st century: Hexosaminidase A enzyme assay is essential for accurate testing. *Am J Med Genet A.* 149A (11):2444–2447.
- Schroder M (1989). Isolation of a cDNA encoding the human GM2 activator protein. *FEBS Lett.* 251(1-2):197-200.
- Schroder M, Schnabel D, Suzuki K, Sandhoff K (1991). A mutation in the gene of a glycolipid-binding protein (GM2 activator) that causes GM2-gangliosidosis variant AB. *FEBS Lett.* 290(1-2):1-3.
- Schroder M, Schnabel D, Hurwitz R, Young E, Suzuki K, Sandhoff K (1993). Molecular genetics of GM2-gangliosidosis AB variant: a novel mutation and expression in BHK cells. *Hum Genet.* 92:437-440.
- Schwarz JM, Rodelsperger C, Schuelke M, SeelowD (2010). Mutation Taster evaluates disease-causing potential of sequence alterations. *Nat Methods.* 7(8):575–576.
- Scott SA, Sedelmann L, Liu L, Luo M, Desnick RJ, Kornreich R (2010). Experience with carrier screening and prenatal diagnosis for sixteen Ashkenazi Jewish genetic diseases. *Hum Mut.* 31; 1240-50.
- Shapiro BE, Pastores GM, Gianutsos J, Luzy C, Kolodny EH (2009). Miglustat in late-onset Tay-Sachs disease: a 12-month, randomized, controlled clinical study with 24 months of extended treatment. *Genet Med.* 2009;11:425–33.

- Shapria E, Blitzer MG, Miller JB, et al (1989). Fluorometric assays in Biochemical Genetics: A laboratory Manual Oxford university press, 19-46.
- Sheth J, Mistri M, Sheth F, Shah R, Bavdekar A, Godbole K, et al (2014a). Burden of Lysosomal Storage Disorders in India: Experience of 387 Affected Children from a Single Diagnostic Facility. *JIMD Rep.* 12:51-63.
- Sheth J, Mistri M, Datar C, Kalane U, Patil Shekhar, Kamate M, et al (2014b). Expanding the spectrum of HEXA mutations in Indian patients with Tay-Sachs disease. *MGM Rep.* 1:425-430.
- Shirabe T, Hirokawa M, Asaki H (1980). An autopsy case of Tay-Sachs disease – with special reference to axonal swelling of the central nervous system and freeze-fracture replication studies of the membranous cytoplasmic bodies. *Folia Psychiatr Neurol Jpn.* 34:515-523.
- Shore S, Tomczak J, Grebner EE, Myerowitz R (1992). An unusual genotype in an Ashkenazi Jewish patient with Tay-Sachs disease. *Hum Mutat.* 1(6):486-490.
- Skoog W, Beck W (1956) Studies on the fibrinogen, dextran and phytohemagglutinin methods of isolating leukocytes. *Blood* 11:436-454.
- Sonderfeld S, Brendler S, Sandhoff K, Galjaard H, Hoogeveen AT (1985) Genetic complementation in somatic cell hybrids of four variants of infantile GM2-gangliosidosis. *Hum Genet.* 71:196-200
- Specola N, Vanier MT, Goutieres F, Mikol J, Aicardi J (1990). The juvenile and chronic forms of GM2 gangliosidosis: Clinical and enzymatic heterogeneity. *Neurology.* 40:145-150.
- Srivastava SK, Beutler E (1973). Hexosaminidase-A and hexosaminidase-B: Studies in Tay-Sachs' and Sandhoff's diseases. *Nature.* 241:463.
- Srivastava SK, Wiktorowicz JE, Awasthi YC (1976). Interrelationship of hexosaminidases A and B: Confirmation of the common and unique subunit theory. *Proc Natl Acad Sci.* 73:2833-2837.
- Staretz-Chacham O, Lang TC, La Marca ME, Krasnewich D, Sidransky E (2009). Lysosomal Storage Disorders in the Newborn. *Pediatrics.* 123(4):1191-1207.
- Strecker G, Herlant-Peers MC, Fournet B, Montreuil J, Dorland L, Haverkamp J, et al (1977). Structure of seven oligosaccharides excreted in the urine of a patient with Sandhoff's disease (GM2 gangliosidosis-variant O). *Eur J Biochem.* 81:165.
- Stockley TL, Ray PN (2003). Multiplexed Fluorescence Analysis for mutations causing Tay-Sachs disease in Methods in Molecular Biology: Neurogenetics Methods and Protocols edited by Potter NT Humana Press vol-217:131-142.
- Suzuki K (1965). The pattern of mammalian brain gangliosides. III. Regional and developmental differences. *J Neurochem.* 12:969-979.
- Suzuki Y (2005). Sialobiology of influenza: molecular mechanism of host range variation of influenza viruses. *Biol Pharm Bull.* 28:399-408.

- Svennerholm L (1962). The chemical structure of normal human brain and Tay-Sachs gangliosides. *Biochem Biophys Res.* 9:436-441.
- Takahashi K, Naito M, Suzuki Y (1987). Lipid storage disease: Part III. Ultrastructural evaluation of cultured fibroblasts in sphingolipidoses. *Acta Pathol Jpn.* 37:261-272.
- Tallman JF, Brady RO, Quirk JE, Villalba M, Gal AE (1974). Isolation and relationship of human hexosaminidases. *J Biol Chem.* 249: 3489-3499.
- Tanaka A, Ohno K, Sandhoff K, Maire I, Kolodny EH, Brown A, et al (1990a). GM2-gangliosidosis B1 variant: analysis of beta-hexosaminidase alpha gene abnormalities in seven patients. *Am J Hum Genet.* 46(2):329-39.
- Tanaka A, Punnett HH, Suzuki K (1990b). A new point mutation in the beta-hexosaminidase alpha subunit gene responsible for infantile Tay-Sachs disease in a non-Jewish Caucasian patient (a Kpn mutant). *Am J Hum Genet.* 47(3):568-74.
- Tanaka A, Sakuraba H, Isshiki G, Suzuki K (1993). The major mutation among Japanese patients with infantile Tay-Sachs disease: a G-to-T transversion at the acceptor site of intron 5 of the beta-hexosaminidase alpha gene. *Biochem Biophys Res.* 192(2):539-546.
- Tanaka A, Sakazaki H, Murakami H, Isshiki G, Suzuki K (1994). Molecular genetics of Tay-Sachs disease in Japan. *J Inherit Metab Dis.* 17(5):593-600.
- Tanaka A, Fujimaru M, Choeh K, Isshiki G (1999). Novel Mutations, including the second most common in Japan, in the B-hexosaminidase A subunit gene, a simple screening of Japanese patients with Tay-sach's disease. *J Hum Genet.* 44:91–95.
- Tanaka A, Hoang LT, Nishi Y, Maniwa S, Oka M, Yamano T (2003). Different attenuated phenotypes of GM2 gangliosidosis variant B in Japanese patients with HEXA mutations at codon 499, and five novel mutations responsible for infantile acute form. *J Hum Genet.* 48(11):571-574.
- Tandon A (2002). Therapeutic Options for Tay-Sachs Disease. Einstein Quart. *J Biol Med.* 19:10-12.
- Tay W (1881). Symmetrical changes in the region of the yellow spot in each eye of an infant. *Tr Ophth Soc U Kingdom.* 1:155.
- Tegay DH (2012). GM2 Gangliosidoses - Introduction and Epidemiology at Medscape Updated: Mar 9, 2012.
- Tettamanti G, Bonali F, Marchesini S, Zambotti V (1973). A newprocedure for the extraction, purification and ractionation of brain gangliosides. *Biochim Biophys Acta.* 296(1):160–170.
- Tews I, Perrakis A, Oppenheim A (1996). Bacterial chitobiase structure provides insight into catalytic mechanism and the basis of Tay-Sachs disease. *Nature Structural Biology* 3:638–648.
- Thomas GH (1994). Pseudodeficiencies of lysosomal hydrolases. *Am J Hum Genet.* 54(6):934–940.

- Tomczak J, Grebner EE (1994). Three novel beta-hexosaminidase A mutations in obligate carriers of Tay-Sachs disease. *Hum Mutat.* 4(1):71-72.
- Triggs-Raine BL, Feigenbaum ASJ, Natowicz M (1990). Screening for carriers of Tay-Sachs disease among Ashkenazi Jews. A comparison of DNA-based and enzyme-based tests. *N Engl J Med.* 323(1):6–12.
- Triggs-Raine BL, Akerman BR, Clarke JT (1991). Sequence of DNA flanking the exons of the HEXA gene, and identification of mutations in Tay-Sachs disease. *Am J Hum Genet.* 49:1041–1054.
- Triggs-Raine BL, Mules EH, Kaback MM, Lim-Steele JS, Dowling CE, Akerman BR, et al (1992). A pseudodeficiency allele common in non-Jewish Tay-Sachs carriers: implications for carrier screening. *Am J Hum Genet.* 51(4):793-801.
- Triggs-Raine B, Richard M, Wasel N, Prence EM, Natowicz MR (1995). Mutational analyses of Tay-Sachs disease: studies on Tay-Sachs carriers of French Canadian background living in New England. *Am J Hum Genet.* 56(4):870-879.
- Trop I, Kaplan F, Brown C, Mahuran D, Hechtman P (1992). A glycine250--> aspartate substitution in the alpha-subunit of hexosaminidase A causes juvenile-onset Tay-Sachs disease in a Lebanese-Canadian family. *Hum Mutat.* 1(1):35-39.
- Tropak M, Mahrun (2010). Tay-Sachs disease. In: Encyclopedia of life science (ELS). John wiley & Sons, Ltd.
- Tse R, Vavouglis G, Hou Y, Mahuran DJ (1996). Identification of an active acidic residue in the catalytic site of beta-hexosaminidase. *Biochemistry* 35(23):7599-7607.
- Turpin JC, Baumann N (2003). Presenting psychiatric and cognitive disorders in adult neurolipidoses. *Rev Neurol (Paris)*. 159:637-647.
- Ul-Haque A (1995). Fine needle aspiration cytology of Tay-Sachs disease. A case report. *Acta Cytol.* 39:762-765.
- Varki A, Hooshmand F, Diaz S, Varki NM, Hedrick SM (1991). Developmental abnormalities in transgenic mice expressing sialic acid specific 9-O-acetylesterase. *Cell.* 65:65.
- Vellodi A (2005). Lysosomal storage disorders. *Br J Haematol.* 128(4):413-431.
- Verma IC (2000). Burden of genetic disorders in India. *Indian J Pediatr* 67(12):893-898.
- Verma PK, Rangnath P, Dalal AB, Phadke SR (2012). Spectrum of Lysosomal Storage disorders at a Medical Genetics Center in North India. *Indian Pediatr* 49(10):799-804.
- Von Figura K, Hasilik A (1986). Lysosomal enzymes and their receptors. *Ann Rev Biochem.* 55:167-193.
- Wakamatsu N, Kobayashi H, Miyatake T (1992). A novel exon mutation in human b-hexosaminidase b subunit gene affecting the 3' splice site selection. *J Biol Chem* 267:2406–2413.

- Wendeler M, Sandhoff K (2009). Hexosaminidase assays. *Glycoconj J.* 26 (8):945-952.
- Wicklow BA, Ivanovich JL, Plews MM, Salo TJ, Noetzel MJ, Lueder GT, et al (2004). Severe subacute GM2 gangliosidosis caused by an apparently silent HEXA mutation (V324V) that results in aberrant splicing and reduced HEXA mRNA. *Am J Med Genet A.* 127A(2):158-66.
- Wu GS, Lu ZH, Wang JF, Wang Y, Xie X, Meyenhofer MF, et al (2005). Enhanced susceptibility to kainate-induced seizures, neuronal apoptosis, and death in mice lacking gangliotetraose gangliosides: Protection with LIGA 20, a membrane-permeant analog of GM1. *J Neurosci.* 25:11014–11022.
- Xie B, McInnes B, Neote K, Lamhonwah AM, Mahuran D (1991). Isolation and expression of a full-length cDNA encoding the human GM2 activator protein. *Biochem Biophys Res.* 177(3):1217-1223.
- Xie B, Kennedy JL, McInnes B, Auger D, Mahuran D (1992). Identification of a processed pseudogene related to the functional gene encoding the GM2 activator protein: localization of the pseudogene to human chromosome 3 and the functional gene to human chromosome 5. *Genomics.* 14(3):796-798.
- Xie B, Rigat B, Smiljanic-Georgijev N, Deng H, Mahuran D (1998). Biochemical Characterization of the Cys¹³⁸Arg Substitution Associated with the AB Variant Form of GM₂ Gangliosidosis: Evidence That Cys¹³⁸Is Required for the Recognition of the GM₂ Activator/GM₂ Ganglioside Complex by β-Hexosaminidase A. *Biochemistry.* 37(3):814-821.
- Xie B, Wang W, Mahuran D J (1992). A cys138-to-arg substitution in the G-M2 activator protein is associated with the AB variant form of GM2 gangliosidosis. *Am J Hum Genet.* 50:1046-1052.
- Yamano T, Shimada M, Okada S, Ytaka T, Kato T, Yabuuchi H (1982). Ultrastructural study of biopsy specimens of rectal mucosa. Its use in neuronal storage disease. *Arch Pathol Lab Med.* 106:673-677.
- Yoshikawa H, Yamada K, Sakurgawa N (1992). MRI in the early stage of Tay-Sachs disease. *Neuroradiology.* 34:394-395.
- Yu RK, Nakatani Y, Yanagisawa M (2009). The role of glycosphingolipid metabolism in the developing brain. *J Lipid Res.* 50 (l):S440–S445.
- Yu RK, Tsai YT, Ariga T, Yanagisawa M (2011). Structures, biosynthesis, and functions of gangliosides-an overview. *J Oleo Sci.* 60:537–544.
- Yu RK, Tsai YT, Ariga T (2012). Functional roles of gangliosides in neurodevelopment: An overview of recent advances. *Neurochem Res.* 37:1230–1244.
- Zhang X, Kiechle FL (2004). Review: Glycosphingolipids in health and disease. *Ann Clin Lab Sci.* 34:3-13.
- Zimran AT, Gelbart B, Westwood GA, Grabowski, Beutler E (1991). High frequency of the Gaucher disease mutation at nucleotide 1226 among Ashkenazi Jews. *Am J Hum Genet.*

49(4):855–859.

Zokaeem G, Bayleran J, Kaplan P, Hechtman P, Neufeld EF (1987). A shortened beta-hexosaminidase alpha-chain in an Italian patient with infantile Tay-Sachs disease. *Am J Hum Genet.* 40:537-547.