ERNDIM 2025 SYMPOSIUM

ERNDiM

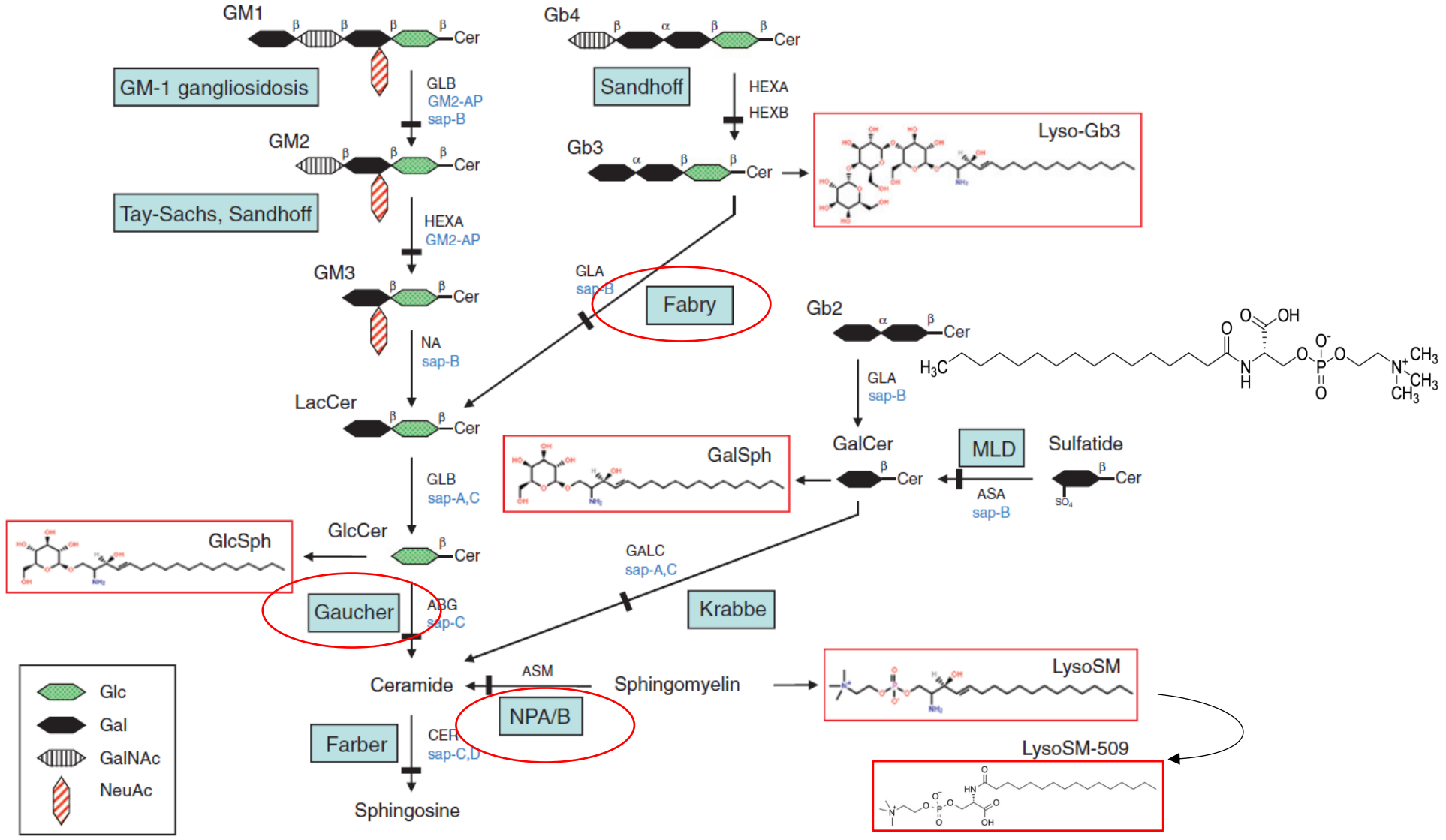
Thursday 9th
Friday 10th
October 2025
Madrid SPAIN
Crowne Plaza Madrid
Centre Retiro

History and updates on the use of Biomarkers in lysosomal diseases: FABRY, GAUCHER, NPC, ASMD

Sara Boenzi
Laboratory of Metabolic diseases and Hepatology, Bambino Gesù Children's Hospital, IRCCS – Rome - Italy

Bambino Gesù
OSPEDALE PEDIATRICO

MAIN BIOMARKERS

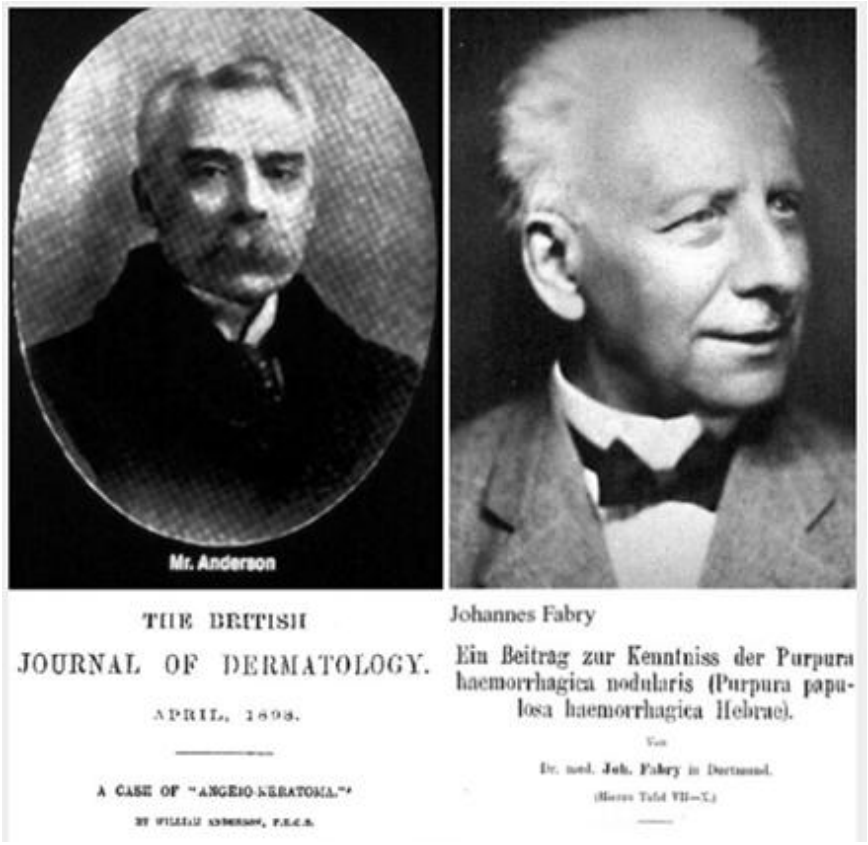


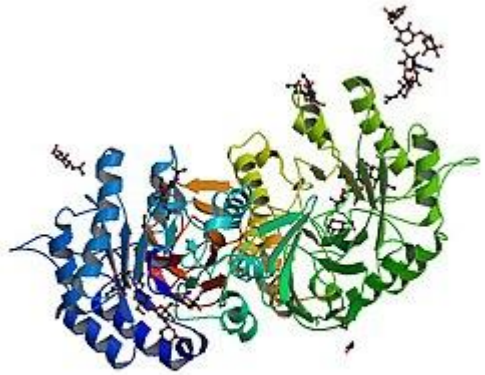
N-palmitoyl-O-phosphocholineserine
(Maekawa et al 2019)

Polo et al. 2017 modified

Fabry disease: Hystory

Anderson-Fabry disease was first described in 1898 separately and simultaneously by a German dermatologist (Johannes Fabry) and an English dermatologist (William Anderson), who identified the typical skin lesion of the disease, consisting of reddish maculopapular cutaneous angiectasias.



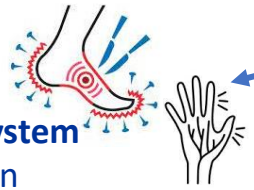


- **1967:** α-galactosidase A
- **2001:** Enzyme replacement therapy (ERT) becomes commercially available, providing recombinant α-galactosidase A to patients with Fabry disease.

Fabry disease clinical manifestations

Fabry disease

mainly affected organs

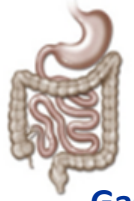


Periferal nervous system
neuropathic pain

Central nervous system
Disfunction of nervous system, pain, psychiatric manifestations, stroke, transient ischemic attack, white matter lesions

Heart
Arrithmias, LVH, aortic dilatation mitral and aortic valve disease, myocardial fibrosis

Kidney
microalbuminuria, proteinuria, renal insufficiency

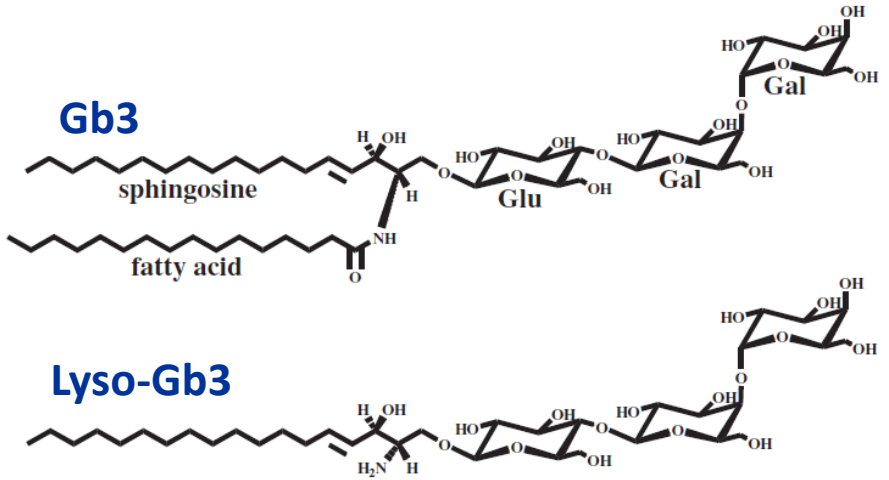


Gastrointestinal tract
nausea, vomiting, diarrhea, abdominal pain

Ocular
Corneal deposits, lenticular opacities

Fabry disease diagnosis

Fabry disease is an X-linked genetic disease, characterized by the accumulation of specific glycosphingolipids, primarily globotriaosylceramide (Gb3) and its deacylated form globotriaolsylsphingosine (lyso-Gb3) in biological fluids, vascular endothelium, heart, and kidneys.



Boutin et al. 2012

✓ **Analysis of biomarkers in body fluids**

✓ **α-galactosidase A activity**

✓ **Confirmation by genetic test in the *GLA* gene**

Fabry disease biomarkers

Molecular Genetics and Metabolism 100 (2010) 257–261

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

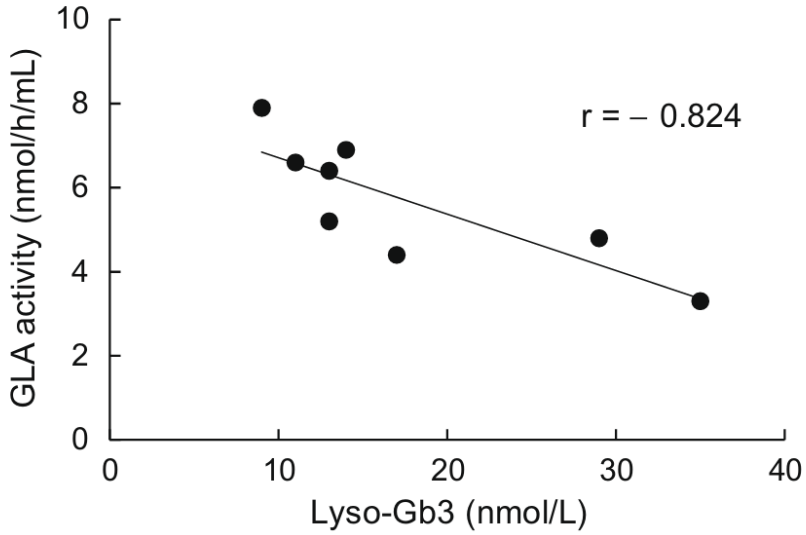
journal homepage: www.elsevier.com/locate/ymgme

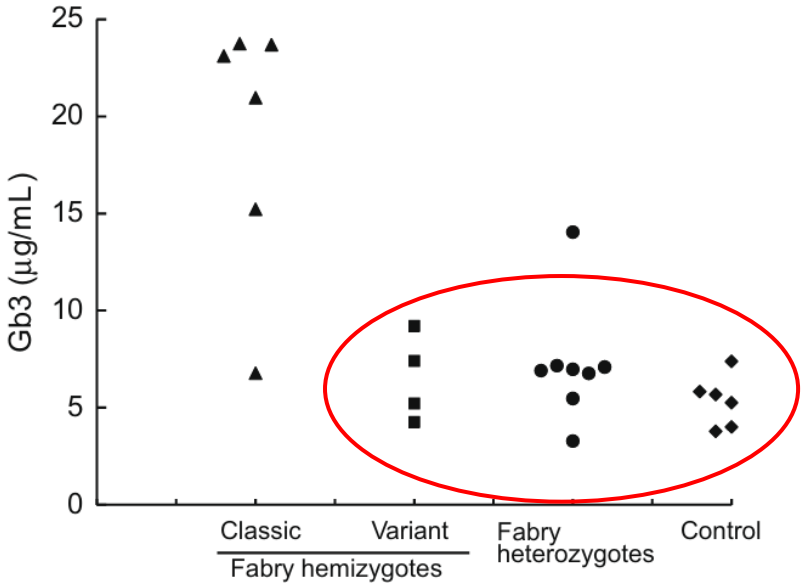
Plasma globotriaosylsphingosine as a biomarker of Fabry disease

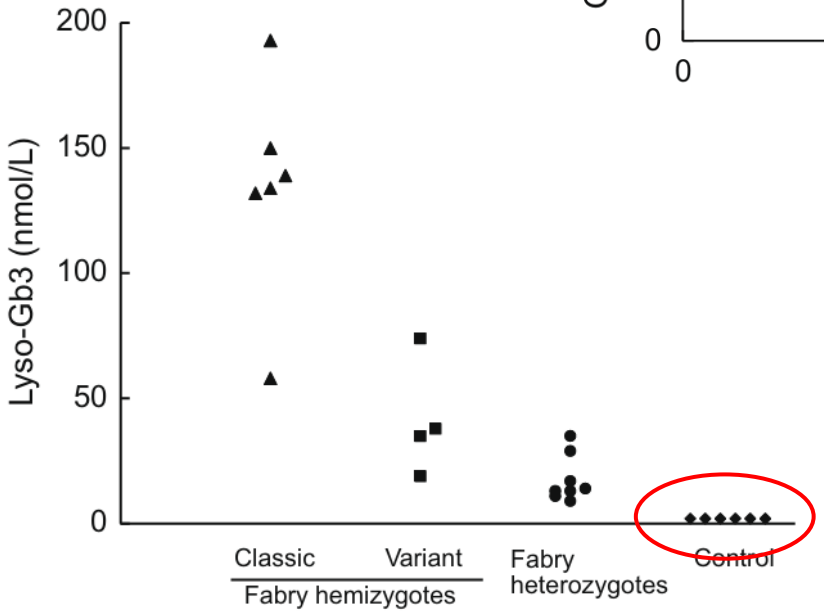
Tadayasu Togawa [a], Takashi Kodama [a], Toshihiro Suzuki [a], Kanako Sugawara [b], Takahiro Tsukimura [a], Toya Ohashi [c], Nobuyuki Ishige [d], Ken Suzuki [d], Teruo Kitagawa [d], Hitoshi Sakuraba [a,b,*]

[a] Department of Analytical Biochemistry, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan
[b] Department of Clinical Genetics, Meiji Pharmaceutical University, 2-522-1 Noshio, Kiyose, Tokyo 204-8588, Japan
[c] Department of Gene Therapy, Institute of DNA Medicine, The Jikei University School of Medicine, 3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan
[d] Tokyo Health Service Association, 1-2 Sadohara-cho, Ichigaya, Shinjuku-ku, Tokyo 162-8402, Japan

Negative correlation between Lyso-Gb3 plasma concentration and AGAL activity.







Fabry disease biomarkers

analytical chemistry

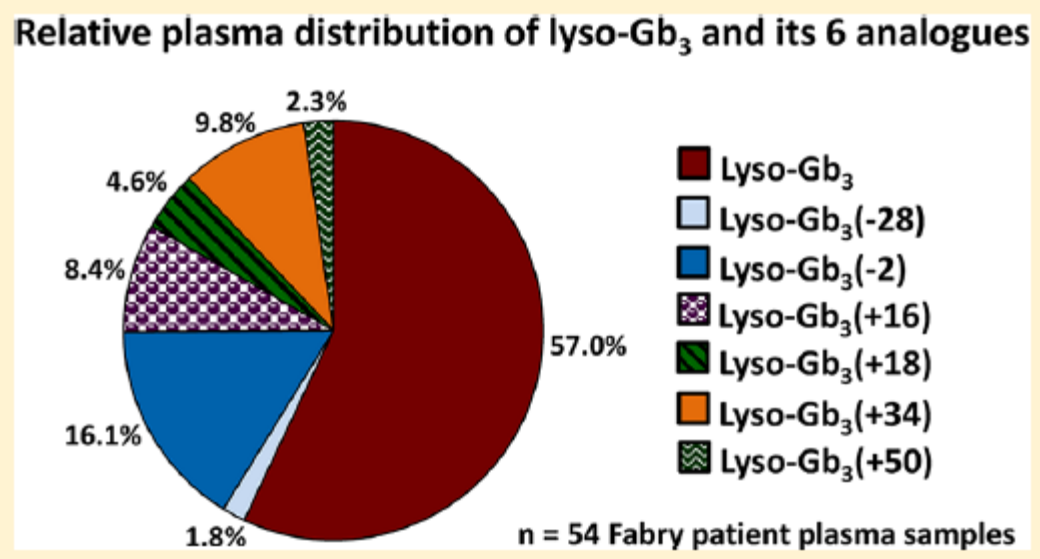
Article

pubs.acs.org/ac

Multiplex Tandem Mass Spectrometry Analysis of Novel Plasma Lyso-Gb_3-Related Analogues in Fabry Disease

Michel Boutin and Christiane Auray-Blais*

Service of Genetics, Department of Pediatrics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, 3001 12th Avenue North, Sherbrooke, Québec J1H 5N4, Canada



- ✓ lyso-Gb3 and its related analogues in plasma are higher in Fabry males compared to Fabry females and higher for untreated males compared to treated males and decrease significantly after the beginning of enzyme replacement therapy (ERT) treatment.

- ✓ In plasma, lyso-Gb3 is significantly more abundant than its related analogues

Boutin et al. 2014

Fabry disease: plasma Lyso-Gb3

Clinica Chimica Acta 414 (2012) 273–280

Contents lists available at SciVerse ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

LC–MS/MS analysis of plasma lyso-Gb_3 in Fabry disease☆

Michel Boutin, René Gagnon, Pamela Lavoie, Christiane Auray-Blais *

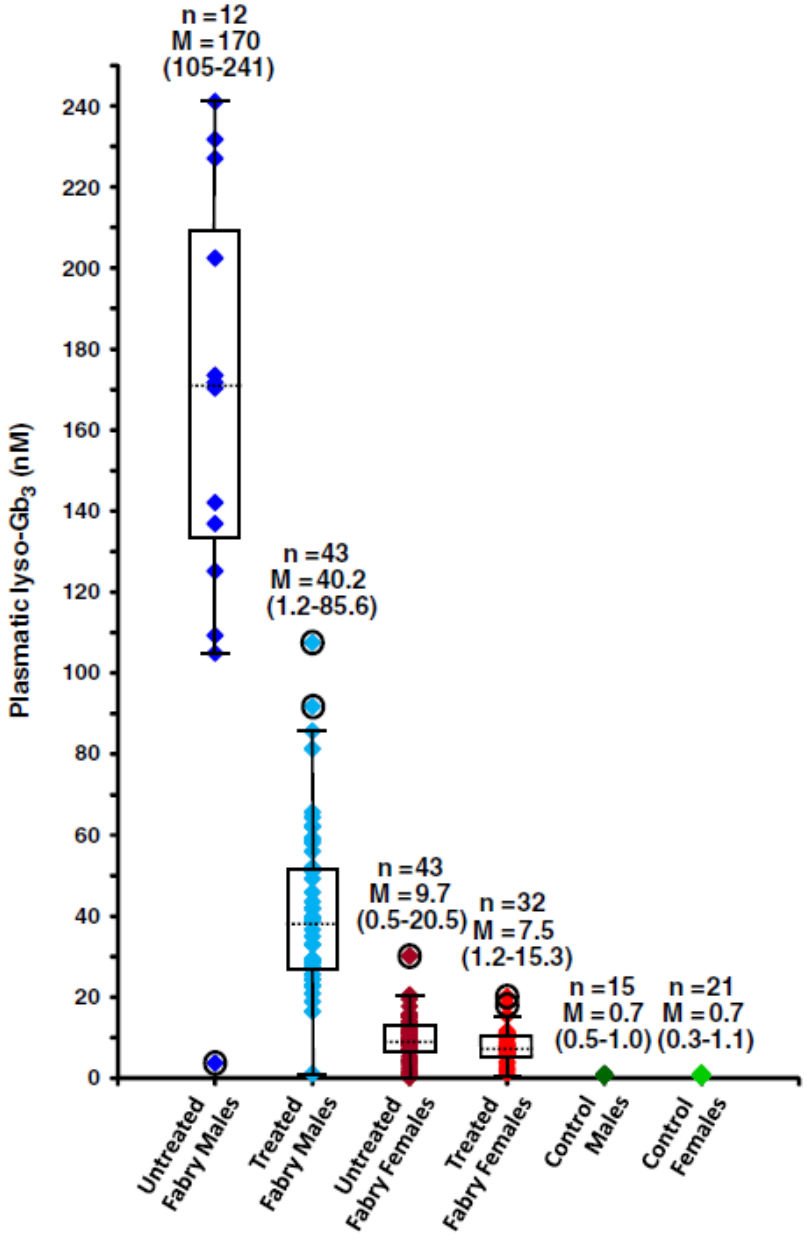
Service of Genetics, Department of Pediatrics, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Sherbrooke, Quebec, Canada

Fabry disease is an X-linked genetic disease, more severe in hemizygous males compared to heterozygous females.

Hemizygous Males: always affected, and reduced AGAL activity

Heterozygous females: they are not merely carriers, broad spectrum of manifestations is possible due to X-chromosome inactivation.

Boutin et al. 2012



Molecular Genetics and Metabolism 123 (2018) 148–153

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

Genotype, phenotype and disease severity reflected by serum LysoGb3 levels in patients with Fabry disease

Albina Nowak [a,*], Thomas P. Mechtler [b], Thorsten Hornemann [c], Joanna Gawinecka [c], Eva Theswet [a], Max J. Hilz [d], David C. Kasper [b]

[a] Department of Internal Medicine, University Hospital Zurich and University of Zurich, Rämistrasse 100, 8091 Zürich, Switzerland
[b] ARCHIMED Life Science, Leberstrasse 20, 1110 Vienna, Austria
[c] Institute for Clinical Chemistry, University Hospital Zurich and University of Zurich, Rämistrasse 100, 8091 Zürich, Switzerland
[d] University College London, Institute of Neurology, Queen Square, London WC1N 3BG, United Kingdom

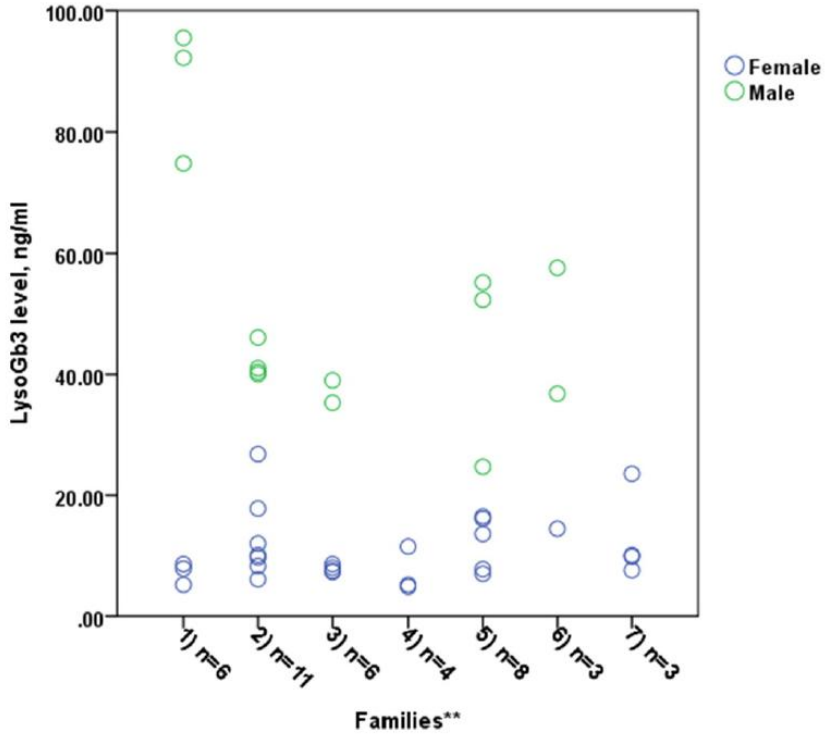
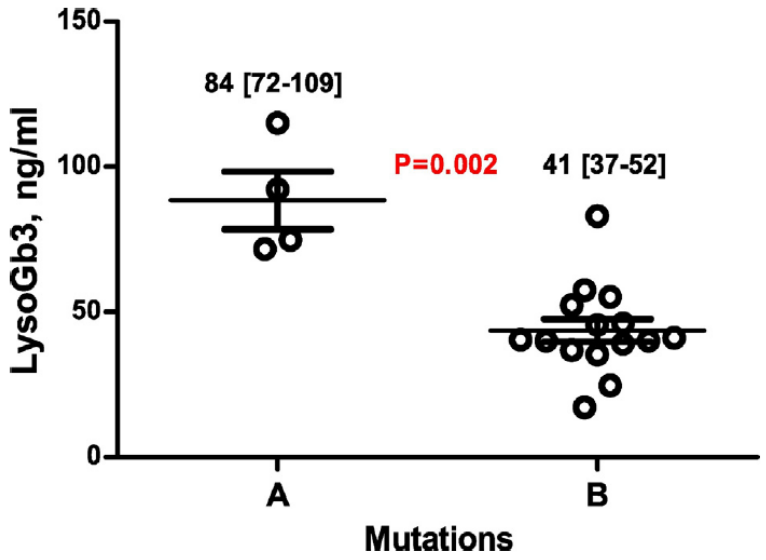


Fig. 2. Plasma LysoGb3 levels per family*. *Families with at least three family members were plotted.

- ✓ Lyso-Gb3 is higher in cases with severe variants in *GLA* gene (frameshift and nonsense) and useful in variants of uncertain significance (VUS)
- ✓ in females, lysoGb3 did not depend on mutation severity

Serum LysoGb3 levels in affected males*



*males with the same ERT preparation (α-agalsidase) at a stable dose of at least 5 years

Clinica Chimica Acta 501 (2020) 27–32

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

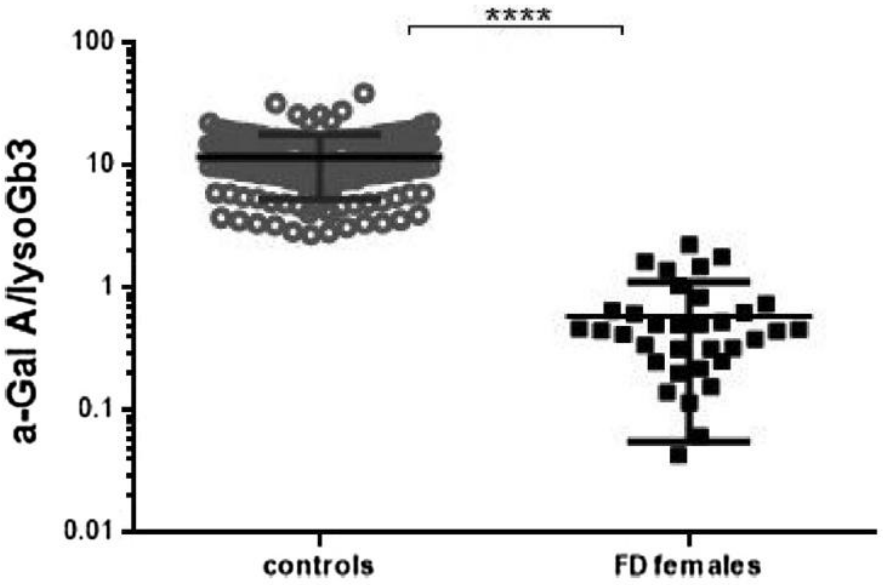
α-Galactosidase A/lysoGb3 ratio as a potential marker for Fabry disease in females

G.V. Baydakova[a], A.A. Ilyushkina[a,*], S. Moiseev[c], I.O. Bychkov[a], N.V. Nikitina[b], T.A. Buruleva[d], E.Y. Zakharova[a]

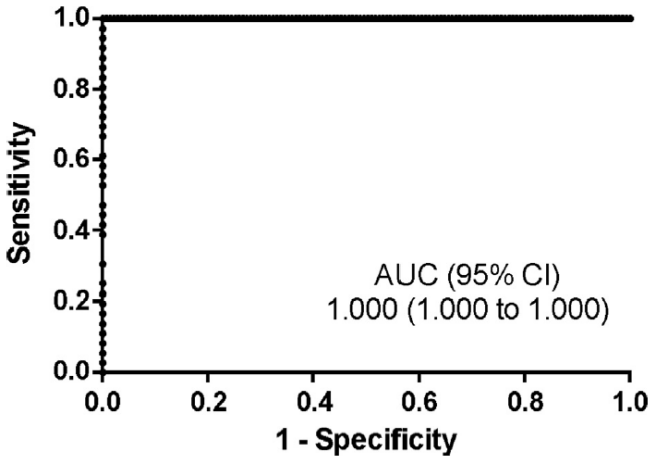
[a] Federal State Budgetary Institution "Research Centre for Medical Genetics", Moscow, Russia
[b] Clinical Diagnostic Center "Maternal and Child Health", Ekaterinburg, Russia
[c] Sechenov First Moscow State Medical University, Moscow, Russia
[d] City Clinical Hospital №52, Moscow, Russia

40-70% of female carriers may have normal AGAL activity

✓ AGAL/LysoGb3 ratio increases the sensitivity in famales



ROC curve for a-Gal A/LysoGb3 for FD female patients



Sensitivity and specificity of α-Gal A/lysoGb3 ratio.

Cut-off	Sensitivity%	95% CI	Specificity%	95% CI
< 1.58	91,67	77,53–98,25%	100,0	97,38–100,0%
< 1.72	94,44	81,34–99,32%	100,0	97,38–100,0%
< 2.03	97,22	85,47–99,93%	100,0	97,38–100,0%
< 2.50	**100,0**	**90,26–100,0%**	**100,0**	**97,38–100,0%**
< 2.80	100,0	90,26–100,0%	99,28	96,06–99,98%
< 2.88	100,0	90,26–100,0%	98,56	94,90–99,83%
< 3.02	100,0	90,26–100,0%	97,84	93,82–99,55%

G.V. Baydakova et al. Clin Chim Acta 2020

Lyso-Gb3 in DBS

Molecular Genetics and Metabolism 121 (2017) 320–324

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

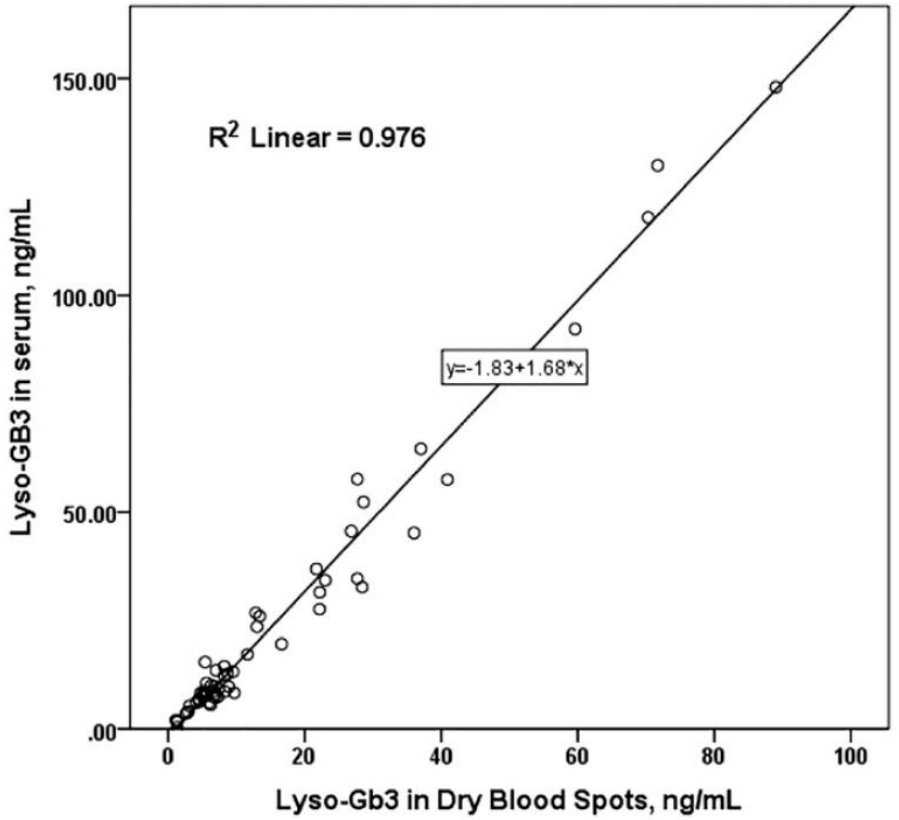
journal homepage: www.elsevier.com/locate/ymgme

Correlation of Lyso-Gb3 levels in dried blood spots and sera from patients with classic and Later-Onset Fabry disease

Albina Nowak [a,*], Thomas Mechtler [b], David C. Kasper [b], Robert J. Desnick [c]

[a] Department of Internal Medicine, University Hospital Zurich, University of Zurich, Rämistrasse 100, 8091 Zürich, Switzerland
[b] ARCHIMED Life Science, Leberstrasse 20, 1110 Vienna, Austria
[c] Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, USA

- ✓ Lyso-Gb3 analysis in DBS is less sensitive than plasma
- ✓ Lyso-Gb3 levels in sera can be estimated from the DBS concentration by multiplying the DBS value by 1.5.
- ✓ Poor correlation between DBS and sera in healthy controls due to the very low Lyso-Gb3 levels, which are at the limits of the assays sensitivity.



biomolecules

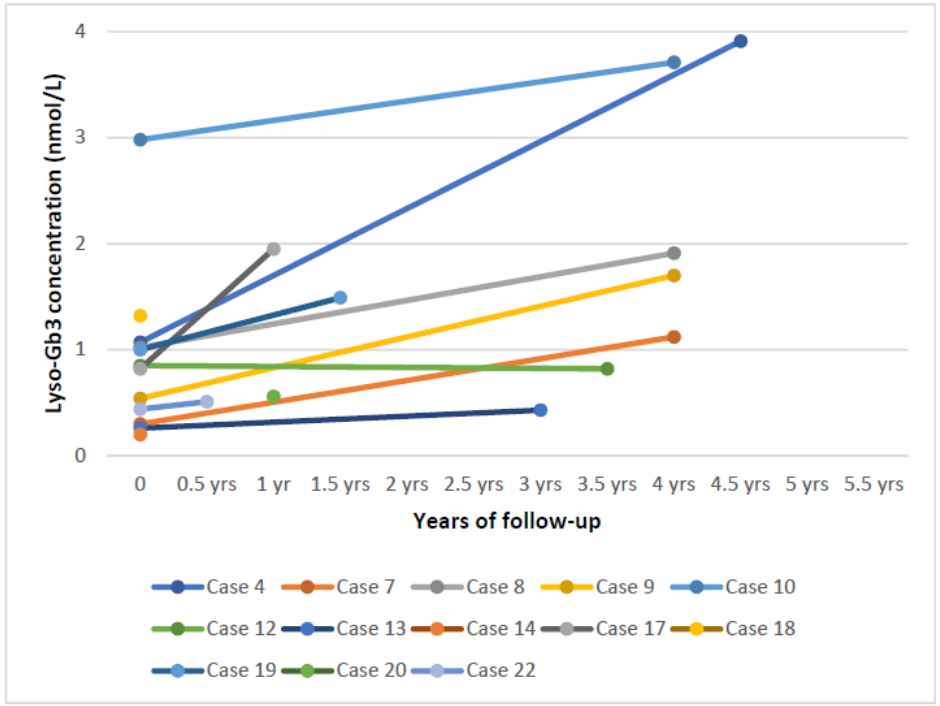
MDPI

Article

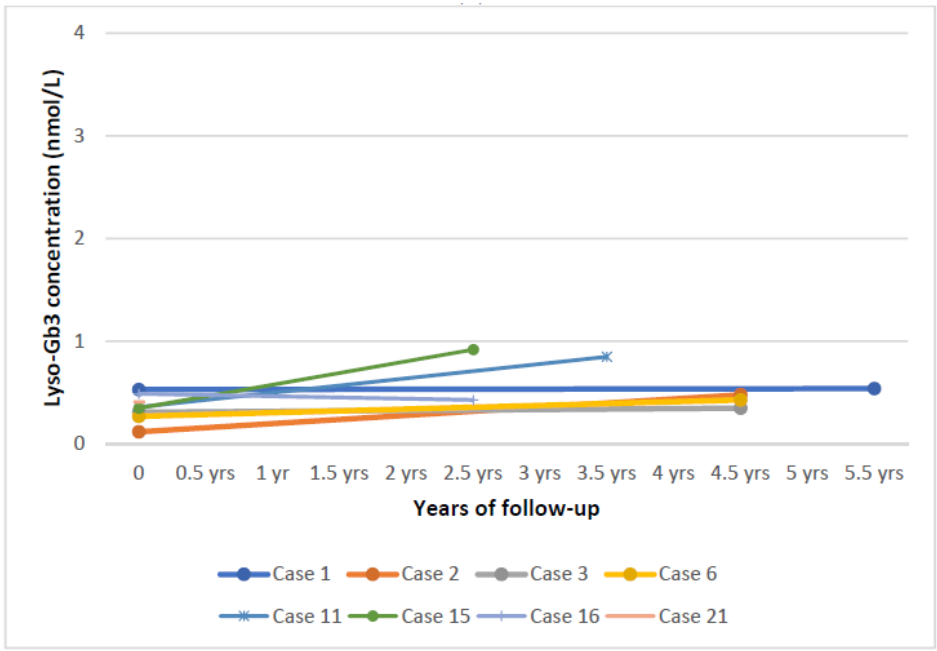
Newborn Screening for Fabry Disease in Northeastern Italy: Results of Five Years of Experience

Vincenza Gragnaniello [1,†], Alessandro P Burlina [2,†], Giulia Polo [1], Antonella Giuliani [1], Leonardo Salviati [3], Giovanni Duro [4], Chiara Cazzorla [1], Laura Rubert [1], Evelina Maines [5], Dominique P Germain [6] and Alberto B Burlina [1,*]

- ✓ 173,342 newborns in 5 years
- ✓ The screening method used α-galactosidase A enzyme activity and Lyso-Gb3 analysis in dried blood samples via a multiplex MS/MS assay.
- ✓ Genetic testing: 22 males were confirmed to be carriers of *GLA* gene variants; all were asymptomatic
- ✓ The incidence was 1:7879



Trend in plasma lyso-Gb3 levels over time in patients carrying later-onset variants. (cut-off 1.3 nmol/L)



Plasma lyso-Gb3 levels over time in subjects carrying benign and unclassified variants (including p.Ala143Thr).

Gaucher disease

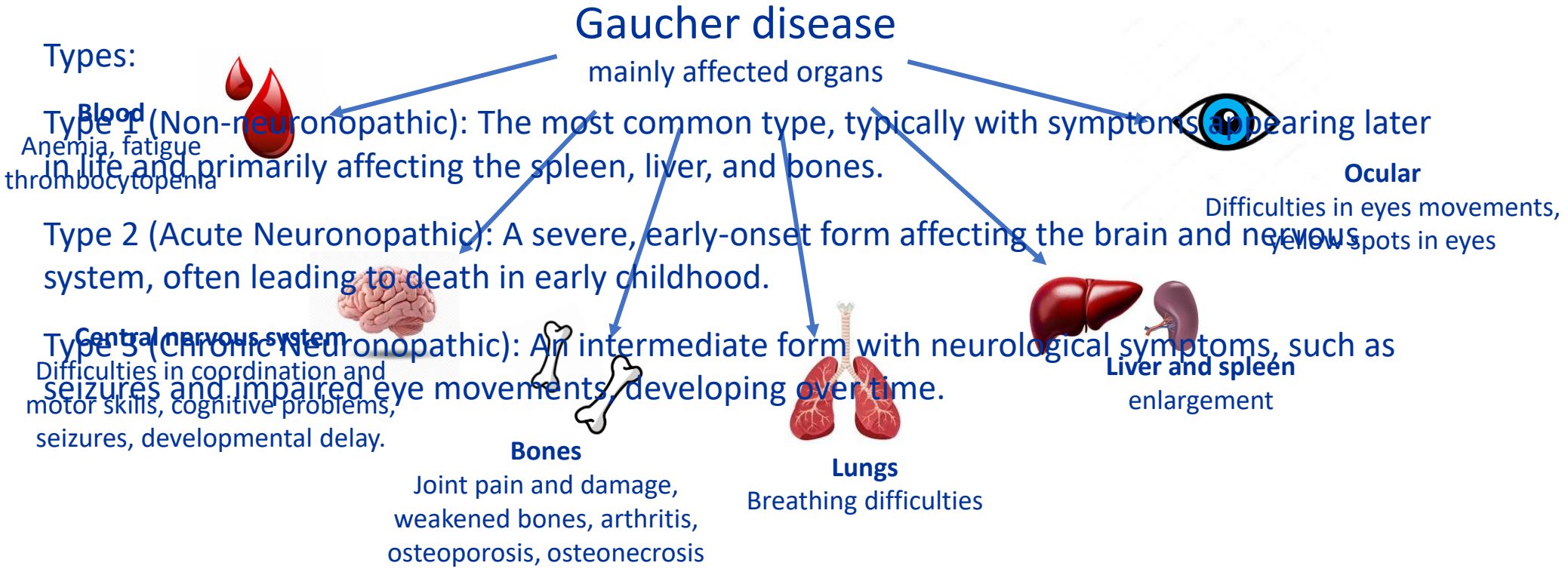
Gaucher disease was first described in 1882 by French physician Philippe Gaucher.

The underlying enzyme deficiency was identified in the 1960s;

In 1984, the gene cloning allowed the development of enzyme replacement therapy (ERT) in the 1990s, which significantly improved treatment for the non-neurological form of the disease.

Gaucher disease clinical manifestations

GD, the most prevalent lysosomal storage disorder, is an autosomal recessive inborn error of metabolism characterized by the toxic accumulation of glucocerebroside lipids within multiple organs.
GD results from mutations in the *GBA1* gene, leading to deficient glucocerebrosidase activity within lysosomes.



Types:

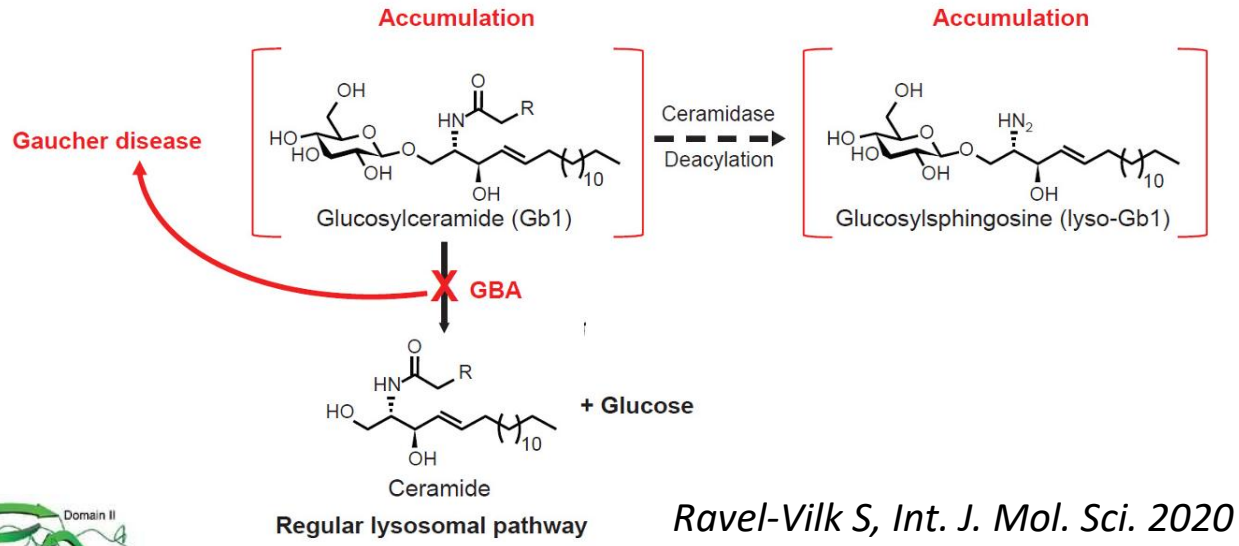
Type 1 (Non-neuronopathic): The most common type, typically with symptoms appearing later in life and primarily affecting the spleen, liver, and bones.

Type 2 (Acute Neuronopathic): A severe, early-onset form affecting the brain and nervous system, often leading to death in early childhood.

Type 3 (Chronic Neuronopathic): An intermediate form with neurological symptoms, such as seizures and impaired eye movements, developing over time.

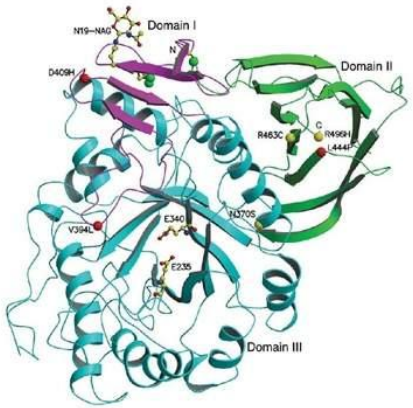
Gaucher disease diagnosis

- ✓ **Analysis of plasma biomarker (Lyso-Gb1)**



Ravel-Vilk S, Int. J. Mol. Sci. 2020

- ✓ **Glucocerebrosidase activity**



- ✓ **Confirmation by genetic test in *GBA1* gene**

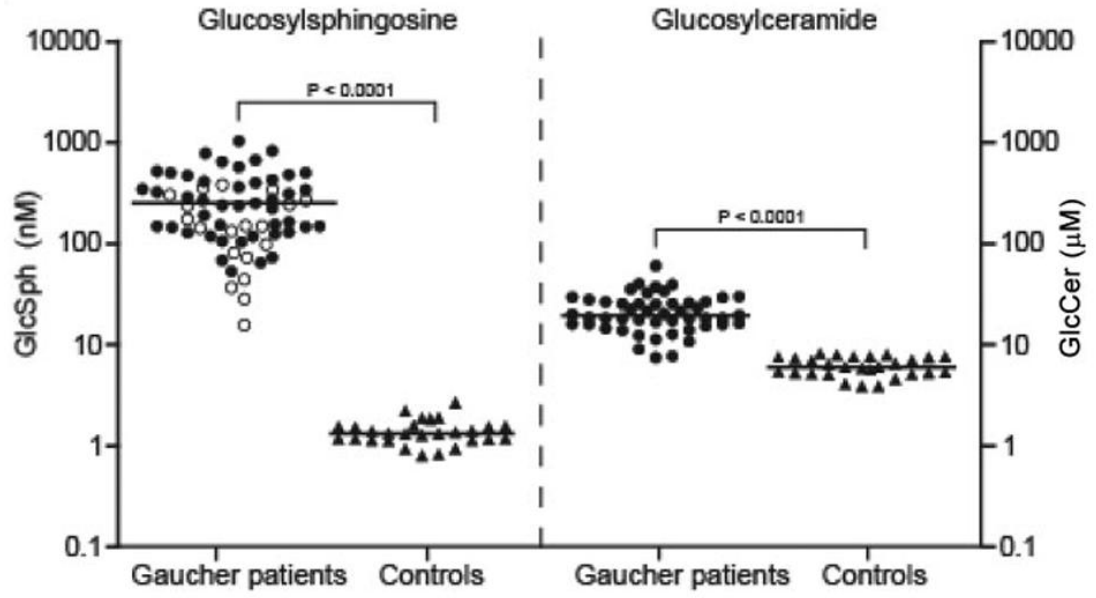
Gaucher disease

e-*Blood*

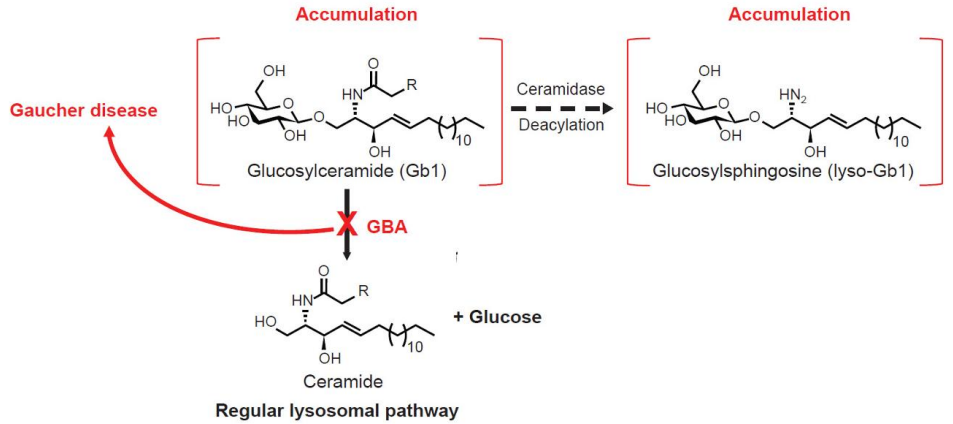
Elevated plasma glucosylsphingosine in Gaucher disease: relation to phenotype, storage cell markers, and therapeutic response

Nick Dekker,[1] Laura van Dussen,[2] Carla E. M. Hollak,[2] Herman Overkleeft,[3] Saskia Scheij,[1] Karen Ghauharali,[1] Mariëlle J. van Breemen,[1] Maria J. Ferraz,[1] Johanna E. M. Groener,[1] Mario Maas,[4] Frits A. Wijburg,[5] Dave Speijer,[1] Anna Tylki-Szymanska,[6] Pramod K. Mistry,[7] Rolf G. Boot,[1] and Johannes M. Aerts[1]

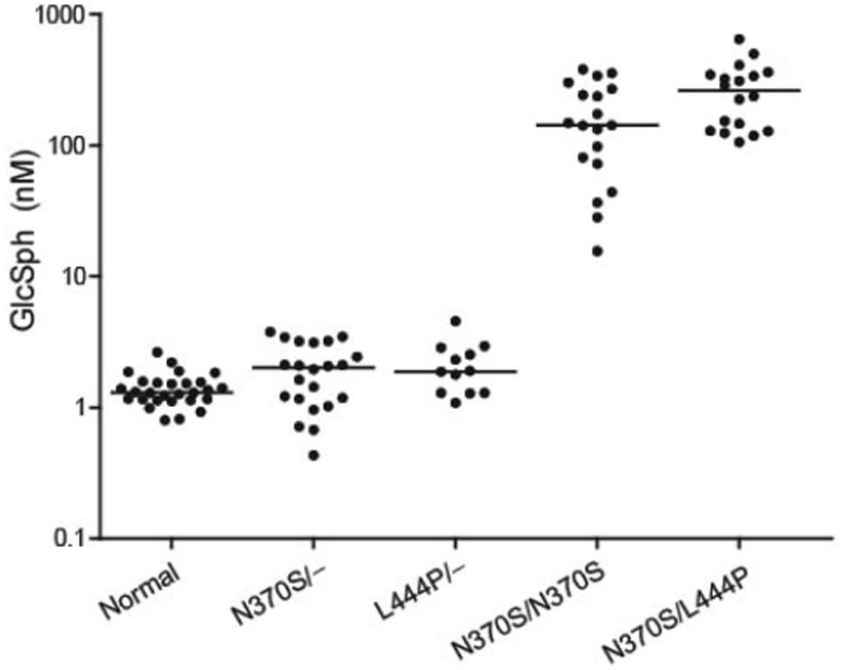
[1]Department of Medical Biochemistry, Academic Medical Center, Amsterdam, The Netherlands; [2]Department of Internal Medicine Endocrinology and Metabolism, Academic Medical Center, Amsterdam, The Netherlands; [3]Leiden Institute of Chemistry, Leiden University, Leiden, The Netherlands; [4]Department of Radiology, Academic Medical Center, Amsterdam, The Netherlands; [5]Department of Pediatrics, Academic Medical Center, Amsterdam, The Netherlands; [6]Department of Metabolic Diseases, Children's Memorial Health Institute, Warsaw, Poland; and [7]Department of Pediatric Gastroenterology & Hepatology, Yale University School of Medicine, New Haven, CT



Dekker et al. 2011



Relation between disease severity and glucosylsphingosine levels



Gaucher disease: DBS

International Journal of *Molecular Sciences*

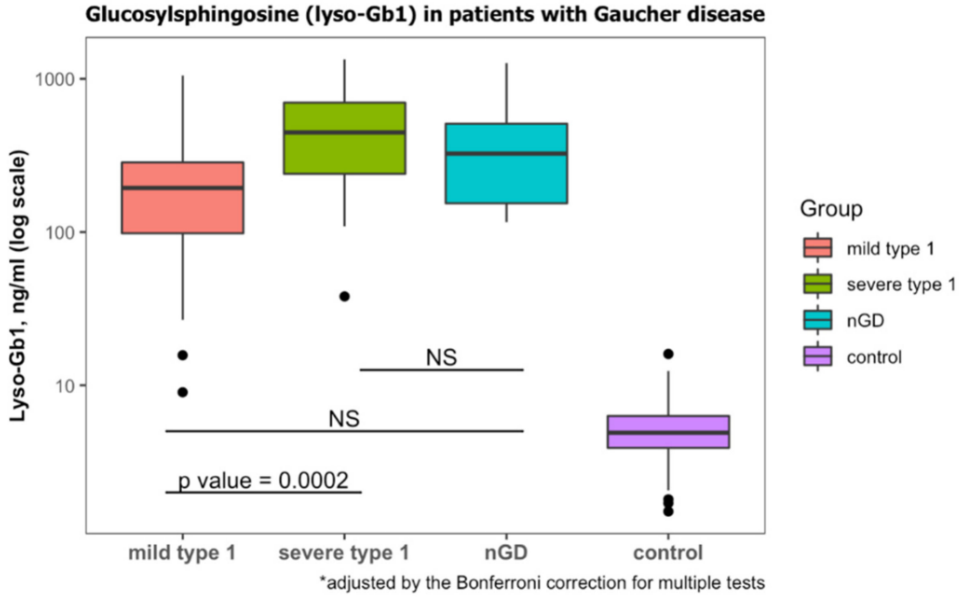
MDPI

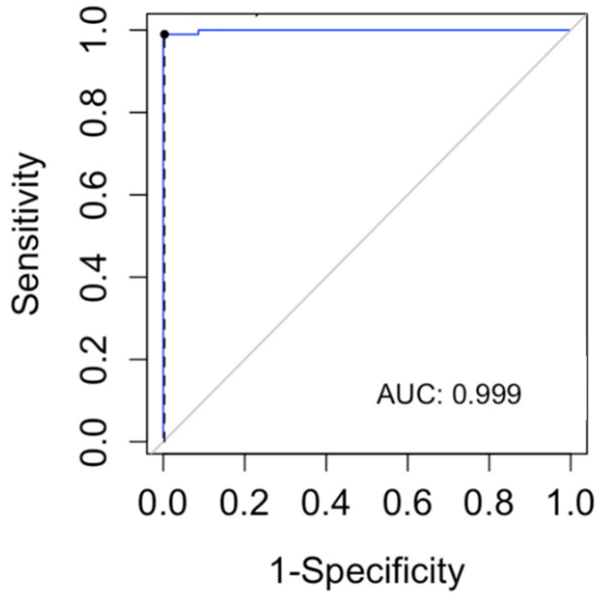
Article

Gaucher Disease Diagnosis Using Lyso-Gb1 on Dry Blood Spot Samples: Time to Change the Paradigm?

Tama Dinur [1], Peter Bauer [2], Christian Beetz [2], Guido Kramp [2], Claudia Cozma [2], Marius-Ionuț Iurașcu [2], Michal Becker-Cohen [1], Majdolen Istaiti [1], Arndt Rolfs [2,3,4], Ari Zimran [1,5] and Shoshana Revel-Vilk [1,5,*]

- 444 screened subjects
- age: 21 (1–78) years





Cut-off 9 ng/mL
sensitivity 100%
specificity 91,3%

- ✓ The Authors proposed a paradigm change for the diagnosis of GD based on lyso-Gb1 measurements and confirmatory *GBA1* mutation analyses in DBS.
- ✓ Lyso-Gb1 levels of the diagnosed with nGD (neuronopathic GD) were non-significantly different from mild GD1 and severe GD1.

Niemann Pick disease: Hystory

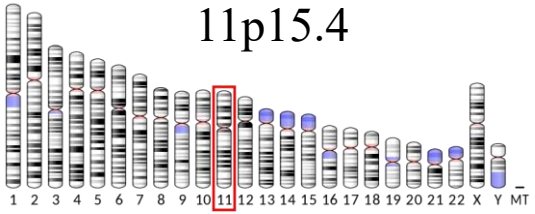
Albert Niemann
Berlin 1880–1921

Ludwig Pick
(1868–1944)

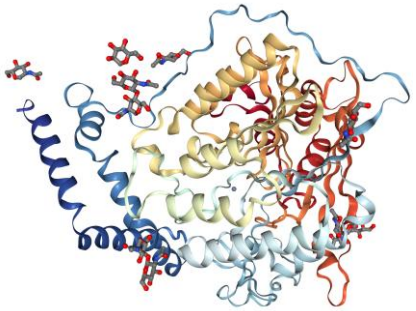
- **1914** Albert Niemann describes first patient
- **1927** Ludwig Pick recognizes NPC from Gaucher's disease
- **1958** A. Crocker and S. Farber group NPA, NPB and NPC
- **1966** R. Brady identifies the NPA/B enzyme defect (ASMD)
- **1996** M. Vanier: recognition of 2 complementary groups of NPCs and cloning of *NPC1*
- **2000** *NPC2* gene cloned
- **2006** Therapeutic authorization for Miglustat
- **2011** Plasma cholestan-3β,5α,6β-triol (Triol) and 7-ketocholesterol (7-KC) proposed as biomarkers of NPC
- **2014** Plasma lysosphingomyelin proposed as a biomarker for NPA/B
- **2015** Discovery of lysosphingomyelin-509 in plasma as a biomarker **of NPC.**
- **2019** Discovery of the structure of lysosphingomyelin-509 (Maekawa) as a phosphatidylserine**.**
- **2020** ERT therapies for ASMD
- **2024-2025** New therapies for Niemann-Pick Disease Type C (NPC) include the FDA-approved arimoclomol and the European-approved levacetylleucine, both approved in combination with the existing drug miglustat to slow disease progression and improve neurological symptoms.

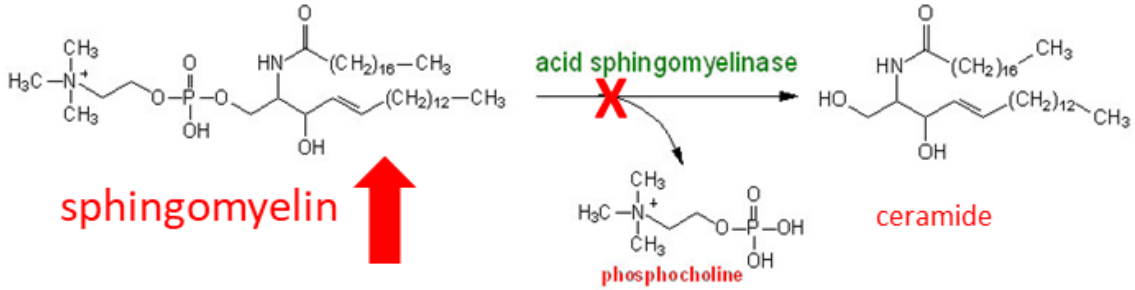
Acid sphingomyelinase deficiency (ASMD)

mutation in *SMPD1* gene



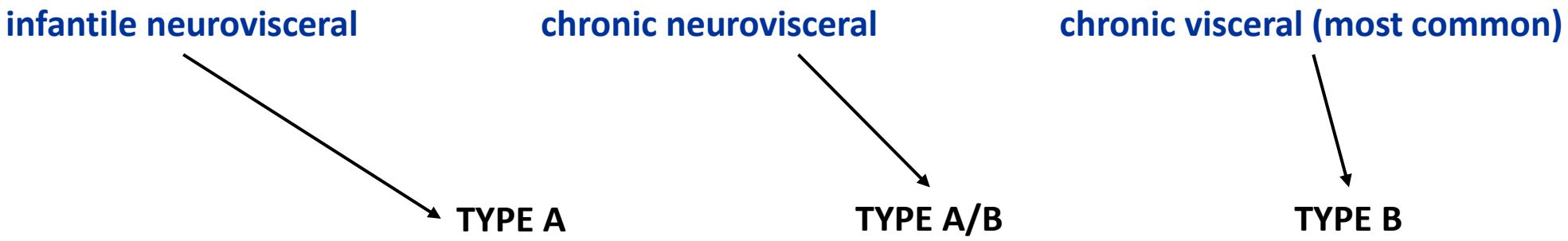
→ Acid sphingomyelinase deficiency





sphingomyelin accumulation in spleen, liver and lungs lysosomes

Three types of ASMD, differing in severity and symptom onset:



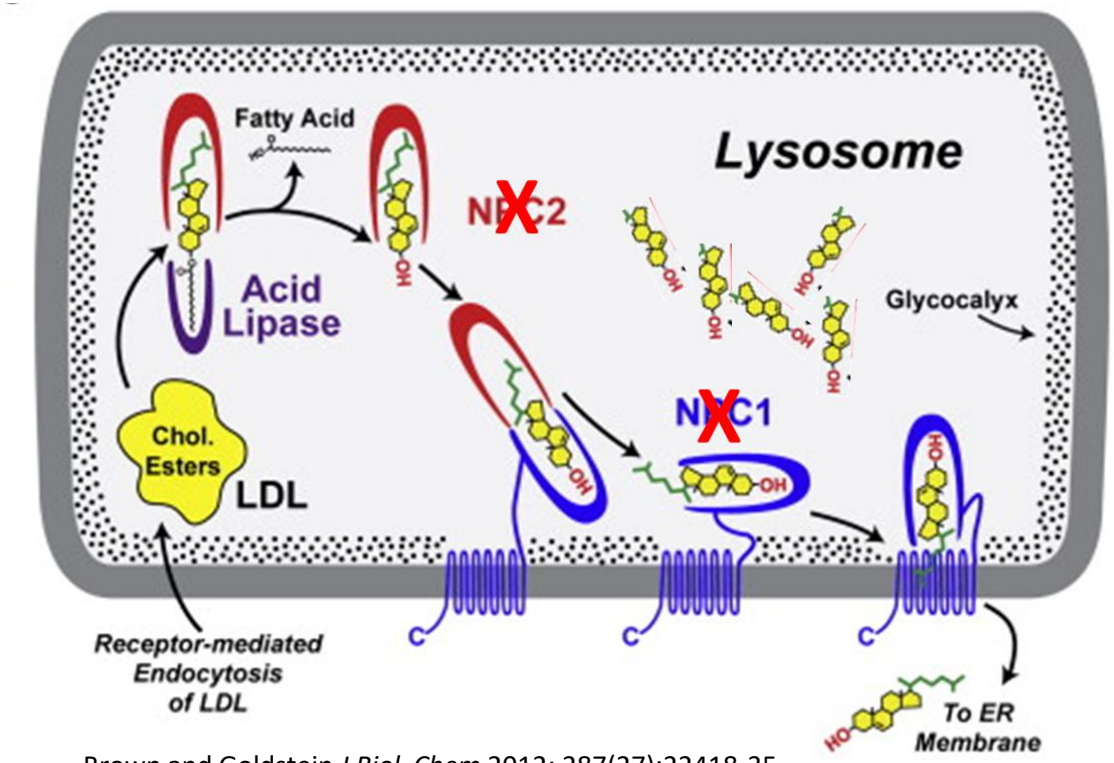
ASMD	TYPE A	TYPE A/B	TYPE B
First appearance of symptoms	Early infancy	Infancy to childhood	Infancy to childhood
Organ involvement	Multiorgan, including neurodegeneration	Variable multiorgan, typically including neurodegeneration	Variable multiorgan, limited or no neurodegeneration
Rate of symptom progression	Rapid	Variable	Variable, slower
Severity	Most severe	Moderate severity	Least severe

The level of residual activity of ASMase cannot predict the ASMD phenotype.

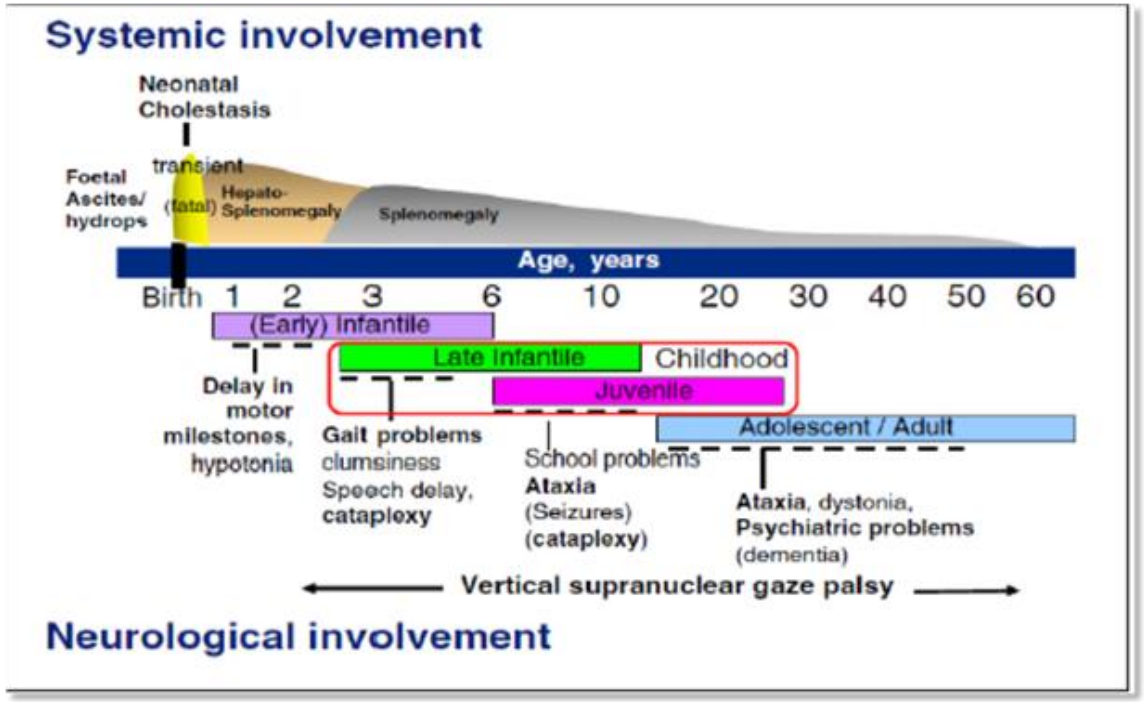
Wasserstein et al. *Mol Gen Metab* 2019

Niemann-Pick type C Mechanism & Clinical manifestations

It is not an enzymatic defect



Brown and Goldstein *J Biol Chem* 2012; 287(27):22418-35



Vanier MT. *J Inherit Metab Dis*. 2015;38:187–99

Biomarkers for Niemann-Pick disease Type C and ASMD

- ✓ **Oxysterols**: 3β,5α,6β-cholestantriol (Triol) and 7-ketocholesterol (7-KC)
- ✓ **Lyso-sphingomyelin** (Lyso-SM) and **lyso-sphingomyelin 509** (Lyso-SM-509, N-palmitoyl-O-phosphocholineserine)
- ✓ **Bile acids**: 3β,5α,6β-trihydroxycholanic acid and its glycine conjugate

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Sci Transl Med. 2010 November 3; 2(56): 56ra81. doi:10.1126/scitranslmed.3001417.

Cholesterol oxidation products are sensitive and specific blood-based biomarkers for Niemann-Pick C1 disease

Forbes D. Porter[1], **David E. Scherrer**[2], **Michael H. Lanier**[2], **S. Joshua Langmade**[2], **Vasumathi Molugu**[2], **Sarah E. Gale**[2], **Dana Olzeski**[2], **Rohini Sidhu**[2], **Dennis J. Dietzen**[3], **Rao Fu**[1], **Christopher A. Wassif**[1], **Nicole M. Yanjanin**[1], **Steven P. Marso**[4], **John House**[4], **Charles Vite**[5], **Jean E. Schaffer**[2], and **Daniel S. Ory**[2,*]

Supplemental Material can be found at:
http://www.jlr.org/content/suppl/2011/04/24/jlr.D015735.DC1.html

methods

A sensitive and specific LC-MS/MS method for rapid diagnosis of Niemann-Pick C1 disease from human plasma

Xuntian Jiang,* Rohini Sidhu,* Forbes D. Porter,† Nicole M. Yanjanin,† Anneliese O. Speak,§ Danielle Taylor te Vruchte,§ Frances M. Platt,§ Hideji Fujiwara,* David E. Scherrer,* Jessie Zhang,* Dennis J. Dietzen, Jean E. Schaffer,* and Daniel S. Ory[1,*]**

Diabetic Cardiovascular Disease Center* and Department of Pediatrics,**Washington University School of Medicine, St. Louis, MO; Program in Developmental Endocrinology and Genetics,† *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the National Institutes of Health, Department of Health and Human Services, Bethesda, MD; and Department of Pharmacology,§ University of Oxford, Oxford, UK

Jiang X, *et al*. *J Lipid Res*. 2011;52:1435-4;
Porter F, *et al*. *Sci Transl Med*. 2010;2:56ra81

Oxysterols: NP-C patients vs Controls

Clinica Chimica Acta 437 (2014) 93–100

Contents lists available at ScienceDirect

Clinica Chimica Acta

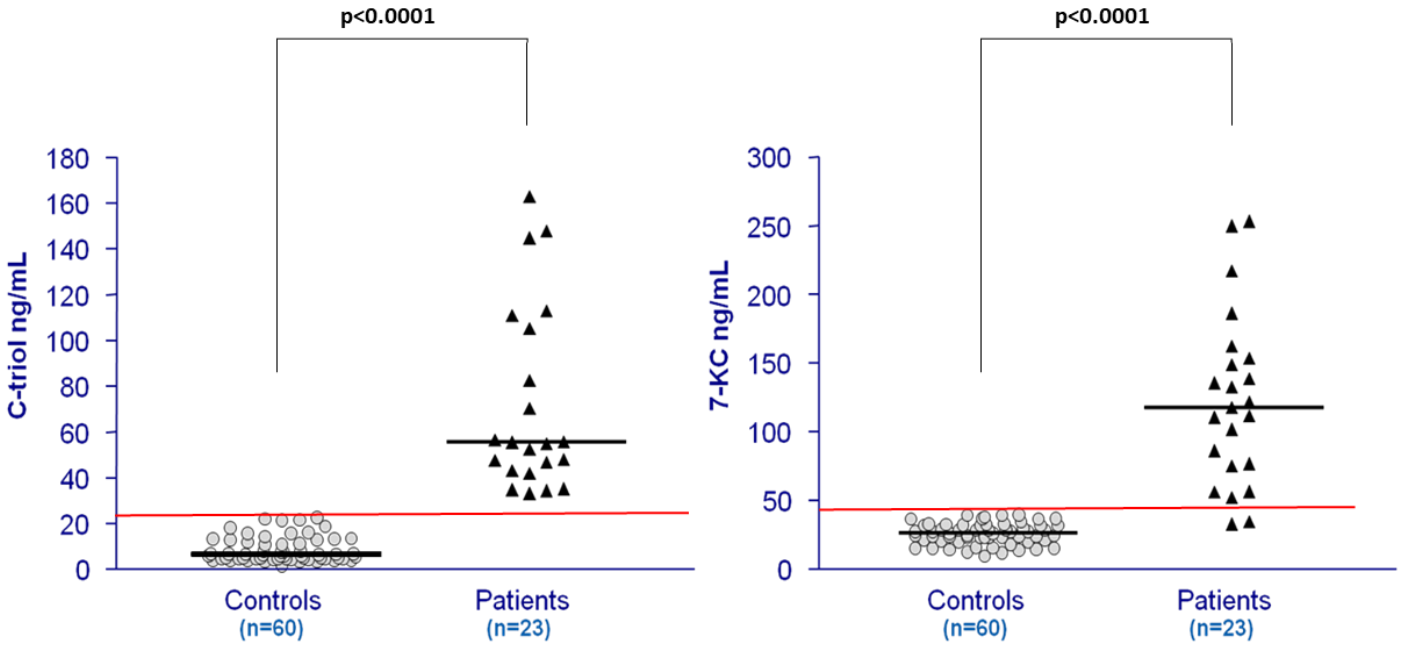
journal homepage: www.elsevier.com/locate/clinchim

A new simple and rapid LC–ESI-MS/MS method for quantification of plasma oxysterols as dimethylaminobutyrate esters. Its successful use for the diagnosis of Niemann–Pick type C disease

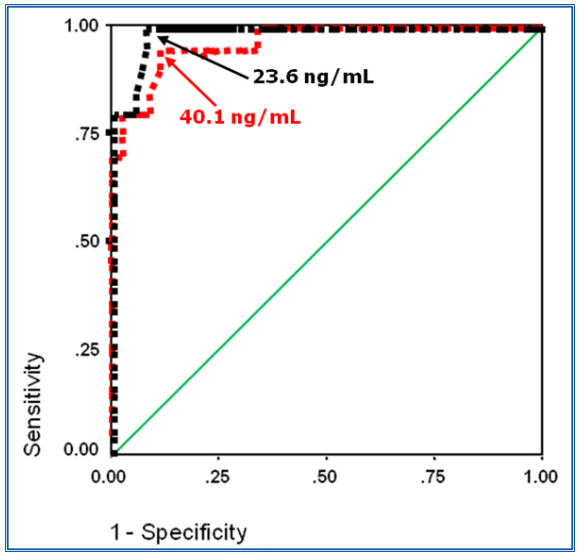
Sara Boenzi [a,*], Federica Deodato [b], Roberta Taurisano [b], Diego Martinelli [b], Daniela Verrigni [c], Rosalba Carrozzo [c], Enrico Bertini [c], Anna Pastore [a], Carlo Dionisi-Vici [b], David W. Johnson [d]

[a] Laboratory of Metabolic Biochemistry, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[b] Division of Metabolism, Department of Pediatric Medicine, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[c] Unit for Neuromuscular and Neurodegenerative Diseases, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[d] Department of Biochemical Genetics, Women's and Children's Hospital, North Adelaide 5006, South Australia, Australia

Oxysterols as dimethylaminobutyrate derivatives



Receiver Operating Characteristic (ROC)

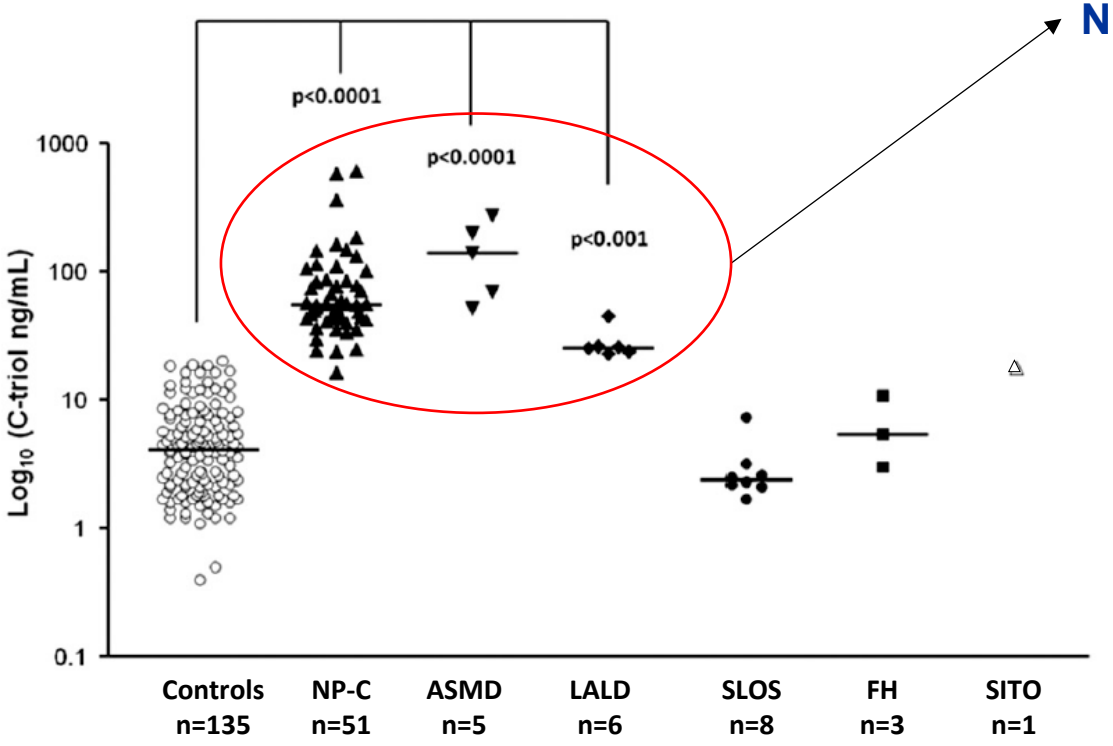


Triol AUC: 0.998
Cut-off: 23.7 ng/mL
Specificity: 98.3%
Sensitivity: 100%

7-KC AUC: 0.972
Cut-off: 40.1 ng/mL
Specificity: 85.0%
Sensitivity: 95.5%

Boenzi S, *et al*. *Clinica Chimica Acta.* 2014;437;93–100

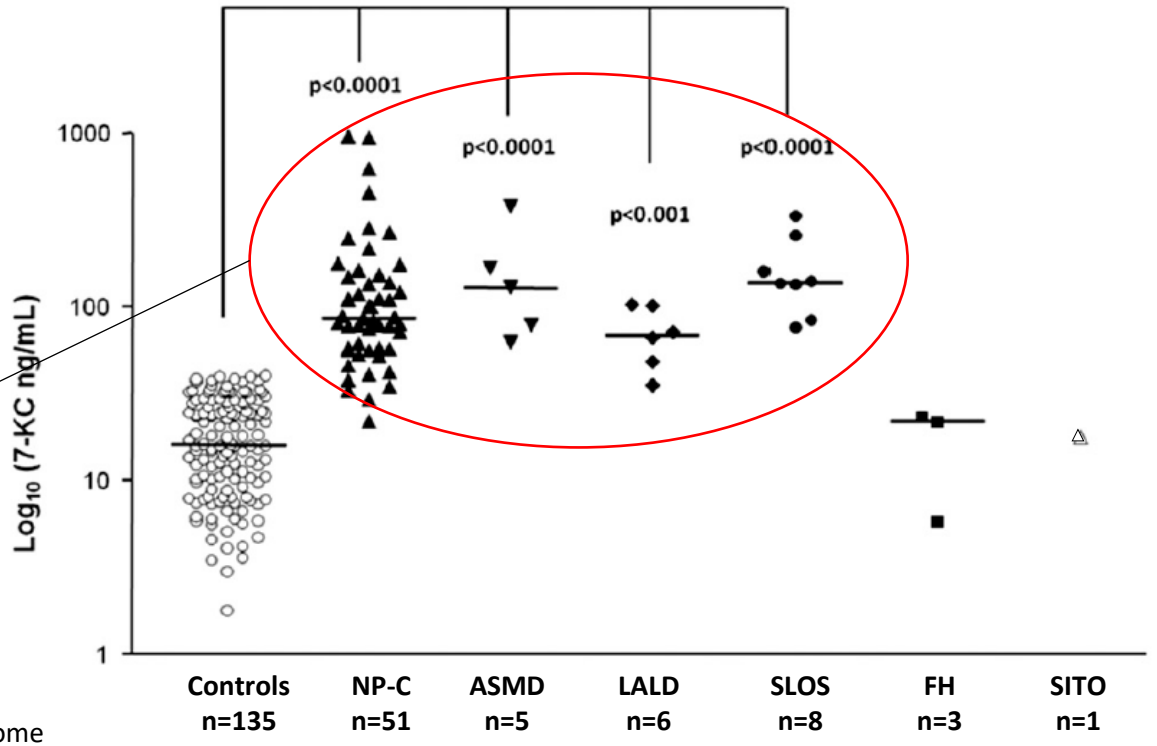
Oxysterols



NP-C, ASMD and LALD

Non-specific biomarkers for NP-C

NP-C, ASMD, LALD and SLOS

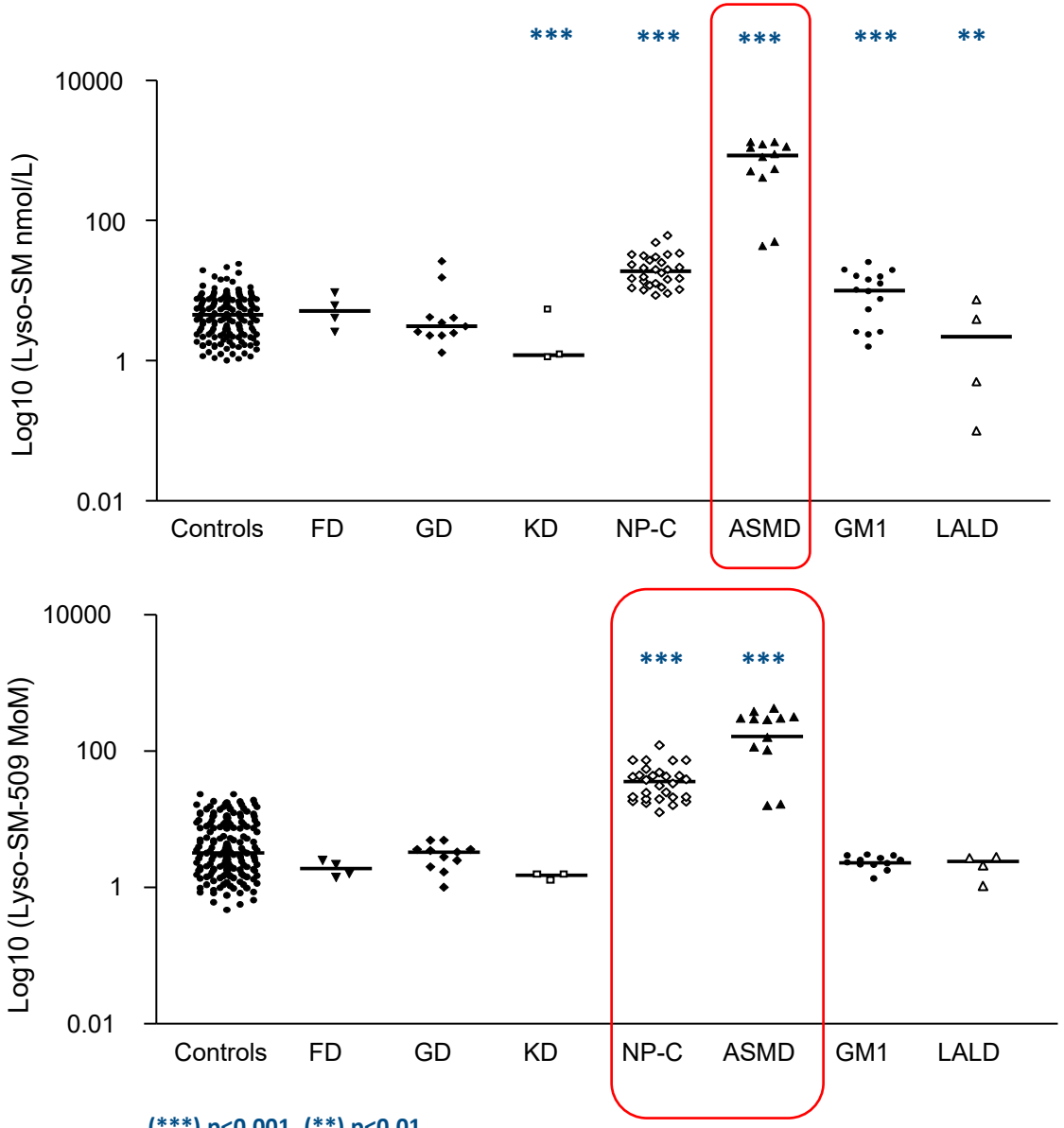


7-KC, 7-ketocholesterol; ASMD, acid sphingomyelinase deficiency (NP-B);
C-triol, cholestane-3β,5α,6β-triol; LALD, Lysosomal acid lipase deficiency; SLOS, Smith-Lemli-Opitz syndrome

Boenzi S, *et al*. *J Lipid Res*. 2016;57:361–7

Lyso-sphingolipids: lyso-SM and lyso-SM-509 for differential diagnosis

Disease	Patients	No. of samples
FD	2	4
GD	5	11
KD	2	3
NP-C	13	28
ASMD	4	12
GM1	5	15
LALD	3	4
Controls	160	160

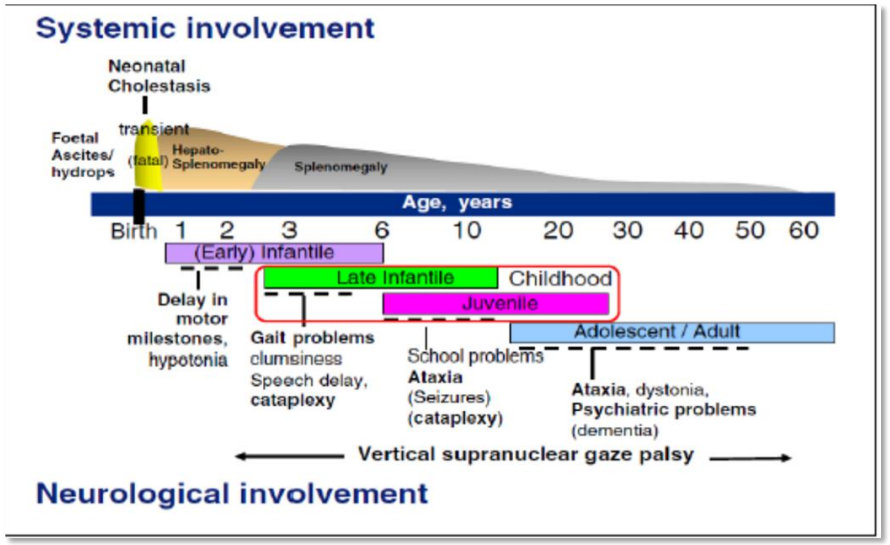


(***) p<0.001, (**) p<0.01

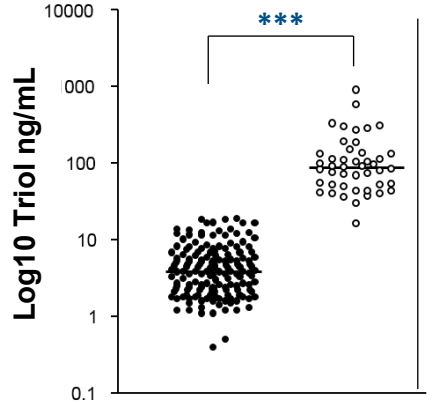
ASMD, acid sphingomyelinase deficiency; FD, Fabry disease; GD, Gaucher disease; KD, Krabbe disease; GM1, GM1 gangliosidosis; LALD, lysosomal acid lipase deficiency; MoM, multiple of the median

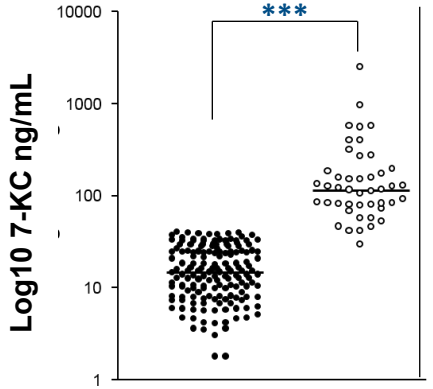
Biomarkers vs NP-C phenotype

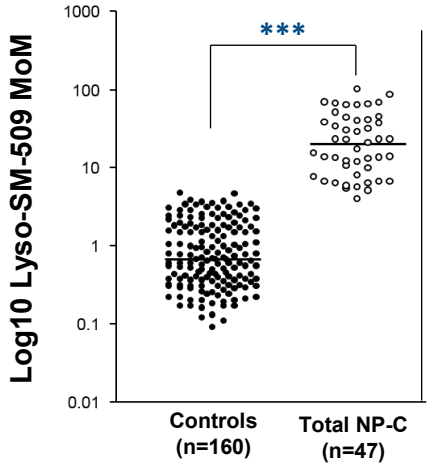
Phenotype	Patients
NP-C total	14
Perinatal-visceral	2
Early infantile	4
Late infantile	3
Juvenile	5
Controls	160



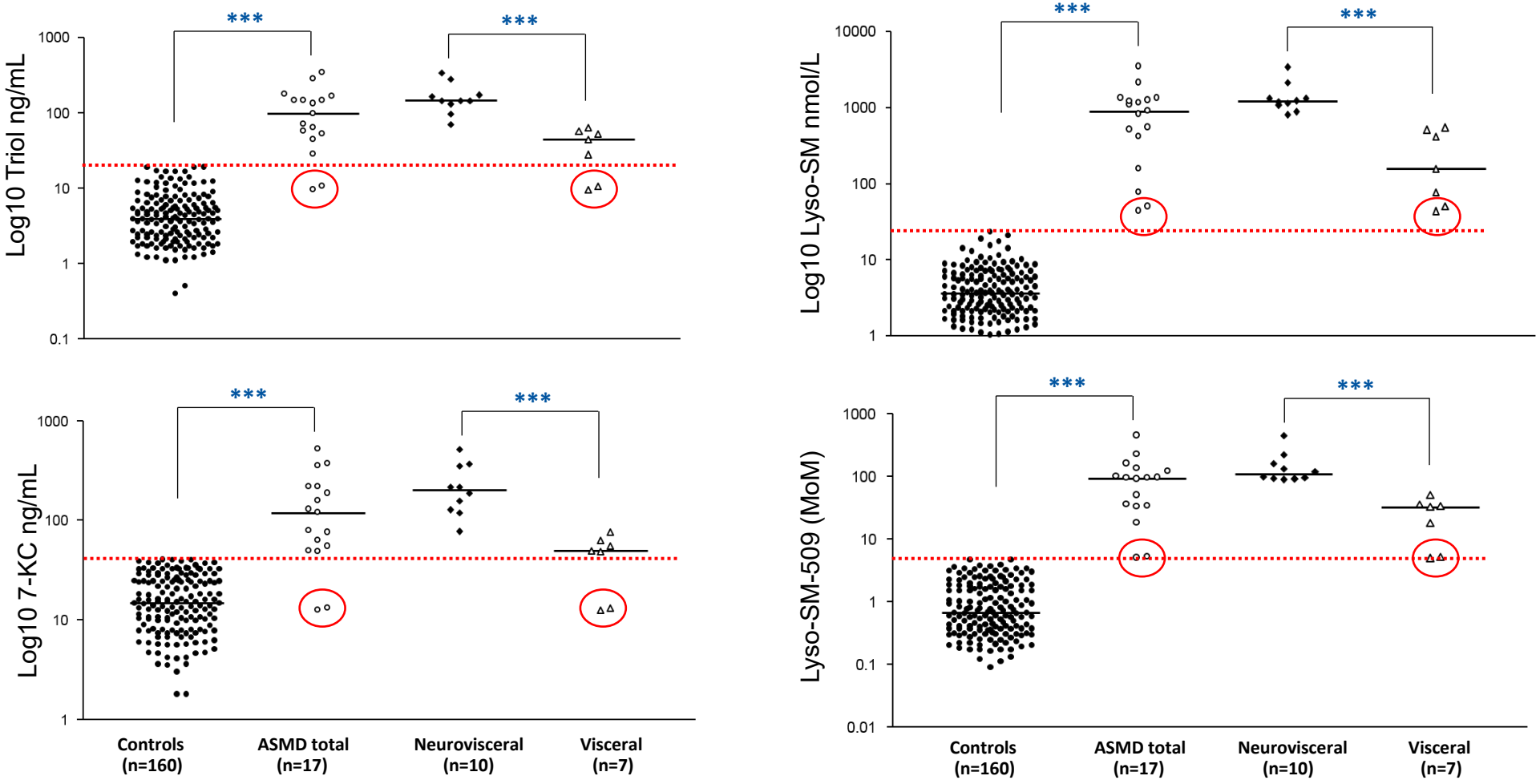
Vanier MT. *J Inherit Metab Dis*. 2015;38:187–99





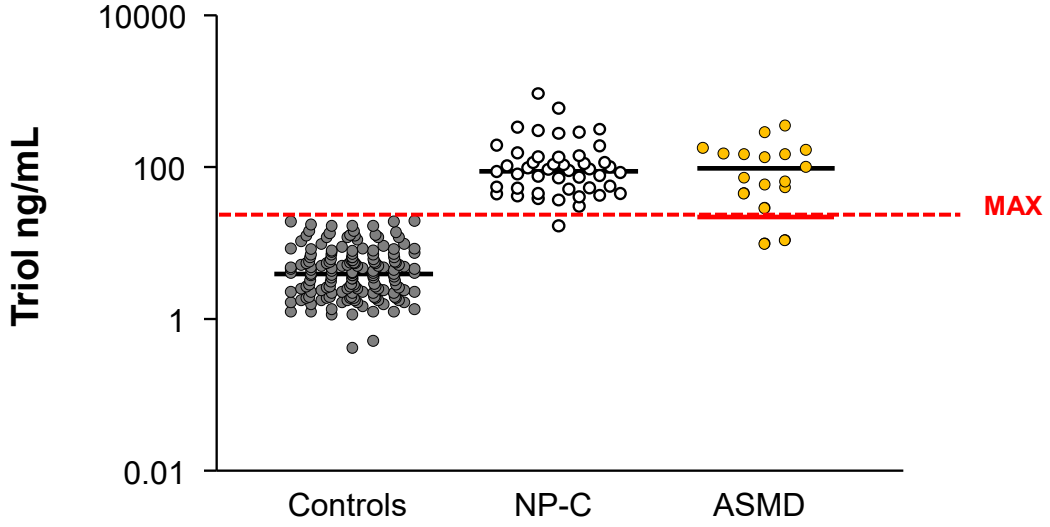


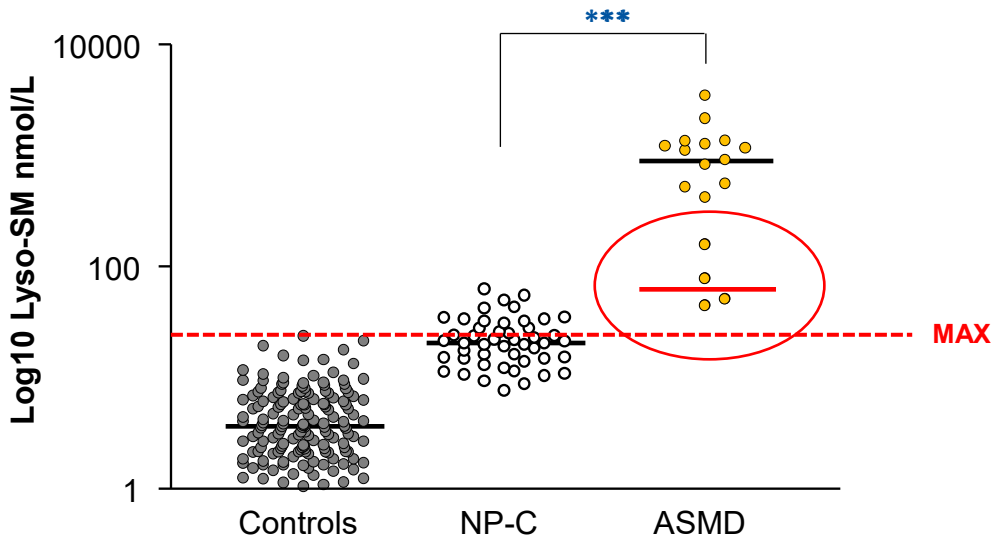
Biomarkers vs ASMD phenotype

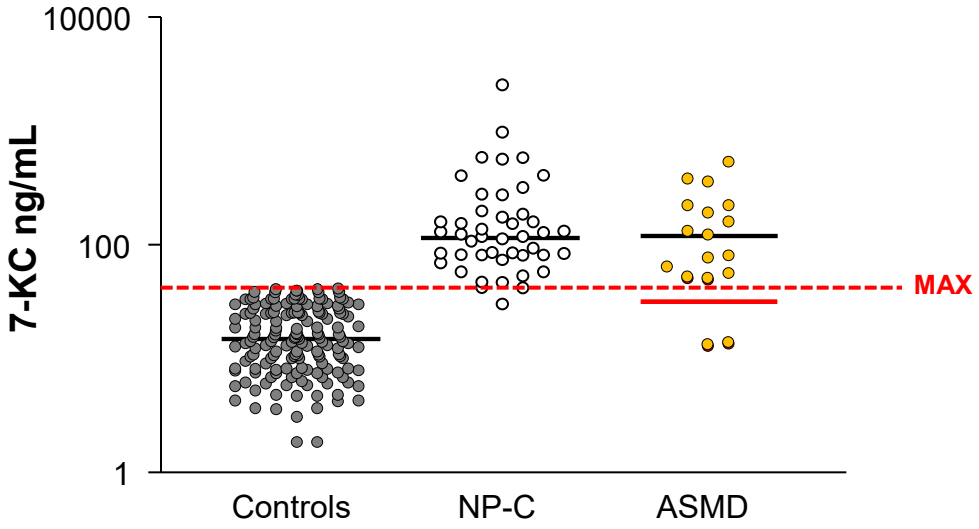


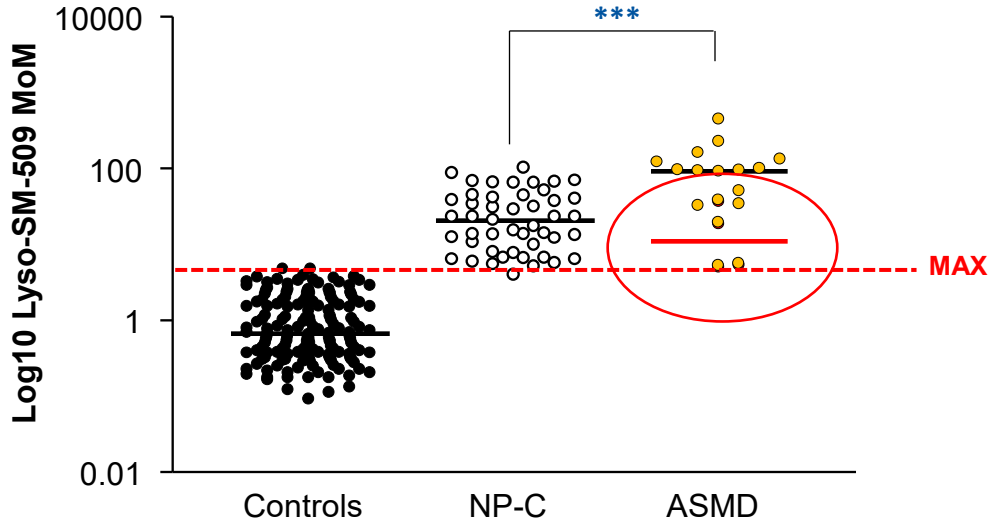
** p<0.001
*** p<0.0001

Comparison between NP-C and ASMD









NP-C and ASMD biomarkers on DBS

Molecular Genetics and Metabolism 111 (2014) 209–211

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

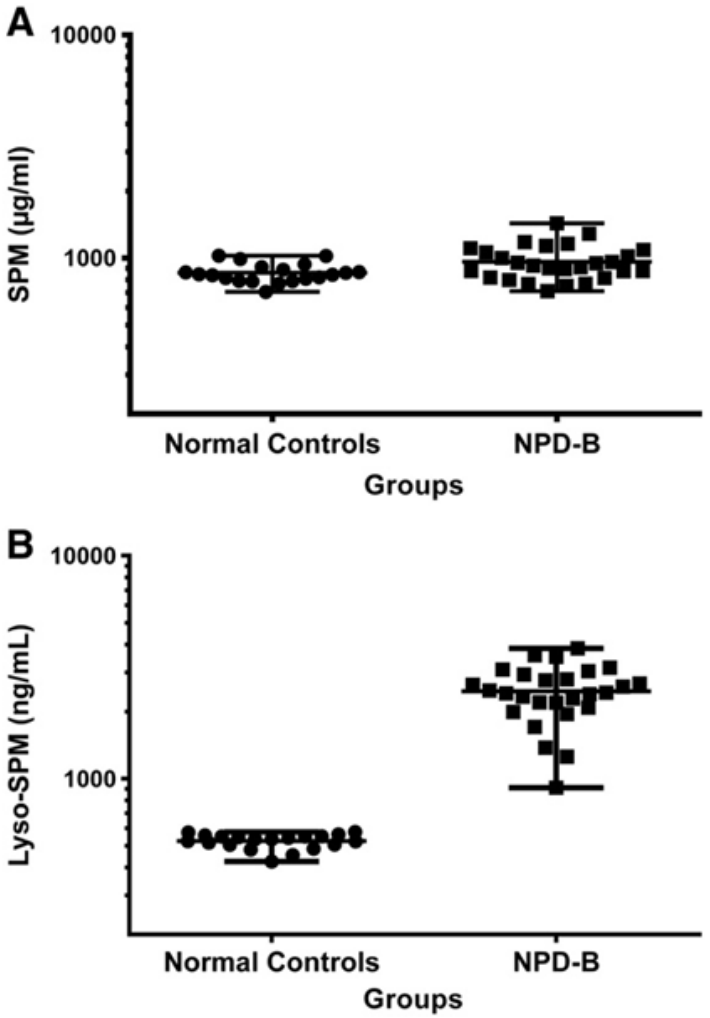
Short Communication

Lyso-sphingomyelin is elevated in dried blood spots of Niemann–Pick B patients

Wei-Lien Chuang [a], Joshua Pacheco [a], Samantha Cooper [a], Margaret M. McGovern [b], Gerald F. Cox [a], Joan Keutzer [a], X. Kate Zhang [a,*]

[a] Genzyme Corporation, a Sanofi Company, One Mountain Road, Framingham, MA 01701-9322, USA
[b] Department of Pediatrics, Stony Brook University School of Medicine, Stony Brook, New York, NY 11794-8111, USA

In DBS, Lyso-Sphingomyelin is a better biomarker than Sphingomyelin

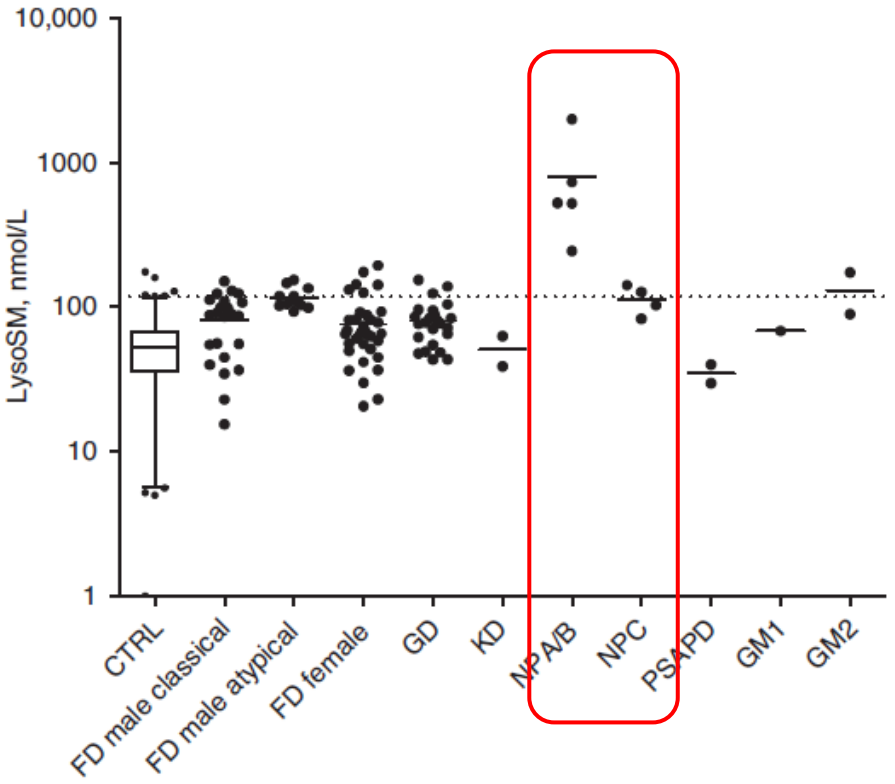


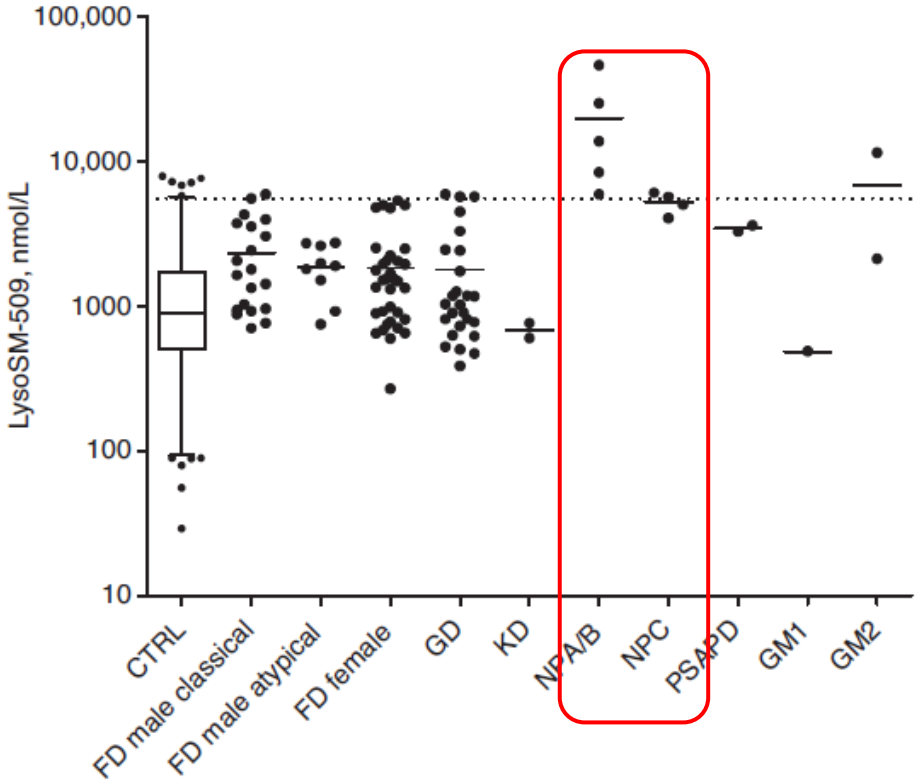
NP-C and ASMD biomarkers on DBS

DE GRUYTER Clin Chem Lab Med 2019; 57(12): 1863–1874

Giulia Polo, Alessandro P. Burlina, Enzo Ranieri, Francesca Colucci, Laura Rubert, Antonia Pascarella, Giovanni Duro, Albina Tummolo, Andrea Padoan, Mario Plebani and Alberto B. Burlina*

Plasma and dried blood spot lysosphingolipids for the diagnosis of different sphingolipidoses: a comparative study





NP-C and ASMD biomarkers

Plasma oxysterols

- ✓ High sensitivity for identification of NP-C and ASMD
- ✓ Oxysterols are not specific biomarkers for NP-C
- ✓ Oxysterols concentrations correlate with patient's age and disease phenotype

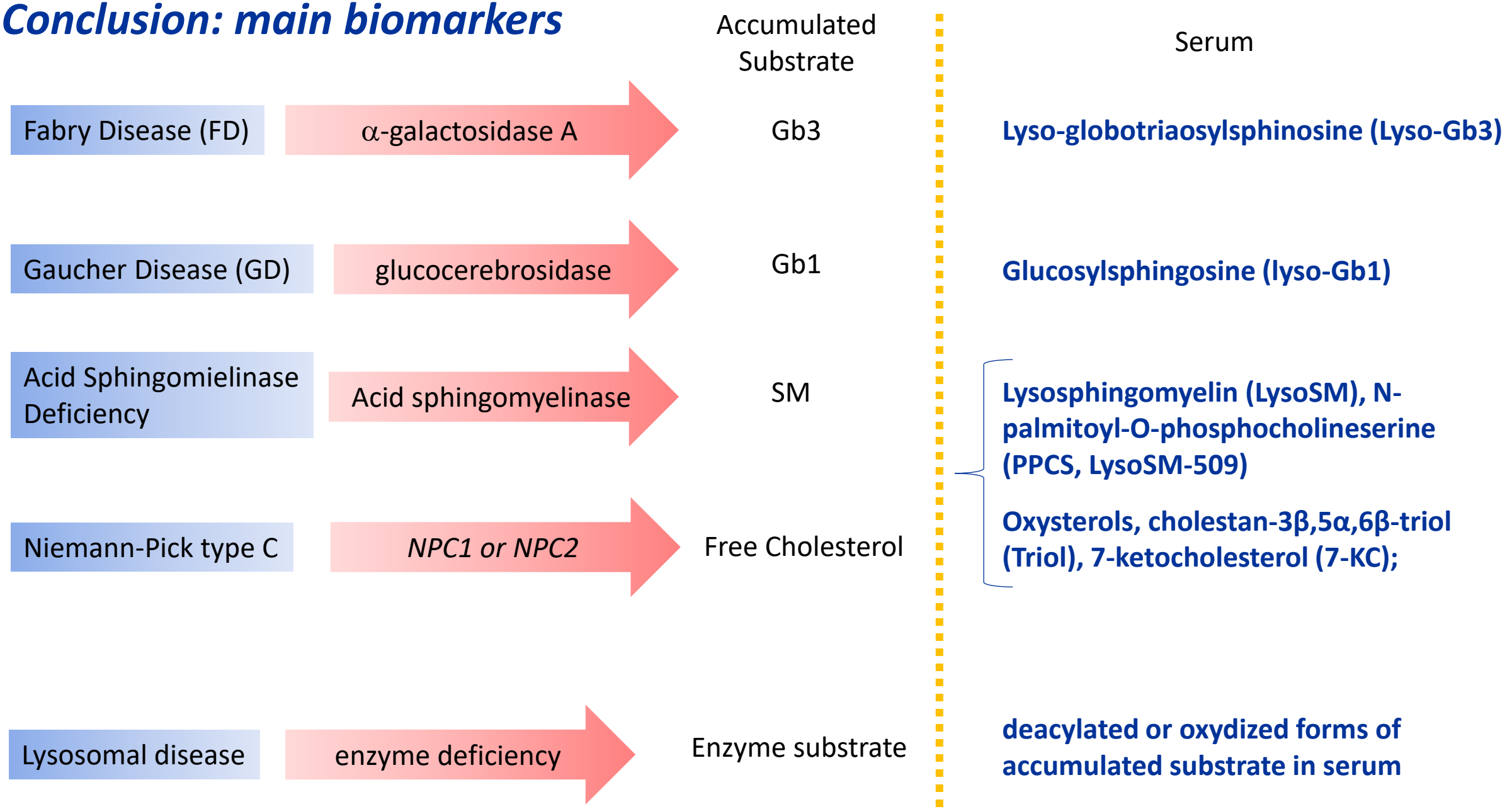
- ✓ Oxysterols analysis do not allow for discrimination between NP-C and ASMD
- ✓ Risk of false positives results: a careful sample storage and treatment is necessary
- ✓ Oxysterols analysis not suitable on dried blood spots

NP-C and ASMD biomarkers

Plasma lyso-sphingolipids

- ✓ **High sensitivity and specificity for NP-C and ASMD diagnosis**
- ✓ **Measurement of Lyso-SM and Lyso-SM-509 allows for discrimination between NP-C and ASMD**
- ✓ **Lyso-sphingolipids concentrations correlate with patient's age and phenotype**
- ✓ **Lyso-sphingolipids are more stable compounds compared to oxysterols**
- ✓ **The analysis requires an easy sample preparation procedure**
- ✓ **Lyso-sphingolipids analysis is not fully suitable on dried blood spots**

Conclusion: main biomarkers



Thank you for the attention!!