

Gaucher Disease Biomarker: Lyso-GL-1

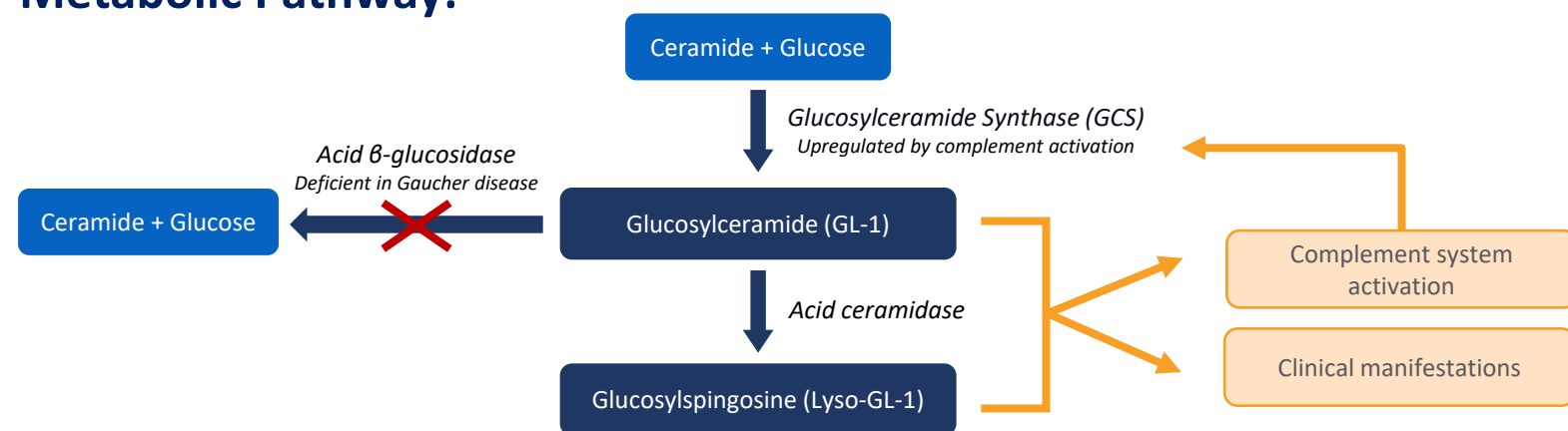
Disease Overview

Gaucher disease type 1 (GD1) is one of the most common lysosomal disorders (LSDs).

- Gaucher disease (GD) is caused by a deficiency of the enzyme acid β -glucosidase (glucocerebrosidase), encoded by the *GBA1* gene. Deficiency of this enzyme leads to a buildup of glucosylceramide (GL-1) and glucosylsphingosine (also called lyso-GL-1, lyso-GB-1, or glucopsychosine) in cells of the macrophage monocyte lineage.¹
- Accumulation of these lipids throughout the body leads to progressive anemia, thrombocytopenia, and hepatosplenomegaly. Skeletal disease in GD includes displacement of normal marrow cells with disease-affected cells, bone pain, osteopenia, osteonecrosis, and pathologic fractures.^{1,2}
- Macrophage proliferation leads to elevated levels of numerous inflammatory and proinflammatory proteins, such as angiotensin-converting enzyme, tartrate-resistant acid phosphatase, and chitotriosidase, as well as chemokines and cytokines.^{3,4,5}

Biomarker: Glucosylsphingosine (Lyso-GL-1, Lyso-GB-1)

Metabolic Pathway:



Glucosylsphingosine (lyso-GL-1) is the deacylated form of glucosylceramide (GL-1). Both lyso-GL-1 and GL-1 accumulate in GD as a direct result of β -glucosidase deficiency, making lyso-GL-1 a highly specific biomarker.

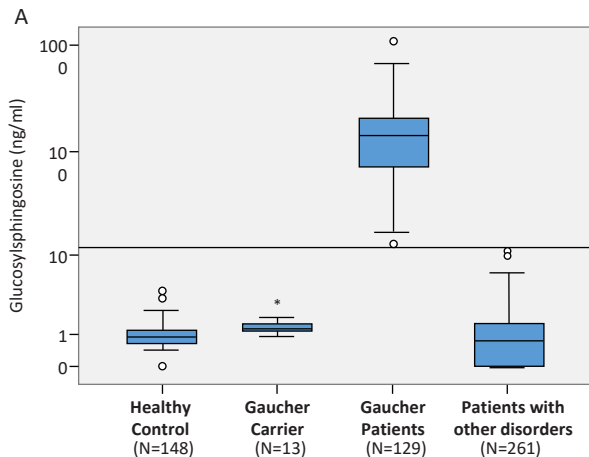
In vitro studies have demonstrated the following:⁶

- Lyso-GL-1 is cytotoxic to some cell types and pro-inflammatory in others.
- Lyso-GL-1 is damaging to specific neurons, impairs cytokinesis, and interferes with osteoblasts, immune regulation, and signal transduction.

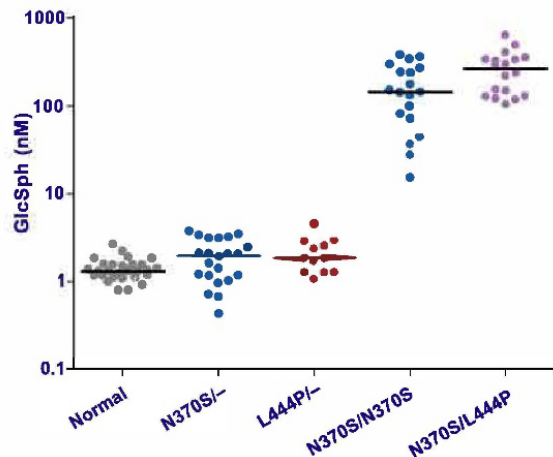
Preclinical data and evidence from 20 patients with Gaucher disease showed that excessive lyso-GL-1 has a role in dysregulating humoral immunity by promoting chronic B-cell activation and gammopathy, which can evolve into multiple myeloma.⁶

In patients with GD1, lyso-GL-1 correlates with chitotriosidase, CCL18, spleen volume, liver volume,⁷ platelets, and hemoglobin.⁸ Splenectomized patients have been shown to have higher lyso-GL-1 levels than non-splenectomized patients.⁷

Utility of Lyso-GL-1 in the Diagnostic Setting



Adapted from: Rolfs A, et al. *PLoS One*. 2013;8(11):e79732



Adapted from: Dekker N, et al. *Blood*. 2011;118(16):e118-27.

- Glucosylsphingosine (Lyso-GL-1) in GD patients was compared to healthy controls, GD1 carriers, and patients with other LSDs.⁹
- The horizontal bar marks the 12 ng/ml level which differentiated between GD1 and non-GD1 patients in this study.
- Notably, only GD patients feature pathological values of lyso-GL-1.

- There is clear differentiation between GD1 patients and healthy controls.¹⁰ There also appears to be differentiation by genotype with N409S (N370S)/L483P (L444P) patients having higher average levels than N409S (N370S) homozygotes, suggesting lyso-GL-1 levels correlate with disease severity.¹⁰
- Carriers of either pathogenic variants have levels similar to normal controls.¹⁰

Lyso-GL-1 testing options:

Some laboratories offering Lyso-GL-1 testing are listed below. There may be other laboratory tests appropriate for your patient. Other testing options can be found at www.concertgenetics.com or www.ncbi.nlm.nih.gov/gtr. Consult each laboratory for a full range of options. Content is current at time of printing and tests may not be available in all states; please call laboratory to confirm test availability and all logistics. Sanofi does not review or control the content of non-Sanofi websites. These listings do not constitute an endorsement by Sanofi of information provided by any other organizations, nor an endorsement by Sanofi of any one laboratory.

Lab	Test Name & Code	Sample Requirements	Kits	Average TAT	Mobile Blood Draw	Billing	Contact
Centogene	Lyso-Gb1	WB: 1ml EDTA (lavender) tube; DBS card: 10 circles	Blood, DBS	15 d	No	Inst, Self-pay, Ins	P: 617-580-2102 W: www.centogene.com
Clinical Mass Spectrometry Laboratory at Cincinnati Children's Hospital Medical Center	Lyso GL-1 (LAB88770)	Frozen plasma 0.2mL Dried Plasma Spot card: 2 spots	No	3 d	No	Inst	P: 513-636-4203 E: pathology@cchmc.org W: https://www.cincinnatichildrens.org/service/c/clinical-labs
Duke (DUHS) Biochemical Laboratory	Lyso-Gb1 (LAB9856)	Plasma 1 mL	No	28 d	No	Inst	P: 919-613-8400 W: https://testcatalog.duke.edu/
The Lantern Project (performed at Revvity Omics)	Lyso-GL-1 (for diagnostic purposes, must be bundled with enzyme and/or GBA sequencing) [†]	DBS card: 2 circles	DBS	3 d	Yes	No charge*	P: 866-354-2910 E: genomics@revvity.com W: www.LanternProjectDx.com
Mayo Clinic Laboratories	Glucosylsphingosine (GPSYW/GPSY/GPSYP)	WB: 1ml EDTA (lavender) tube; DBS card: 2 spots; Plasma: 0.3 ml	Blood	2-9 d	Yes	Inst, Ins, (account required)	P: 800-533-1710 E: mcl@mayo.edu W: www.mayocliniclabs.com
Revvity Omics	Glucosylsphingosine (Lyso-GB1) Monitoring, B0030	DBS: 2 spots	DBS	3 d	No	Inst, Self-Pay	P: 866-354-2910 W: www.revvity.com
Sanofi Rare Disease Specialty Testing Program (performed at Labcorp)	Lyso-GL-1	Plasma: 1 ml (from EDTA/lavender tube)	Blood*	14 d	No~	No charge* (specific account required)	P: 888-681-1701 E: RareDiseaseProgram@labcorp.com

Because performance specifications for Lyso-GL-1 assays are unique to each laboratory, interlaboratory results are not comparable.¹¹

d=days, DBS=dried blood spots, Ins=Insurance, Inst=Institutional, TAT= turn around time, WB=whole blood
 *Testing is performed at no charge; local charges may apply for sample collection, processing or shipping. †Lyso-GL-1 as part of The Lantern Project is for diagnostic assistance only, not monitoring of existing patients.
 ‡Individual testing supplies can be ordered.
 ~Phlebotomy is covered if performed at a Labcorp Patient Service Center (PSC).
 1. Baris HN, et al. *Pediatr Endocrinol Rev*. 2014;12:72-81. 2. McGovern MM, et al. *Orphanet J Rare Dis*. 2017;12:41. 3. Mucci JM, Rozenfeld P. *Gene*. 2012;509:51-59. 4. Mistry PK, et al. *Proc Natl Acad Sci USA*. 2010;107:19473-19478. 5. Danilov SM, et al. *Mol Genet Metab*. 2018;123:501-510. 6. Revel-Vilk S, et al. *Int J Mol Sci*. 2020;21(19):7159. 7. Murugesan V, et al. *Am J Hematol*. 2016;91:1082-1089. 8. Arkadir D, et al. *Am J Hematol*. 2018;93:E140-E142. 9. Rolfs A, et al. *PLoS One*. 2013;8(11):e79732. 10. Dekker N, et al. *Blood*. 2011;118:e118-27. 11. Burd EM. *Clin Microbiol Rev*. 2010;23(3):550-576.
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