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

- Gaucher disease is caused by a deficiency of the enzyme acid β-glucosidase (glucocerebrosidase), encoded by the GBA 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 is caused by displacement of normal marrow cells with disease-affected cells, resulting in bone pain, osteopenia, osteonecrosis, and 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.\(^3,4,5\)

**Disease Overview**

**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 Gaucher disease as a direct result of acid β-glucosidase deficiency, making lyso-GL-1 a highly specific biomarker.

A biologically active molecule implicated in the pathophysiology of Gaucher disease, lyso-GL-1 is known to:

- Mediate osteoblastic dysfunction and alter intracellular calcium homeostasis.\(^6\)
- Be a potent antigen for type II natural killer T cells,\(^7\) which
  - Trigger proliferation of B cells that differentiate into anti-lyso-GL-1- and anti-GL-1-autoantibody-secreting plasma cells,\(^8\) which
    - Activate the complement pathway leading to chronic inflammation,\(^7,8\) triggering a feedback loop that increases expression of glucosylceramide synthase (GCS), leading to increased production of GL-1 and lyso-GL-1.\(^9\)

In patients with Gaucher type I, lyso-GL-1 correlates with chitotriosidase, CCL18, spleen volume, liver volume,\(^10\) platelets, and hemoglobin.\(^11\) Splenectomized patients have been shown to have higher lyso-GL-1 levels than non-splenectomized patients.\(^10\)
Utility of Lyso-GL-1 in the Diagnostic Setting

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

Lyso-GL-1 testing options:

<table>
<thead>
<tr>
<th>Lab</th>
<th>Test Name &amp; Code</th>
<th>Sample Requirements</th>
<th>Kits</th>
<th>Avg TAT</th>
<th>Mobile Blood Draw</th>
<th>Billing</th>
<th>Contact</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Lantern Project (performed at PerkinElmer Genomics)</td>
<td>Lyso-GL1</td>
<td>DBS card: 2 circles</td>
<td>DBS</td>
<td>3 d</td>
<td>Yes</td>
<td>No charge*</td>
<td>P: 866-354-2910 E: <a href="mailto:genomics@perkinelmer.com">genomics@perkinelmer.com</a> W: <a href="http://www.LanternProjectDx.com">www.LanternProjectDx.com</a></td>
</tr>
<tr>
<td>Mayo Clinic Laboratories</td>
<td>Glucopsychosine (GPS/GPSY or GPSYW)</td>
<td>WB: 1ml EDTA (lavender) tube; DBS card: 2 spots; Plasma: 0.3 ml</td>
<td>Blood</td>
<td>14-20 d</td>
<td>Yes</td>
<td>Inst, Ins (account required)</td>
<td>P: 800-533-1710 E: <a href="mailto:mcl@mayo.edu">mcl@mayo.edu</a> W: <a href="http://www.mayocliniclabs.com">www.mayocliniclabs.com</a></td>
</tr>
<tr>
<td>Sanofi Genzyme Rare Disease Specialty Testing Program (performed at LabCorp)</td>
<td>Lyso-GI-1</td>
<td>Plasma: 1 ml (from EDTA/lavender tube)</td>
<td>Blood*</td>
<td>14 d</td>
<td>No*</td>
<td>No charge (account required)</td>
<td>P: 888-681-1701 E: <a href="mailto:RareDiseaseProgram@LabCorp.com">RareDiseaseProgram@LabCorp.com</a> W: <a href="http://www.labcorp.com">www.labcorp.com</a></td>
</tr>
<tr>
<td>Sema4</td>
<td>Lyso-GL1</td>
<td>WB: 1-2 ml EDTA (lavender) or heparin (green) tube; Frozen plasma: 0.5-1 ml</td>
<td>Blood</td>
<td>5 d</td>
<td>Yes</td>
<td>Inst, Ins, Self-Pay</td>
<td>P: 800-298-6470 E: <a href="mailto:clientservices@sema4.com">clientservices@sema4.com</a> W: <a href="http://www.sema4.com">www.sema4.com</a></td>
</tr>
</tbody>
</table>

d=days, DBS=dried blood spots, Ins=Insurance, Inst=Institutional, WB=whole blood, w=weeks.
*Testing is performed at no charge; local charges may apply for sample collection, processing or shipping. †Lyso-GL1 as part of The Lantern Project is for diagnostic assistance only, not monitoring of existing patients. 
Individual testing supplies can be ordered. Plebotomy is covered if performed at a LabCorp Patient Service Center (PSC).

Sanofi Genzyme does not review or control the content of non-Sanofi Genzyme websites. These listings do not constitute an endorsement by Sanofi Genzyme of information provided by any other organizations. The following is a selection of laboratories whose Gaucher testing program includes lyso-GL-1 (glucosylsphingosine or glucopsychosine). This is not an exhaustive list of labs that offer one or the other or an endorsement of any one lab. Other testing options can be found at www.concertgenetics.com or www.ncbi.nlm.nih.gov/gtr. Content is current at time of printing and tests may not be available in all states; please call laboratory to confirm test availability, sample shipping information, and all other logistics.

References: