A next generation health information company
Enable physicians and patients to more seamlessly engage the digital universe of data, knowledge and understanding to better diagnose, treat, and prevent disease.
A Spinout of the Mount Sinai Health System

- Mount Sinai Health System is one of the largest and most respected academic medical centers and health systems in the United States, featuring 7 hospital campuses and Icahn School of Medicine. Mount Sinai has more than 6,000 physicians and 140 ambulatory practice locations throughout the Tri-State Area.

- Icahn School of Medicine is an international leader in medical and scientific training, biomedical research, and patient care, featuring more than 5,000 faculty.

- Mount Sinai has made a substantial investment toward the future of genetic research and diagnostics and are committed to developing next generation treatments.
<table>
<thead>
<tr>
<th>Institution by Rank</th>
<th>Change in Ranking from 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baylor College of Medicine</td>
<td>1  → 1</td>
</tr>
<tr>
<td>Washington University</td>
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</tr>
<tr>
<td>Stanford University</td>
<td>4  → 3</td>
</tr>
<tr>
<td>Icahn School of Medicine</td>
<td>31 → 4</td>
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<tr>
<td>North Carolina, Chapel Hill</td>
<td>6  → 5</td>
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<tr>
<td>Harvard Medical School</td>
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<tr>
<td>University of Washington</td>
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<tr>
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<td>Columbia University</td>
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<tr>
<td>University of Chicago</td>
<td>7  ← 14</td>
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</tbody>
</table>
Sema4 has grown rapidly over the past 5 years.
Advanced technologies have given rise to an explosion in the digital universe that is fundamentally transforming life as we know it. (Over 1 trillion gigabytes of information was created and replicated in 2011; growth continues to accelerate—a factor of 9 growth in the last 5 years; roughly 2 zettabytes of data added a year now; estimated 20-30% is usable.)

You know you're getting old and being left behind when...

27 million people watched the 'League of Legends' World Championship (more than the World Series or NBA Finals).
Advances in DNA sequencing technologies have now added to this explosion
These types of rapid technology advances are delivering massive scales of data around individuals, that if appropriately integrated, can dramatically alter our ability to predict disease risk or diagnose, treat, or even prevent disease.
On the molecular side, significant cohorts profiled at an unprecedented depth

<table>
<thead>
<tr>
<th>Tissue</th>
<th># Cases</th>
<th># Controls</th>
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<tbody>
<tr>
<td>AOR</td>
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<td>SF</td>
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<tr>
<td>SKLM</td>
<td>530</td>
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</tr>
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</table>
Providing for the first time extensive maps of disease

The thickness of the edges between the tissue and the disease reflect how frequently a disease-causing gene is shared between pairs of diseases and tissues.
Complementing the molecular dimensions is the “Exposome”, the newest “Omic”

“The totality of environmental exposures throughout a lifetime”

-Analogous to the Genome
App enabled use of Geographical Information Systems for the “External Exposome”

- Air Temperature/Climate
- Exposure to green, natural areas
- Daily air pollution
- Social Media Content
- Access to Healthy Foods
- Traffic patterns
The value of a more completely phenotyped and molecularly profiled population
Using EHR data, diabetic patients organized into 3 distinct groups representing different severity, comorbidities and genetic components.

**Subtype 1:**
- More likely to suffer from blindness and vision defects
- Grouping genetically supported

**Subtype 2:**
- Greater risk of infections and cancer
- More immune deficient

**Subtype 3:**
- Higher blood pressure, blood clots, more metabolic syndrome like
- Grouping genetically supported
We can go further to integrate these different dimensions of data to build models.
Simulation on these models enables in silico perturbations the elucidate information flow
Sema4: New MS effort pushing an information driven approach to reinventing medicine
Pioneering today the application of these individual patient trajectories in cancer

Patient tumor and germline are profiled, key drivers identified, tumor constructed in avatar models, those models taken through HTS for identification of drug cocktail.
Medical systems of the future…

Largest car company in the world owns no cars (founded 2009)

> 200,000 drivers in US
> 1,000,000 drivers worldwide

Largest hotel chain in the world owns no hotels (founded in 2008)

Soon the largest medical system in the world will own no hospitals

- Implantable
- Ingestible
- Portable
- Wearable

> 200,000 drivers in US
> 1,000,000 drivers world wide
THE PROBLEM: We do not have the scale of content needed to build these models to realize this vision.

Unique capabilities of coupling what people **need** to know with what they **want** to know for their future.
Which translates into being able to see far more of the clinically actionable genome for much less cost.

- **Carrier of Mendelian Mutations**: Virtually everyone carries loss of function mutations that have the potential to cause serious disease.
- **Fetus with Severe Genetic Lesions**: Roughly 1 in 100 babies will harbor severe genetic lesions that cause catastrophic illness.
- **Child with Genetic Condition**: Roughly 2 in 100 children harbor mutations that result in failure to thrive conditions.
- **Cardiac, Neuro, Heme**: Up to 20% of the population carries variants for blood clotting, heart disease and dementia.
- **Pharmacogenomics**: Virtually everyone carries loss of function mutations that can impact drug response.
- **Heritable Cancer**: Heritable forms of cancer affect up to 10% of the population (breast, ovarian, prostate, colon, etc.).
Our Mission: Enable physicians to more seamlessly engage the digital universe of data, knowledge and understanding to better diagnose, treat, and prevent disease.

Data Acquisition and Management (taking into account more complete information)

Knowledgebase (enabling better tracking)

Advanced Analytics (providing better solutions for the future)

Deep, Dynamic, Adaptive Learning Platform

NLP Curatio ETL

Networks Knowledge Simulator

Molecular Outcomes

Health Graph

Our focus on reproductive health

• Not just a testing company, but an information partner to help physicians help families deliver children free of disease
  • Aid physicians in maximizing patient outcomes
  • Streamline physician workflow
  • Partnering to enable learning healthcare systems
Why do we believe we can growth hack up to big numbers via genetic testing? Not only do we have significant efforts in predictive modeling, but we are leaders in genomic testing

MGTL offers comprehensive testing for numerous genetic disorders through the following 4 panels:

- **Standard Pan-ethnic Panel (4 Disorders)**
- **High Frequency Pan-ethnic Panel (10 Disorders)**
- **Comprehensive Jewish Panel (96 Disorders)** prevalent in Ashkenazi, Sephardic, and/or Mizrahi Jews
- **Expanded Carrier Screening Panel, NGS-based + companion assays; pan-ethnic (281 Disorders)**

Highly competitive vs. commercial competitors (Counsyl, Good Start, Integrated, Recombine)

Major reference partners onboard

---

Comprehensive, pan-ethnic screening panel (281 disorders)
Milestone connection between diagnostic testing and information system
Managing pregnancy and postnatal journey

General surveillance and managing wellness

- Does my baby have any serious medical issues?
- What are the disease risks for my child?
- What medical issues can I pass on to my child?

Preconception → Prenatal → Postnatal

Clinical Genetic Testing
- eGC Mobile Apps
- Non Invasive Prenatal Testing
- Carrier Screening

Direct to Consumer
- Helix Carrier Screening
- NBS from Dx pathways
- Search for Resilience

Web & Mobile Apps
- Educate
- Consent
- Test
- Report

DT Medical Systems
- NBS Dx Pathway for Pharma
- Current Carrier and NiPT DTP

Clinical Genetic Testing
- Current Carrier and NiPT DTP
- NBS Dx Pathway for Pharma
- Search for Resilience

New Born Screening
- eGC Mobile Apps

Non Invasive Prenatal Testing
- Carrier Screening

Search for Resilience
- Does my baby have any serious medical issues?
- What are the disease risks for my child?
- What medical issues can I pass on to my child?
Creating a feedback loop to continually refine test interpretations and expand test utility

Aggregate and Bank Data

Deep, Dynamic, Adaptive Learning System

Information Store

New Born Screening
Non Invasive Prenatal Testing
Carrier Screening
eGC Mobile Apps

Output Layer
Hidden Layer
Input Layer
Existing Customer Journey

MAJOR TAKEAWAY
Anxiety-inducing rollercoaster experience with too many variations.

- Patients bounce back and forth across stakeholders almost at every step.
- Inconsistent service throughout, relying too much on individual interactions.
- GCs are overloaded with logistics and repetitive tasks that steal time from actual counseling.
New Customer Journey

Current Journey

<table>
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<tr>
<th>Referral</th>
<th>Education</th>
<th>Panel Selection</th>
<th>Sample Collection</th>
<th>Waiting</th>
<th>Results Ready</th>
<th>Cell Interpretation</th>
<th>Personal Research</th>
<th>Order Partner</th>
<th>Testing</th>
<th>Sample Collection</th>
<th>Waiting</th>
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<th>Cell Interpretation</th>
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</tbody>
</table>

eGC Journey

Dr
Self (eGC)
GC
Mount Sinai
To: Stephanie Arnold
See Status of Your Test

Create your account today.
Access to your results, records and health data. All in one place.

Create Account
Live Consult Demo

Please select your role to launch the demo

PATIENT
Sarah Wagner  
Patient

COUNSELOR
Janelle McCarthy  
Genetic Counselor  
Mount Sinai

SCENARIO
Upon her Carrier Screening test, Sarah Wagner (patient) has scheduled a Live Consult session with Janelle McCarthy (genetic counselor).
This prototype demonstrates the key aspects of the Live Consult session.
Stephanie Arnold

Tests

Expanded Carrier Screening Test

Test Date: 1/31/17
Referring Physician: Robert Smith, M.D.

- Sample Received: 2/1/17
- Analysis Complete: 2/15/17
- Consult: 2/17/17, 10 am
- Results Available: 2/17/17

View Results
NextStep™ Consulting Session

Begins at 12:30 EST, 02.12.2016

Call in Number 555-555-5555
NextStep™
Live Consult Session

Genetic Counselor: Janelle McCarthy

WHAT WILL BE COVERED
Summary
Result Interpretation
Risk Overview
Recommendations
NextStep™
Results Summary

REDUCE RISK
No variants were detected in 279 Genes.

VARIANT FOUND
- Condition 1 - Lorem Ipsum
- Condition 2 - Lorem Ipsum
**Condition 1 - Lorem Ipsum - ABCD Gene**

**Condition Description**

Cystic fibrosis (CF) is a genetic condition characterized by the production of abnormally thick, sticky mucus, particularly in the lungs and digestive system. While it is normal to have mucus lining the organs of the respiratory, digestive, and reproductive systems in order to lubricate and protect them, in people with CF this mucus is thick and sticky. This abnormal mucus results in the clogging and obstructing of various systems in the body. CF is a chronic condition that worsens over time.
Condition 1 - Lorem Ipsum - HEXA Gene

Inheritance Diagram
## Reduced Risk for 279 Conditions

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>GENE</th>
<th>FREQUENCY</th>
<th>DETECTION RATE</th>
<th>VARIANT</th>
<th>RESIDUAL RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abetalipoproteinemia - AR</td>
<td>MTTP</td>
<td>1 in 186</td>
<td>&gt;95%</td>
<td>NOT FOUND</td>
<td>1 in 3701 Reduced</td>
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</table>
Recommendations & Next Steps

NEXT

• **Test your partner** Testing your partner will check if he is also a carrier of Tay-Sachs and Mediterranean Fever. Testing will give you a more conclusive understanding of your risk.

AFTER PARTNER TESTING

• **Consideration of residual risk** After a negative carrier screen is recommended, especially in the case of a positive family history for a specific disorder.

DURING PREGNANCY

• **Fetal DNA Test** Nemo enim ipsam voluptatem quia voluptas sit aspernatur aut odit aut fugit, sed quia consequuntur magni dolores eos qui ration.

AFTER BIRTH

• **Carrier Testing** If you and your partner carry a condition likely to affect your child we recommend testing your child after birth so they can.
Your Sema4 account.
Access to your results, records and health.
All in one place.
Dr. John Smith

Notifications

![Alert Icon] Abnormal Result Found Abigail Smith, Sample #23802830

Tests

<table>
<thead>
<tr>
<th>Name</th>
<th>DOB</th>
<th>Sample</th>
<th>Test</th>
<th>Date</th>
<th>Physician</th>
<th>Status</th>
<th>Results Viewed</th>
<th>Consult</th>
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<tbody>
<tr>
<td>Abigail Smith</td>
<td>1/12/83</td>
<td>23802830</td>
<td>Next Step</td>
<td>1/12/16</td>
<td>Smith, John</td>
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<td>Y</td>
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<tr>
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<td>Smith, John</td>
<td>Final</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>
Welcome back, Jane

Your CarrierCheck results are ready.

This report will help you understand what your results mean and give you some suggestions on what to do next.

What We Found

We analyzed your DNA to see if you are a carrier of **gene variants (or changes) associated with 65 inherited conditions**. Carriers are usually healthy, but may have an increased risk of having a child with a genetic disease.

<table>
<thead>
<tr>
<th>Carrier</th>
<th>Negative</th>
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<tr>
<td>1 Condition</td>
<td>64 Conditions</td>
</tr>
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</table>

You tested **positive** for one of the gene variants that we screened for. You tested **negative** for most of the gene variants that we screened for.
Dr. John Smith

Tests

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<td>Final</td>
<td>Y</td>
<td>Y</td>
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</tbody>
</table>
**Results Summary**

**POSI TIVE for Smith-Lemli-Opitz Syndrome**
One copy of the c.964-1G>C mutation

Negative for all other mutations tested in the other 280 diseases

**Recommendations**
Testing the partner for this condition and genetic counseling

**Interpretation Summary**
This patient carries one copy of the DHCR7 c.964-1G>C mutation and is at least a carrier for Smith-Lemli-Opitz syndrome. The negative results for the other gene mutations do not completely exclude the possibility that this patient is a carrier for other diseases. Please refer to the accompanying tables for residual carrier risks in individuals for the corresponding ethnic groups, assuming a negative family history and the patient is not affected with one of the diseases.

**What is Smith-Lemli-Opitz Syndrome**
Characteristic facial features, microcephaly, intellectual disability, and behavioral problems (e.g. autism). Abnormalities of the heart, lungs, kidneys, gastrointestinal tract, fingers/toes and genitalia are also common. Variable severity of symptoms.
Dr. John Smith

Notifications

⚠ **Abnormal Result Found** Abigail Smith. Sample #23802830

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Peace of Mind
One test, 281 genetic disorders. Your peace of mind.

Introducing Next Step. Guiding you to insights about your baby’s development. The only screen backed with years of clinical research from Mount Sinai and researchers from around the world.

Need to register a kit?

One screening, 281 Answers.
The Next Step Genetic Test.
THE END

WE LOOK FORWARD TO EXPLORING WAYS TO PARTNER!!!