Simons Searchlight is an international research program with the goal of accelerating science and improving lives for people with rare genetic neurodevelopmental disorders.
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Simons
SEARCHLIGHT
Priorities for Searchlight Data Collection

- Longitudinal
- Feasible, scalable
- Facilitate investigation by researchers
- Standardized, validated, sensitive measures
- Participant-centered - high-priority useful data
What are the **goals** of Simons Searchlight?

Our mission is to shed light on these conditions by collecting high quality natural history data and building strong partnerships between researchers, industry and families.

- Collect detailed **medical and behavioral histories** along with **blood samples**
- Synthesize the information you provide and **share results back to families**
- **Freely share data** and samples with qualified researchers
- **Connect** participants and researchers from around the world
- Promote better understanding of these **genetic changes**
Information for Families

- Personalized reports: SCQ, SRS, CBCL and Vineland located on your dashboard

- Summary snapshots on your gene page

- Presentations at conferences and meetings

The Vineland Daily Living Skills scale is a survey of everyday self-care, household skills and responsibilities. For younger children, this might include dressing or potty-training, and for older children, this might include helping to clean the house or using money.

The Vineland Socialization scale is a survey of social skills. For younger children, this might include playing with others, and in older children, this might include following social "rules".

Thank you for contributing to the Simons VIP study!

Please remember these results are based on your responses to an online computerized research survey. They are not monitored or evaluated by a professional, and they do not represent a clinical evaluation or clinical feedback. No questionnaire is 100 percent accurate. If you ever have any questions or concerns, please talk to your doctor.
Simons Searchlight participants can donate a blood sample

Blood collection steps

**Step 1:** A blood sample kit is mailed to you free of charge
**Step 2:** Make an appointment at a local Quest Labs to have the blood drawn
**Step 3:** The lab mails the kit back to Simons Searchlight

Questions? Email coordinator@simonssearchlight.org
How will the sample be used in research and why is this important?

Induced pluripotent stem cells

Infinity BiologiX

Simons Foundation Autism Research Initiative
Nancy Lurie Marks Family Foundation

New York Stem Cell Foundation
6 – 9 months

Simons Searchlight

Questions? Email coordinator@simonssearchlight.org
What are induced pluripotent stem cells (iPSCs)?
Quality of Life Inventory - Disability

(18 individuals with MED13L)

Health & Well-being
- Is in good health: 83%
- Sleeps well: 72%
- Has energy for daily activities: 94%
- Is alert and aware: 100%

Activities & the Outdoors
- Enjoys moving their body: 83%
- Enjoys feeling steady during activities: 72%
- Enjoys physical activities: 83%
- Enjoys outings: 56%
- Enjoys time outdoors: 72%

Feelings & Emotions
- In a good mood: 89%
- Smiles: 94%
- Expresses happiness using body language: 78%
- Laughs or giggles: 89%

Notes: This graphic reflects the percentage of people who reported “Often” or “Very Often” for each question. We gratefully acknowledge Dr. Jenny Downs of the Telethon Kids Institute.
Quality of Life Inventory - Disability
(18 individuals with MED13L)

**Family & Friends**
- Happy when they are understood: 61%
- Feels relaxed while making eye contact: 72%
- Initiates greetings with others: 67%
- Happy to be included: 83%
- Enjoys socializing at mealtimes: 56%
- Enjoys interacting with others: 83%
- Excited by upcoming activities: 61%

**Daily Life**
- Expresses their needs: 56%
- Makes own choices for activities: 61%
- Likes using technology: 72%
- Helps with routines: 44%
- Enjoys making things: 50%

Notes: This graphic reflects the percentage of people who reported "Often" or "Very Often" for each question. We gratefully acknowledge Dr. Jenny Downs of the Telethon Kids Institute.
The MED13L Registry in Simons Searchlight
Progress of Individuals with MED13L

**STEP 1**
Sign up online.

**STEP 2**
Provide your genetic lab report.

**STEP 3**
Share your important medical history.

**STEP 4**
Fill out surveys.

**STEP 5**
Provide a blood sample if you are interested.

**STEP 6**
Update us every year.

We are a long-term study, gathering new information from you every year.
MED13L Biospecimens

12 individuals contributed to the available biospecimens

<table>
<thead>
<tr>
<th>Available Sample</th>
<th>MED13L Carriers</th>
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<tbody>
<tr>
<td>Induced pluripotent stem cells (iPSCs)</td>
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<tr>
<td>Lymphoblastoid cell lines</td>
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<td>Whole blood DNA</td>
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<td>Saliva DNA</td>
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* 6 iPSCs coming soon
# MED13L iPS Cells

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<td>6</td>
<td>p.Pro866Leu</td>
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<td>Upcoming</td>
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</table>

- Researchers worldwide can request (non- and for-profit), nominal fee $120/sample
- Request through SFARI Base
- Researchers can submit requests now
### Variants Observed in MED13L

**57 individuals**

<table>
<thead>
<tr>
<th>Variant Category</th>
<th>Number</th>
<th>Breakpoints</th>
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Variants as of June 2022
9 people with VUS or additional variants, not shown
* Indicates biological relatives
### Variants Observed in MED13L
57 individuals (continued)

<table>
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<th>Variant Category</th>
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Variants as of June 2022
9 people with VUS or additional variants, not shown
Variants Observed in MED13L

Frameshift or nonsense

Missense

Variants

p.Met1?
p.Trp88*
p.Arg148*
p.Gln185*
p.Gln185Serfs*7
p.Lys250Argfs*12

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p.Ala729Argfs*12
p.Pro866Leu
p.Pro879Leu
p.Leu971Phefs*36
p.Arg977Val

p.Gln1157*
p.Pro1210Argfs*13
p.Trp1359*
p.His1363Ilefs*25
p.Glu1374Lysfs*14
p.Glu1405*
p.Tr1470Asnfs*9
p.Tyr1513*
p.Gln1537*
p.Pro1573Leufs*27
p.Ser1605*
p.Tr1636Metfs*24

p.Ile1659Thrfs*8
p.Thr1663Cysfs*43
p.Arg1760*
p.Thr1815fs
p.Asn1824Metfs*28
p.Tyr1830Cys
p.Arg1900*
p.Asp1911Tyr
p.Cys1932Trpfs*12
p.Arg1974*
p.Gln1981*
p.Leu1997Phefs*19

p.Gln2186*
p.Ser2163Leu

Functional Regions

6 VUS, not shown
Protein structure of MED13L
Simons Searchlight
MED13L Medical History Data

28 participants with pathogenic or likely pathogenic variants
Age at Most Recent Medical History Interview
(28 individuals)

Age Range
2yr(s) - 30yr(s)

24
Participants under 18

Average Age
8 yr(s)
Developmental and Behavioral Conditions
(28 individuals)

- OCD: 1 (4%)
- Language Delay/Impairment: 25 (89%)
- Intellectual Disability/Developmental Delay: 27 (96%)
- Autism: 10 (36%)
- Anxiety: 2 (7%)
- ADHD: 1 (4%)
Neurological Problems
(28 individuals)

- Tic Disorder: 2 (7%)
- Small Head Size: 2 (7%)
- Movement Disorder: 3 (11%)
- Low Muscle Tone: 22 (79%)
- Large Head Size: 3 (11%)
- High Muscle Tone: 5 (18%)
- Coordination Problems: 9 (32%)
Seizure course in 14 individuals completing the Seizure History survey:

- Seizure onset was from 5 months of age through adulthood
  - Average age of first seizure is 7 years
- 6 (43%) of individuals with seizures have had to take medication for their seizures
  - 5 (36%) continue to take preventative medication for their seizures (1 resolved)
- 4 (29%) of caregivers reported that their child’s seizures are under control
  - Average age at seizure control was 6 years

* Additional people completed the Seizure History survey as compared to the medical history interview
Heart
(28 individuals)

Total People with Congenital Heart Disease: 3 (11%)
Patent Ductus Arteriosus: 2 (7%)
Bicuspid Aortic Valve: 1 (4%)
Endocrinologic (28 individuals)

- Short Stature: 3 (11%)
- Hypothyroidism: 1 (4%)
- Failure to Thrive: 7 (25%)
Vision Problems
(28 individuals)

- **Ptosis**: 2 (7%)
- **Nearsighted**: 6 (21%)
- **Lazy Eye**: 1 (4%)
- **Farsighted**: 9 (32%)
- **Crossed Eyes**: 6 (21%)
- **Cataract**: 1 (4%)
- **Astigmatism**: 6 (21%)

* 3 resolved through surgery
† 1 resolved through surgery
Additional Medical Issues
(28 individuals)

Scoliosis 2(7%)
Genital 2(7%)
Kidney 3(11%)
Heart 3(11%)
G-Tube Surgery 3(11%)
Endocrinologic 8(29%)
Gastro 15(54%)
Vision 19(68%)
Medication Use
(18 individuals)

- **Sleep**: 4 (22%)
- **Severe Behavior**: 1 (6%)
- **Antiepileptic drugs (AEDs)**: 4 (22%)
- **Sedatives**: 1 (6%)
- **Gastrointestinal**: 2 (11%)
- **Asthma, Respiratory, Allergy**: 2 (11%)
- **Antidepressants**: 2 (11%)

[*1 additional person reported taking antiepileptic medication, over and above those reporting seizures in the medical history]*
Vineland Adaptive Behavior Scales Developmental Growth Charts (Vineland-3)
Expressive Language Development
(13 individuals)

![Graph showing expressive language development over age at evaluation. The x-axis represents age at evaluation, ranging from 0 to 18+ years. The y-axis represents Vineland Age Equivalent, ranging from 0 to 4 years. The graph includes scattered data points and a trend line indicating an increase in Vineland Age Equivalent with age. There is a dashed line at 1 year which represents the age at which the individual begins to use single words to request.

Uses single words to request.
Personal Care Skills
(13 individuals)

Vineland Age Equivalent
(in years)

Age at Evaluation

Dresses self

Feeds self with fork and spoon
Social Development
(13 individuals)

Vineland Age Equivalent
(in years)

Age at Evaluation

Shows interest in friends

Makes eye contact during social interactions
Gross Motor Development
(9 individuals)

Vineland Age Equivalent
(in years)

Age at Evaluation

Hops/jumps

Walks without help
Child Behavior Checklist (CBCL)
Most young children do not have significant behavior problems.
Child Behavior Checklist

Behavioral and Emotional Concerns
Ages 6-18 Years (17 individuals)

- Looking at behavior over time in our small group of pre-teens and teens, behavioral problems tend to **decrease**.
Child Behavior Checklist

Top Behavioral and Emotional Concerns

Ages 1.5-5 Years (22 individuals)

- Difficulty waiting
- Scared to attempt new things
- Doesn't respond when spoken to
- Impatient
Child Behavior Checklist

Top Behavioral and Emotional Concerns
Ages 6-18 Years (17 individuals)

- Overeats
- Demands frequent attention
- Frequently distracted
- Hyperactive
Summary: MED13L Medical and Behavioral Phenotypes

Common issues
- Intellectual disability and developmental delay
- Language delay
- Hypotonia (low muscle tone)

Other issues
- Autism
- Coordination problems
- Hypertonia (high muscle tone)
- Seizures
- Growth issues
- Eye/vision issues
- Anxious
- Impatience
- Overeating
- Attention/hyperactivity
Thank you