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

- Participant-centered
- High-priority useful data
- Facilitate investigation by researchers
- Longitudinal
- Feasible, scalable
- Standardized, validated, sensitive measures
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

Simons Searchlight Registry Update

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

Questions? Email coordinator@simonssearchlight.org
What are induced pluripotent stem cells (iPSCs)?

Simons Searchlight Participant → Blood Cells → iPSCs → Specialized Differentiated Cells → Disease Modelling → Nerve Cells, Liver Cells, Other Tissue Cells

Drug Screening and Discovery

Questions? Email coordinator@simonssearchlight.org
The HIVEP2 Registry in Simons Searchlight
Progress of Individuals with HIVEP2

**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.

Login for more...
HIVEP2 Biospecimens

12 individuals contributed to the available biospecimens

<table>
<thead>
<tr>
<th>Available Sample</th>
<th>HIVEP2 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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<tr>
<td>Whole blood DNA</td>
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<tr>
<td>Saliva DNA</td>
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* 4 iPSCs not yet available but coming soon
## HIVEP2 iPS Cells

<table>
<thead>
<tr>
<th></th>
<th>p. nomen</th>
<th># of Carriers</th>
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<tbody>
<tr>
<td>1</td>
<td>p. Arg943*</td>
<td>1</td>
<td>Upcoming</td>
</tr>
<tr>
<td>2</td>
<td>p. Arg943*-corrected</td>
<td>1</td>
<td>Upcoming</td>
</tr>
<tr>
<td>3</td>
<td>p. Gln1248*</td>
<td>1</td>
<td>Upcoming</td>
</tr>
<tr>
<td>4</td>
<td>p. Leu1718Alafs*16</td>
<td>1</td>
<td>Upcoming</td>
</tr>
</tbody>
</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 HIVEP2
**23 individuals**

<table>
<thead>
<tr>
<th>Variant Category</th>
<th>Number</th>
<th>p.nomen</th>
<th>Variant Classification</th>
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<td>Likely pathogenic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glu408Lys</td>
<td>Likely pathogenic</td>
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</table>

<table>
<thead>
<tr>
<th>Variant Category</th>
<th>Number</th>
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<th>Variant Classification</th>
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<td></td>
<td></td>
<td>Gln969*</td>
<td>Pathogenic</td>
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<tr>
<td></td>
<td></td>
<td>Arg1028*</td>
<td>Pathogenic</td>
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<tr>
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<td>Gln1157*</td>
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<td>Gln1173*</td>
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<tr>
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<td>2</td>
<td>Tyr1177Ilefs*2</td>
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<td>Gln1248*</td>
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<td>Gln1896*</td>
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<td></td>
<td>2*</td>
<td>Ser1967Cysfs*2</td>
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<tr>
<td></td>
<td></td>
<td>Gln2322*</td>
<td>Likely pathogenic</td>
</tr>
</tbody>
</table>

Variants as of July 2022
8 VUS in Simons Searchlight; not shown
* indicates biological relatives
Variants Observed in HIVEP2
23 individuals

Variants

- p.Asp397Tyr
- p.Glu408Lys
- p.Arg943*
- p.Gln969*
- p.Arg1028*
- p.Gln1157*
- p.Gln1173*
- p.Tyr1177Ilefs*2
- p.Gln1248*
- p.Leu1718Alafs*16
- p.Gln1896*
- p.Ser1967Cysfs*2
- p.Arg1979*
- p.Arg2223*
- p.Gln2291*
- p.Gln2322*

Functional regions

- Zinc finger
- Nuclear localization signal
- Serine-rich region
- Asp/Glu-rich acidic region

8 VUSs in Simons Searchlight; not shown
Protein Structure of HIVEP2
Quality of Life Survey
We gratefully acknowledge Dr. Jenny Downs of the Telethon Kids Institute.

* This graphic shows the number and proportion of individuals reported to experience each aspect of health and well-being Often or Very Often.
Quality of Life Inventory - Disability

(5 individuals with HIVEP2)

**Family & Friends**

- Happy when they are understood: 3
- Feels relaxed while making eye contact: 2
- Initiates greetings with others: 4
- Happy to be included: 4
- Enjoys socializing at mealtimes: 4
- Enjoys interacting with others: 5
- Excited by upcoming activities: 5

**Daily Life**

- Expresses their needs: 1
- Makes own choices for activities: 3
- Likes using technology: 5
- Helps with routines: 1
- Enjoys making things: 2

We gratefully acknowledge Dr. Jenny Downs of the Telethon Kids Institute
Simons Searchlight
HIVEP2 Medical History Data

13 Male Participants
19 Participants
6 Female

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

Age Range
1yr(s) - 42yr(s)

18 Participants under 18

Average Age
10 yr(s)
Developmental and Behavioral Conditions
(19 Individuals)

- Language Delay/Impairment: 14 (74%)
- Intellectual Disability/Developmental Delay: 17 (89%)
- Autism: 7 (37%)
- Anxiety: 2 (11%)
- ADHD: 5 (26%)
Neurological Problems
(19 individuals)

- Tic Disorder: 3 (16%)
- Small Head Size: 5 (26%)
- Movement Disorder: 4 (21%)
- Low Muscle Tone: 16 (84%)
- Coordination Problems: 7 (37%)
- Cerebral Palsy: 3 (16%)
Endocrinologic
(19 individuals)

- Short Stature: 1 (5%)
- Precocious Puberty: 1 (5%)
- Obesity: 1 (5%)
- Failure to Thrive: 2 (11%)
Vision Problems
(19 individuals)

- Nearsighted: 2 (11%)
- Lazy Eye: 3 (16%)
- Farsighted: 8 (42%)
- *Crossed Eyes: 5 (26%)
- Cataract: 1 (5%)
- Astigmatism: 4 (21%)

* 2 resolved through surgery
Additional Medical Issues
(19 individuals)

- Urinary Reflux: 1 (5%)
- Seizures: 1 (5%)
- Genital: 1 (5%)
- Endocrinologic: 5 (26%)
- Gastro: 11 (58%)
- Vision: 14 (74%)
Antiepileptics
* Some used for behavior
Child Behavior Checklist (CBCL)
Child Behavior Checklist

Behavioral and Emotional Concerns
Ages 1.5-5 Years (8 individuals)

- Aggression
- Sadness
- Anxiety
- Attention/Hyperactivity
- Oppositional Behavior
Child Behavior Checklist

Behavioral and Emotional Concerns
Ages 6-18 Years (12 individuals)

- Aggression
- Sadness
- Anxiety
- Attention/Hyperactivity
- Oppositional Behavior

- Also, looking at how these behavior issues change over time in a small subset of children with 2-4 timepoints, overall behavioral and emotional problems seem to decrease in most children going through the pre-teen and teen years.
Child Behavior Checklist

Top Behavioral and Emotional Concerns
Ages 1.5-5 Years (8 individuals)

- Chews on non-food items
- Difficulty waiting
- Quickly moves from one activity to the next (short attention)
- Hyperactive
Child Behavior Checklist

Top Behavioral and Emotional Concerns
Ages 6-18 Years (12 individuals)

- Frequently distracted
- Demands frequent attention
- Hyperactive
- Obsessions
Summary: HIVEP2 Medical and Behavioral Phenotypes

Common issues
- Language impairment
- Intellectual disability or developmental delay
- Eye/Vision problems
- Low muscle tone (hypotonia)

Other issues
- Autism
- ADHD (attention/hyperactivity)
- Mood or behavior problems
- Small head size (microcephaly)
- Movement disorders
- Motor coordination issues
Thank you