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

Logan Adams
Tempus

Jamie Atanda
Geisinger

Libby Brooks
Simons Foundation

Alyss Covanagh
Simons Foundation

Wendy Chung
Columbia

Elisheva Dubin
Columbia

Tamar Forman
Simons Foundation

Swami Ganesan
Simons Foundation

LeeAnne Green Snyder
Simons Foundation

Alison Holbrook
Simons Foundation

Jane Hong
Simons Foundation

Stanley Jean
Simons Foundation

Bill Jensen
Simons Foundation

Erica Jones
Simons Foundation

Catherine Kentros
Columbia

Misia Kowanda
Geisinger

Christa Lese Martin
Geisinger

Jay Nestle
Tempus

Tyler Ramsey
Geisinger

Andrea Rondon
Simons Foundation

Danielle Schmidt
Tempus

Kaitlyn Singer
Geisinger

Rebecca Smith
Geisinger

John Spiro
Simons Foundation

Cora Taylor
Geisinger

Jennifer Tjernagel
Simons Foundation

Amanda Tufano
Geisinger

Lauren Walsh
Geisinger

Curtis Weaver
Geisinger
Priorities for Searchlight Data Collection

- Participant-centered, high-priority, useful data
- Longitudinal
- Facilitate investigation by researchers
- 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**

**December 2021**

**Participant Age at Most Recent Interview**

**Developmental & Behavioral Diagnoses**

**Neurological Problems**

**Gastrointestinal Problems**

**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 home 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)?
The CSNK2A1 (OCNDS) Registry in Simons Searchlight
Progress of Individuals with CSNK2A1 (OCNDS)

**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.
## Variants Observed in CSNK2A1 (OCNDS)

**61 individuals**

<table>
<thead>
<tr>
<th>Variant Category</th>
<th>Number</th>
<th>Breakpoints</th>
<th>Variant Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNV breakpoints</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chr20:378136-547319</td>
<td>Likely Pathogenic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chr20:60747-19126923</td>
<td>Pathogenic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chr20:61568-2057916</td>
<td>Pathogenic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chr20:82603-2197239</td>
<td>Pathogenic</td>
<td></td>
</tr>
<tr>
<td>Splice site or intronic</td>
<td>367-1G&gt;A</td>
<td>Pathogenic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>426+1G&gt;T</td>
<td>Likely Pathogenic</td>
<td></td>
</tr>
<tr>
<td>Frameshift or nonsense</td>
<td>p.Glu32Aspfs*14</td>
<td>Pathogenic</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p.Tyr307*</td>
<td>Likely Pathogenic</td>
<td></td>
</tr>
</tbody>
</table>

### Missense

<table>
<thead>
<tr>
<th>Variant Category</th>
<th>Number</th>
<th>p. nomen</th>
<th>Variant Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3*</td>
<td>p.Glu27Lys</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>p.Arg47Gly</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>p.Tyr50Cys</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>p.Arg47Gln</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>p.Tyr50Arg</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Arg80His</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Arg156Glu</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Arg156Tyr</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>p.Arg156Asn</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Asp156Tyr</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Asp156Glu</td>
<td>Likely Pathogenic</td>
</tr>
<tr>
<td></td>
<td>19</td>
<td>p.Lys198Arg</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>p.Arg312Trp</td>
<td>Pathogenic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p.Arg312Gln</td>
<td>Pathogenic</td>
</tr>
</tbody>
</table>

Variants as of July 2022

6 VUS in Simons Searchlight; not shown

* Indicates biological relatives
Variants Observed in CSNK2A1 (OCNDS)
61 individuals

Variants

- p.Arg47Gly
- p.Arg47Gln
- p.Tyr50Cys
- p.Tyr50Ser
- p.Ser51Arg
- p.Val53Leu
- p.Glu27Lys
- p.Glu32Aspfs*14
- c.367-1G>A
- c.426+1G>T
- p.Leu70Arg
- p.Arg80His
- p.Asp156Glu
- p.Asp156Tyr
- p.Asp156Asn
- p.Lys158Arg
- p.Asp175Gly
- p.Gly177Ser
- p.Glu180Lys
- p.Arg191Pro
- p.Ser194Phe
- p.Lys198Arg
- p.Tyr307*
- p.Arg312Trp
- p.Arg312Gln

Functional regions

- ATP/GTP Binding Loop
- Basic cluster
- Activation domain
- Active site
- p+1 loop
- Kinase domain

6 VUS in Simons Searchlight; not shown
Protein Structures of CSNK2A1

7PSU: Structure of protein kinase CK2alpha mutant K198R
6QY7: Human CSNK2A1 bound to ERB-041 (Wild Type)
## CSNK2A1 (OCNDS) Biospecimens

15 individuals contributed to the available biospecimens

<table>
<thead>
<tr>
<th>Available Sample</th>
<th>CSNK2A1 Carriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induced pluripotent stem cells (iPSCs)</td>
<td>9</td>
</tr>
<tr>
<td>Lymphoblastoid cell lines</td>
<td>6</td>
</tr>
<tr>
<td>Whole blood DNA</td>
<td>9</td>
</tr>
<tr>
<td>Saliva DNA</td>
<td>2</td>
</tr>
</tbody>
</table>
# CSNK2A1 (OCNDS) iPS Cells

<table>
<thead>
<tr>
<th>p. nomen</th>
<th># of Carriers</th>
<th>Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>p.Arg47Gln</td>
<td>2</td>
<td>Available</td>
</tr>
<tr>
<td>p.Arg47Gly</td>
<td>1</td>
<td>Available</td>
</tr>
<tr>
<td>p.Tyr50Ser</td>
<td>1</td>
<td>Available</td>
</tr>
<tr>
<td>p.Asp156Glu</td>
<td>1</td>
<td>Available</td>
</tr>
<tr>
<td>p.Lys198Arg</td>
<td>2</td>
<td>Available</td>
</tr>
<tr>
<td>p.Arg312Trp</td>
<td>1</td>
<td>Available</td>
</tr>
<tr>
<td>CNVdel</td>
<td>1</td>
<td>Available</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
Quality of Life Survey
Quality of Life Inventory - Disability

(23 individuals with OCNDS)

Health & Well-being
- Is in good health: 74%
- Sleeps well: 65%
- Has energy for daily activities: 78%
- Is alert and aware: 74%

Activities & the Outdoors
- Enjoys moving their body: 65%
- Enjoys feeling steady during activities: 57%
- Enjoys physical activities: 52%
- Enjoys outings: 43%
- Enjoys time outdoors: 57%

Feelings & Emotions
- In a good mood: 74%
- Smiles: 74%
- Expresses happiness using body language: 74%
- Laughs or giggles: 65%

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**

(23 individuals with OCNDS)

### Family & Friends

- **Happy when they are understood**: 70%
- **Feels relaxed while making eye contact**: 57%
- **Initiates greetings with others**: 57%
- **Happy to be included**: 70%

### Enjoys socializing at mealtimes**: 57%

### Enjoy interacting with others**: 83%

### Excited by upcoming activities**: 78%

### Daily Life

- **Expresses their needs**: 83%
- **Makes own choices for activities**: 70%
- **Likes using technology**: 83%
- **Helps with routines**: 52%
- **Enjoys making things**: 30%

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.
Simons Searchlight
CSNK2A1 (OCNDS) Medical History Data

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

- 0-4: 12 individuals
- 5-9: 16 individuals
- 10-14: 10 individuals
- 15-19: 4 individuals
- 20-24: 1 individual
- 25-29: 1 individual
- 30-34: 1 individual

Age Range: 1yr(s) - 33yr(s)
Participants under 18: 41
Average Age: 9 yr(s)
Developmental and Behavioral Conditions

(44 Individuals)

- **Language Delay/Impairment**: 41 (95%)
- **Intellectual Disability/Developmental Delay**: 39 (91%)
- **Autism**: 9 (21%)
- **Anxiety**: 5 (12%)
- **ADHD**: 5 (12%)
Toilet Training

Toilet Training for Bladder
CSNK2A1 Individuals at least 4 years old (n=36)

- **78%** of children aged 4 or older can use the toilet to urinate
- Average age of learning to use the toilet is just **under 4 years old**
- Children can continue to become potty-trained **after 7 years of age**
- **17%** (6 of 36) of parents consider their child **incontinent** after 4 years of age (has accidents, or wears diapers or pull-ups)

Toilet trained for bowel:
- **75%** of children 4 and older can use the toilet for bowel movements
- Average age of learning to use the toilet is just **under 4 years old**
Neurological Problems
(44 individuals)

- Tic Disorder: 2 (5%)
- Small Head Size: 12 (27%)
- Movement Disorder: 7 (16%)
- Low Muscle Tone: 33 (75%)
- Large Head Size: 1 (2%)
- High Muscle Tone: 1 (2%)
- Cortical Visual Impairment: 1 (2%)
- Coordination Problems: 6 (14%)
- Cerebral Palsy: 2 (5%)
Seizure Disorders
(44 individuals)

Total People with Seizures 12(27%)

- Simple Partial 1(2%)
- Petit Mal 5(11%)
- Myoclonic 2(5%)
- Infantile Spasm 3(7%)
- Grand Mal 6(14%)
- Complex Partial 1(2%)
- Atonic Drop Attack 1(2%)

Seizure course in 20 individuals completing the Seizure History survey:

- Seizures first began between 2 months and 16 years of age
  - Average age of first seizure is 3 years
- 12 (60%) of individuals with seizures have had to take medication for their seizures
  - 6 (30%) continue to take preventative medication for their seizures (6 resolved)
- 8 (40%) 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
(44 individuals)

Total People with Congenital Heart Disease: 2 (5%)
Other: 4 (9%)
Av Canal: 1 (2%)
Surgery
(44 individuals)

GI Surgery-G-Tube: 3 (7%)
Craniofacial Surgery-Facial Cleft Repair: 2 (5%)
Genital
(44 individuals)

Undescended Testicles 49%

Other 12%
Endocrinologic
(44 individuals)

- Short Stature: 19 (43%)
- Irregular Menses: 2 (5%)
- Hypothyroidism: 1 (2%)
- Failure to Thrive: 16 (36%)
Vision Problems
(44 individuals)

- Repetitive Eye Movements: 1 (2%)
- Ptosis: 2 (5%)
- Other: 2 (5%)
- Nearsighted: 3 (7%)
- Lazy Eye: 1 (2%)
- Farsighted: 6 (14%)
- Crossed Eyes: 7 (16%)
- Coloboma: 2 (5%)
- Astigmatism: 14 (32%)
Additional Medical Issues
(44 individuals)

- Structural Birth Defects: 1(2%)
- Kidney: 1(2%)
- Autoimmune: 1(2%)
- Respiratory: 2(5%)
- Immunodeficiency: 2(5%)
- Orthopedic: 3(7%)
- Surgery: 4(9%)
- Heart: 5(11%)
- Genital: 5(11%)
- Vision: 24(55%)
- Endocrinologic: 25(57%)
- Gastro: 29(66%)
Medication Use
(30 individuals)

- Sleep: 8 (27%)
- Seizures: 8 (27%)
- Sedatives Taken for Seizures: 1 (3%)
- Sedatives: 1 (3%)
- Gastrointestinal: 11 (37%)
- Attention, Hyperactivity: 3 (10%)
- Asthma, Respiratory, Allergy: 5 (17%)
- Antidepressants: 2 (7%)
Most Effective Seizure Medications Reported
(20 individuals)

* From the Seizure History Survey
Vineland Adaptive Behavior Scales
Developmental Growth Charts
(Vineland-3)
Expressive Language Development
(17 individuals)

Vineyard Age Equivalent (in years)

Age at Evaluation

Uses single words to request
Personal Care Skills
(17 individuals)

Vineland Age Equivalent (in years)

Age at Evaluation

Dresses self

Feeds self with fork and spoon

SIMONS SEARCHLIGHT
Social Development
(16 Individuals)

- Shows interest in friends
- Makes eye contact during social interaction

Vineland Age Equivalent
(in years)

Age at Evaluation

SIMONS SEARCHLIGHT
Gross Motor Development
(14 individuals)

Vineland Age Equivalent (in years)

Age at Evaluation

Hops/jumps
Walks without help
Child Behavior Checklist (CBCL)
Child Behavior Checklist

Behavioral and Emotional Concerns
Ages 1.5-5 Years (20 individuals)

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

Levels:
- Little to no concern
- Mild
- Significant concern
Child Behavior Checklist

Behavioral and Emotional Concerns
Ages 6-18 Years (26 individuals)

- Looking at behavior changes over time in a small number of pre-teens and teens, most are not showing increasing behavior and emotional problems at adolescence.
Child Behavior Checklist
Top Behavioral and Emotional Concerns
Ages 1.5-5 Years (20 individuals)

- Difficulty waiting
- Quickly frustrated
- Scared to attempt new things
- Impatient
Child Behavior Checklist
Top Behavioral and Emotional Concerns
Ages 6-18 Years (26 individuals)
Summary: CSNK2A1
Medical and Behavioral Phenotypes

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

Other issues
- Autism
- Microcephaly (small head size)
- Seizures
- Low frustration tolerance
- Anxiety
- Obsessions
- Attention problems
Thank you