

SFARI Base

Simons Simplex Collection

Researcher Welcome Packet

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SSC Participation Criteria

Participants were admitted into the Simons Simplex Collection (SSC) in biological family groups. Each family includes one (and only one) child with autism. All siblings must be unaffected.

Participants in the SSC

Proband: the affected child in a family

Parents: biological mother and father of the proband, living at the time of submission, both unaffected with autism — The parents must not be related to each other by blood.

Unaffected designated sibling: the unaffected full sibling closest in age to the proband — The sibling was at least 4 years of age at the time of biospecimen collection.

Other sibling(s): other sibling, opposite in gender to the designated sibling (see other considerations below) — This sibling was at least 4 years of age at the time of biospecimen collection. *We did not collect blood or data on siblings under age 4.

Sibling exception: full sibling requirement was waived for approximately 20 percent of families due to the following exceptions:

- no sibling available
- only half siblings
- full or half siblings younger than 4 years old

Blood samples were collected from the proband, mother, father and designated (full) sibling and sent to a central repository ([RUCDR Infinite Biologics](#); formerly Rutgers University Cell and DNA Repository), where biospecimens were generated.

Inclusion Criteria

Age

The proband was between 4 years and 17 years 11 months of age when the phenotype measures were administered and the data were collected.

All measures were completed within a six-month period for all individuals.

Autism Diagnostic Interview-Revised (ADI-R) Scores

On the ADI-R, the proband met one of the following four (4) criteria:

- standard cutoffs on the social and communication domains,
- standard cutoff on the social domain and within two (2) points of communication domain cutoff,
- standard cutoff on the communication domain and within two (2) points of social domain cutoff, and
- was within one (1) point of the standard cutoffs on both social and communication domains.

All ADI-R data were collected by a reliable examiner.

Autism Diagnostic Observation Schedule (ADOS) Scores

On the ADOS, the proband received a valid and reliable administration, and met cutoffs for autism spectrum or autism:

- The newest ADOS algorithms were used for Modules 1–3.
- Original cutoff algorithms were used for Module 4.

Nonverbal Cognitive Ability

Using the Mullen Scales of Early Learning, the Differential Ability Scales-II, the Wechsler Intelligence Scale for Children-IV or the Wechsler Abbreviated Scale of Intelligence:

- Probands between 4 years and 6 years 11 months of age (48 to 83 months) must have had a nonverbal mental age of at least 24 months. Some exceptions down to 18 months nonverbal mental age were allowed after careful review of diagnosis including observation by videotape.
- Probands 7 years of age or older (84 months or older) must have had a nonverbal mental age of at least 30 months.

Diagnosis

Following the SSC evaluation, the proband received a clinical ‘best estimate diagnosis’ of autistic disorder, Asperger’s disorder or pervasive developmental disorder not otherwise specified (PDD-NOS), according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR).

- The best-estimate diagnosis was based on information from the SSC evaluation, including observation, chart review and ADI-R and ADOS findings.
- The best-estimate diagnosis was made by a psychologist or physician with appropriate credentials and experience requisite for making clinical psychiatric or psychological diagnoses. The diagnostician had direct observation of the proband in making the best estimate diagnosis.

Exclusion Criteria

Families meeting one or more of the following were excluded:

For Probands

Pregnancy and Birth

- fewer than 36 weeks gestation *and* less than 2,000 grams (approximately 4 lbs., 6.5 oz.) at birth
- born with significant injury, abnormality or disease having effects upon the brain
- a history of extensive prenatal or birth complications:
 - A history of significant prenatal/birth injury or brain damage was explored if the proband was in the neonatal intensive care unit or in the hospital for more than three days after birth.

Other Disorders or Limitations

- positive for fragile X syndrome or Down syndrome (trisomy 21)
 - Note 1: If probands met criteria for inclusion based on clinical phenotype measures, no other genetic diagnosis (whether based on macroscopic, microscopic or submicroscopic criteria) is excluded, unless features of the syndrome create secondary exclusionary factors (e.g., blindness, intelligence quotient out of range). The interest in these situations was to identify additional risk factors or modifier genes that may correlate with the autism phenotype.
 - Note 2: 'Clinical arrays' may be administered for purposes of genetic counseling, but results from clinical arrays will not be considered in the research project.
- sensory or motor difficulties that would preclude valid use of the diagnostic instruments
- history of severe nutritional or psychological deprivation
- when English is not equal to proband's primary language in use and fluency

For Full or Half Siblings

- diagnosed with, referred for or suspected of having autism
- suspected of having intellectual disability (mental retardation) or severe learning disability
 - exception: cases documented as Down syndrome (trisomy 21)
- diagnosed with schizophrenia
- diagnosed with a developmental or psychiatric disorder
 - All developmental and psychiatric disorders, and treatment with psychotropic medication, were potential exclusions and were reviewed by consultants.
 - These siblings were met by a site clinician for behavioral observations to confirm inclusion.
- with an Individual Education Plan (IEP) for extensive special education services

- Note 1: IEP must be reviewed. If passed, the sibling should be included as the designated sibling and met by the site clinician.
- extensive special education services to exclude
 - any self-contained special education classroom
 - pull-out time of more than 60 minutes per day
 - paraprofessional aide assignment
 - speech/language therapy for expressive/receptive language or pragmatic language disorder (not articulation)
 - occupational therapy for sensory integration
 - social skills therapy
 - Note 2: For any full siblings less than 4 years old, stringent screening must be done to eliminate any concerns of potential autism. For this reason, if the sibling was receiving any services (even services not considered 'extensive'), the family was put on a waitlist until the sibling reached the age of 4. At that time, they could be reassessed for the SSC.

For Biological Parents

- diagnosed with, referred for or suspected of having autism
- suspected of having intellectual disability (mental retardation) or severe learning disability
- diagnosed with schizophrenia
- parents are third-degree relatives or closer
- neither parent is fluent in English

For Second-Degree Relatives

Second-degree relatives include aunts, uncles, nephews, nieces, grandparents and grandchildren.

- diagnosed with or suspected of having autism

For Third-Degree Relatives

Third-degree relatives include cousins, great-aunts, great-uncles, great-grandmothers, great-grandfathers, half aunts and half uncles.

- diagnosed with or suspected of having autism

Participation in Other Biomaterial Repositories

A family was excluded from participating in the SSC if they had participated or were participating in other autism repositories or repositories of disorders related to autism (e.g., obsessive-compulsive disorder).

Other Considerations

Additional Siblings

If an additional sibling opposite in gender to the designated sibling was available, the site collected blood and all designated sibling measures from that sibling.

Multiplex Families

Simplex families initially enrolled in the study may be discovered to be multiplex after the start of data collection.

If a site later identified/identifies that a sibling, parent or second- or third-degree relative is on the autism spectrum (based on additional information from family follow-up or another source), the family will still be available on SFARI Base and flagged as *multiplex* (in the `families_by_distribution` file).

Previously Excluded Families

Families previously excluded from the core SSC collection for various reasons and released in an ancillary set are now available in the main collection and flagged as *Simons Ancillary Collection* (in the `families_by_distribution` and `individuals_by_distribution` files).

Monozygotic Twins (MZ) with autism

If a family has monozygotic (identical) twins with autism, the proband twin (MZ) protocol in the database was assigned to twin #2 (the proband's twin). The full assessment protocol for the proband was completed on both twins.

SSC@IAN Follow-Up Study

Participation Criteria

Inclusion Criteria

All SSC participants enrolled in the SSC@IAN registry were invited to participate in an online, longitudinal study. For probands and designated siblings who were adults at the time of the study, we first asked a parent to report guardianship status for their adult child (legally independent or dependent). Probands and designated siblings over the age of 18 were invited to participate if they were legally independent. Parents of probands and designated siblings who were minor children or dependent adults were invited to complete surveys about their child(ren). Data were collected on 440 families from the SSC.

Exclusion Criteria

Families in the original SSC who declined to participate in SSC@IAN were not invited to participate in this study.

SSC Available Instruments by Family Role Table

Note: Protocol modifications are sometimes made to accommodate new and/or changed instruments; not all instruments are available for all participants.

Instrument/Activity	Parents	Probands	Unaffected Siblings
Aberrant Behavior Checklist (ABC) Measure of: Aberrant behaviors Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parent Publisher: Slosson		X	
Adult Behavior Checklist for Ages 19 to 59 (ABCL) Measure of: Problem behavior Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parent Publisher: ASEBA			X
Autism Diagnostic Interview-Revised (ADI-R) Measure of: Parent report of behaviors related to autism phenotype Format: Direct interview Administered when: SSC Research Evaluation Administered by: Examiner who has achieved research levels of ADI-R reliability according to SSC standards Administered to: Parent Publisher: WPS		X	
Autism Diagnostic Observation Schedule (ADOS) Measure of: Observational measure of autism phenotype Format: Direct examiner observation Administered when: SSC Research Evaluation Administered by: Examiner who has achieved research levels of ADOS reliability according to SSC standards Publisher: WPS		X	

Instrument/Activity	Parents	Probands	Unaffected Siblings
Brief family physical and dysmorphology examination Measure of: Physical anomalies Format: Direct physical exam Administered when: Physical exam Administered by: Medical or clinical staff Author: Judith Miles	X	X	X
Broad Autism Phenotype Questionnaire (BAPQ) Measure of: Broader autism phenotype Format: Self-report questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Mother and father Publisher: Piven	X		
Child Behavior Checklist for ages 6 to 18 years (CBCL) Measure of: Problem behavior Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parent Regarding whom: Proband and siblings, ages 6 to 18 years Publisher: ASEBA		X	X
Cognitive Testing DAS-II (Differential Ability Scales, Second Edition) Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Administered to: Proband ages 4 to 17 years 11months Publisher: Harcourt Assessments Mullen (Mullen Scales of Early Learning, AGS Edition) Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: Pearson Assessments WASI (Wechsler Abbreviated Scale of Intelligence) Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: Harcourt Assessments WISC-IV (Wechsler Intelligence Scale for Children, Fourth Edition) Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: Harcourt Assessments		X	

Instrument/Activity	Parents	Probands	Unaffected Siblings
Developmental Coordination Disorder Questionnaire (DCDQ) Measure of: motor delays Format: Questionnaire Administered when: Parent Questionnaire Packet Completed by: Parents Author: B.N. Wilson		X	
Diagnosis Summary Form Index of: DSM-IV-TR Diagnoses; Diagnostic Certainty; Clinicians Involved in Making Diagnosis; Deviation IQ, Ratio IQ, and Mental Age scores; Information potentially critical to the evaluation (e.g., undiagnosed problems in parents and siblings). Format: Form Administered when: Following SSC Research Evaluation Completed by: Observing senior psychologist/psychiatrist with clinical/research staff		X	
Interviewer's Clinical Impressions (FHI-I) Measure of: Broader phenotype Format: Rating Administered when: Following ADI-R interview at the SSC Research Evaluation Completed by: ADI-R examiner Publisher: IMGSA	X		
Comprehensive Test of Phonological Processing Non-word Repetition (CTOPP-NR) Measure of: Speech and memory of sounds and non-words Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Administered to: Probands with a verbal mental age of 60 months Publisher: PRO-ED		X	
Parent Substance Use History Form Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Both parents Publisher: SSC	X		
Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4) Measure of: Receptive single-word vocabulary Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: NCS Pearson, Inc.		X	
Purdue Peg Board Measure of: Fine-motor dexterity Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: Lafayette Instrument Co.		X	

Instrument/Activity	Parents	Probands	Unaffected Siblings
Raven's Standard Progressive Matrices Measure of: Nonverbal problem solving Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Clinical/Research staff Publisher: Harcourt Assessments		X	
Repetitive Behavior Scale-Revised (RBS-R) Measure of: Repetitive behaviors Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parents Publisher: Bodfish		X	
Social Communication Questionnaire (SCQ-L) (Parent report) Measure of: Screen of ASD markers Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parents Regarding whom: Parents report on probands (age 4 years to 17 years 11 months) and siblings (age 4 and up) Publisher: WPS		X	X
Social Communication Questionnaire (SCQ-C) (Teacher report) Measure of: Screen of ASD markers Format: Questionnaire Administered when: Included in Teacher Questionnaire Packet Completed by: Teachers Regarding whom: Teachers report on probands age 4 years to 17 years 11 months and siblings age 4 and up Publisher: WPS		X	X
Social Responsiveness Scale (SRS-ARV) — Adult Research Version Measure of: Autistic traits on a continuous scale Format: Questionnaire Administered When: Included in Parent Questionnaire Packet Completed by: Parents Regarding whom: Mother reports on father; father reports on mother; parent reports on adult sibling ages 19 and up Publisher: WPS	X		
Social Responsiveness Scale (SRS) — Parent report Measure of: Autistic traits on a continuous scale Format: Questionnaire Administered when: Included in Parent Questionnaire Packet Completed by: Parents Regarding whom: Parents report on probands (age 4 years to 17 years, 11 months) and siblings (age 4 to 18 years) Publisher: WPS		X	X

Instrument/Activity	Parents	Probands	Unaffected Siblings
Social Responsiveness Scale (SRS) — Teacher report Measure of: Autistic traits on a continuous scale Format: Questionnaire Administered when: Included in Teacher Questionnaire Packet Completed by: Teachers Regarding whom: Teachers report on siblings (age 4 to 18 years) and probands (age 4 years to 17 years 11 months) Publisher: WPS		X	X
SSC Background History Form Index of: Contact information, family demographic information; parent report of proband's developmental milestones Format: Phone interview Administered when: Included in Parent Questionnaire Packet Completed by: Parent Publisher: SSC	X	X	X
SSC Family Pedigree Form Measure of: Phenotype of ancestry Format: Phone interview Administered when: Parent phone interview following return of Parent Questionnaire Packet Administered by: Clinical/Research staff Administered to: Parent Regarding whom: Immediate and extended family of proband Publisher: SSC		X	
SSC Height, Weight, Head Circumference Form Measure of: Physical characteristics Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Physician or clinical/research staff Publisher: SSC	X	X	X
SSC Medical History Interview Measure of: Family medical history Format: Telephone Interview Administered when: Parent phone Interview following return of Parent Questionnaire Packet Administered by: Clinical/Research staff Publisher: SSC	X	X	X
SSC Temperature Form Measure of: Temperature Format: Direct assessment Administered when: SSC Research Evaluation Administered by: Physician or clinical/research staff Publisher: SSC		X	
SSC Treatment History Form Measure: Past participation in therapeutic treatments Format: Phone interview Administered when: Parent phone interview prior to research evaluation Administered by: Clinical/Research staff Administered to: Parent Publisher: SSC		X	

Instrument/Activity	Parents	Probands	Unaffected Siblings
Teacher Report Form (TRF) Measure of: Problem behavior and school functioning Format: Questionnaire Administered when: Included in Teacher Questionnaire Packet Completed by: Teacher most knowledgeable Regarding whom: Siblings (ages 6 to 18 years) and proband (ages 6 years to 17 years 11 months) Publisher: ASEBA		X	X
<u>OR:</u> Caregiver-Teacher Report Form (C-TRF) Measure of: Problem behavior Format: Questionnaire Administered when: Included in Teacher Questionnaire Packet Completed by: Teacher/Daycare provider most knowledgeable Regarding: Siblings between 1 year 6 months and 5 years 11 months of age and probands between 4 years and 5 years 11 months Publisher: ASEBA			
Vineland Adaptive Behavior Scale-II (VABS-II) Measure of: Adaptive behavior Format: Interview Administered when: Parent phone interview regarding siblings and parent interview about proband following ADI-R at SSC Research Evaluation Administered by: Clinical/Research staff Administered to: Parents Publisher: Pearson		X	X

SSC@IAN Follow-Up Study Available Instruments by Role Table

Instrument/Activity	Parents	Probands	New Siblings	Unaffected Siblings
Aberrant Behavior Checklist (ABC) Measure of: Aberrant behaviors Format: Online Questionnaire Completed by: Parent Publisher: Slosson		X		
Adult Behavior Checklist for Ages 19 to 59 (ABCL) Measure of: Problem behavior Format: Online Questionnaire Completed by: Parent Regarding whom: Proband and siblings, ages 6 to 18 years Publisher: ASEBA		X		X
Child Behavior Checklist for ages 6 to 18 years (CBCL) Measure of: Problem behavior Format: Online Questionnaire Completed by: Parent Regarding whom: Proband and siblings, ages 6 to 18 years Publisher: ASEBA		X		X
Communication and Symbolic Behavior Scales (CSBS) Measure of: Communication Delays Format: Online Questionnaire Completed by: Parent Regarding whom: New siblings (baby siblings) Publisher: Brookes			X	

Instrument/Activity	Parents	Probands	New Siblings	Unaffected Siblings
Repetitive Behavior Scale-Revised (RBS-R) Measure of: Repetitive behaviors Format: Online Questionnaire Completed by: Parents Publisher: Bodfish		X		
Social Responsiveness Scale 2 (SRS-2) — Parent report Measure of: Autistic traits on a continuous scale Format: Online Questionnaire Completed by: Parents Regarding whom: Probands (age 4 years to 17 years 11 months) and siblings (age 4 to 18 years) Publisher: WPS		X		X
Social Responsiveness Scale 2 (SRS-2) — Adult (relative/other report) Measure of: Autistic traits on a continuous scale Format: Online Questionnaire Completed by: Parents, spouses or other appointed adults Regarding whom: Parents, independent probands (age >18), siblings (age >18) Publisher: WPS	X	X		X
SSC@IAN Adult Proband Update Form Measure of: Diagnosis, medical and educational updates, employment and living situation Format: Online Questionnaire Completed by: Independent probands >18, parents Regarding Whom: Proband (>18) Publisher: SSC		X		
SSC@IAN ASD Diagnosis and Medical History Update Form Measure of: Diagnosis and brief medical history updates Format: Online Questionnaire Completed by: Parents Regarding Whom: Proband, designated sibling (<18) Publisher: SSC		X		

Instrument/Activity	Parents	Probands	New Siblings	Unaffected Siblings
SSC@IAN Education History Follow-Up Measure of: Education history Format: Online Questionnaire Completed by: Parent Regarding Whom: Proband, designated sibling (age <18) Publisher: SSC		X		X
SSC@IAN Family Medical History Follow-Up Measure of: Family medical history Format: Online Questionnaire Completed by: Parent Publisher: SSC	X	X	X	X
SSC@IAN Medical and Education History Follow-Up Measure of: Medical and educational history Format: Online Questionnaire Completed by: Parents and designated siblings (age >18) Regarding whom: Unaffected siblings Publisher: SSC				X
SSC@IAN Medications History Measure of: Proband medication history Format: Online Questionnaire Completed by: Parent Publisher: SSC		X		

How to access SFARI Base and request SFARI resources

1. Log in to SFARI Base [here](#). If you do not have a SFARI Base account, you may create one. As part of account creation, you will need to affiliate with an institution. If your institution is not registered on SFARI Base, you will be prompted to provide institution details as part of registration. This includes the name and email address for a Signing Official who has authority to represent your institution in a legal agreement, similar to a material transfer agreement.
2. Review your institution's executed Researcher Distribution Agreement (RDA) and agree to the joinder to the RDA. The RDA specifies the legal issues pertaining to research data and specimens, and requires approval from the PI's institution. Each PI and collaborator must agree to the joinder agreement to the RDA for their respective institution.

For institutions that do not yet have an executed RDA, it will be sent to the institutional officer for review and signature upon approval of a request in SFARI Base.

3. Create a SFARI Base project, which includes the title, abstract and an IRB approval or exemption document. Each SFARI project led by a PI must be governed by a protocol approved or exempted by an IRB. A protocol specifies the regulatory issues pertaining to the research and may include co-investigators at multiple institutions. You will need to obtain a PDF copy of the letter of your IRB approval or exempting your protocol.
4. Create a SFARI Base request, which includes specifying the type of resource you would like to request access to (phenotype, genetic or imaging data; biospecimens; and/or research match application). The submitted request will be reviewed by the SFARI science team or appropriate committee.

SSC Sample Consent Form

http://simonsfoundation.s3.amazonaws.com/share/Policies_and_forms/2014/ssc/UMACC_Adult_Consent_03-2011.pdf

If you have additional questions, email collections@sfari.org.