SFARI SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE

SFARI: measuring impact of funding

Natalia Volfovsky
November, 2018

SFARI

https://www.sfari.org

Mission: improve the understanding, diagnosis and treatment of autism spectrum disorders (ASD) by funding innovative research of the highest quality and relevance

SFARI Strategic Priorities:

Identify risk factors whether genetic, environmental or epidemiological.

Use non-human organisms to understand how these risk factors alter brain function and animal behavior.

Promote preclinical and clinical investigations to improve autism diagnosis & therapy.

Promote knowledge dissemination to increase the quality of autism-relevant science

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SFARI Support for Autism Research:

- 2017 budget: **$75 million**
- Since launch in 2003: **>$380 million** in external research support
- >**400 investigators**
- Scientific Resources

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SFARI scientific resources

In addition to funding autism research, SFARI supports a number of key scientific resources for the autism community:

- Cohorts of well-characterized individuals with autism or with specific genetic alterations
    - Simons Simplex Collection (SSC)
    - Simons Variation in Individuals Project (Simons VIP)
    - SPARK
- Tools that enable researchers to keep track of the genetic risk factors for autism (SFARI Gene)
- Autism rodent models
- Biospecimens (blood, fibroblasts, iPSCs) and data (eg. imaging, genetic, phenotypic) from our sponsored research projects (available via SFARI Base)
- Postmortem brain tissue for autism research (available through the collaborative network, Autism BrainNet)
- Therapeutics, including R-baclofen, for investigator-initiated studies in humans and animals (available from Clinical Research Associates, L.L.C., an affiliate of the Simons Foundation)

Measuring Impact of Funding

Fall 2017, the SFARI science team began a conversation with SFARI SAB about a ways of modification of the grant mechanisms to maximize SFARI funding/impact in the autism field.

- Metrics Selection
- Bibliometrics : Publications Trajectories and Relative Citation Ratio
- Assessment of Scientific Resources
- Lessons Learned and Recommendations

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Metrics Selection

What has been the impact of SFARI funding on the autism field?

- Has the resulting science been impactful on the field?

  Relative Citation Ratio (RCR)

- What's the stickiness factor (i.e., do people we bring in stay in the autism field)?

  Publication Trajectory (in progress)

Alice Clayton, Brigitta Gundersen, Julia Sommer, Noah Lawson

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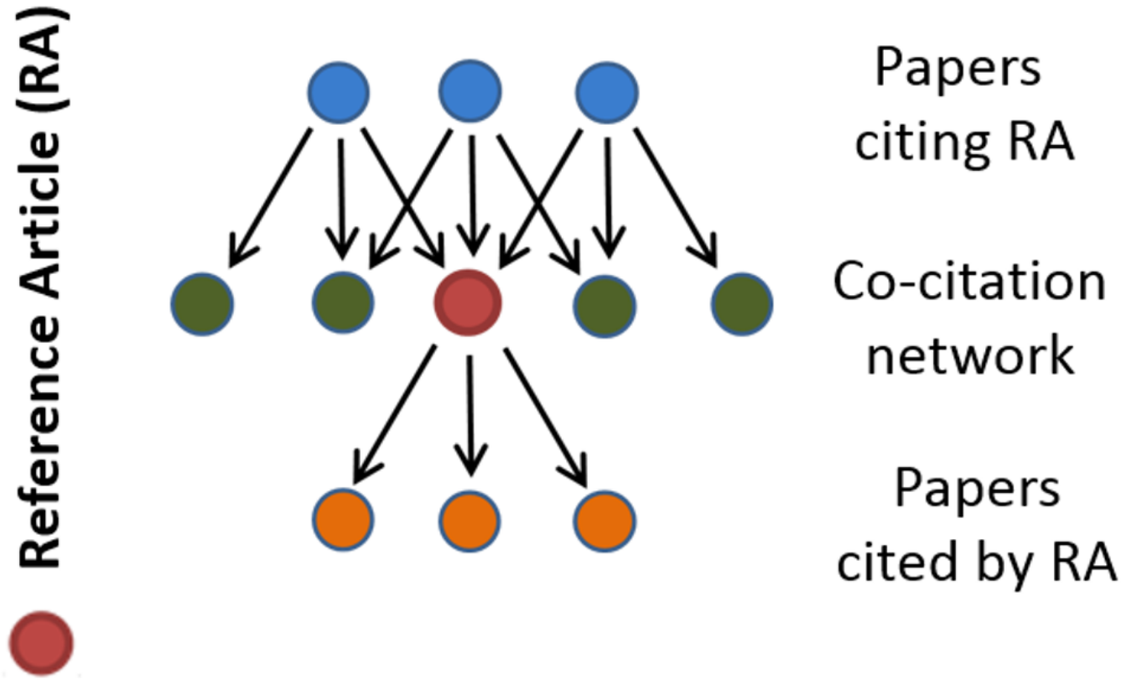
Relative Citation Ratio (RCR)

Has science from SFARI funding been impactful on the field?



RCR: a field-normalized metric that shows the scientific influence of one or more articles relative to the average NIH-funded paper

$$RCR = \frac{Article\ Citation\ Rate}{Expected\ Citation\ Rate}$$

RCR = 1 => 50% NIH publications

Hutchins et al., PLOS Biology 14(9), 2016

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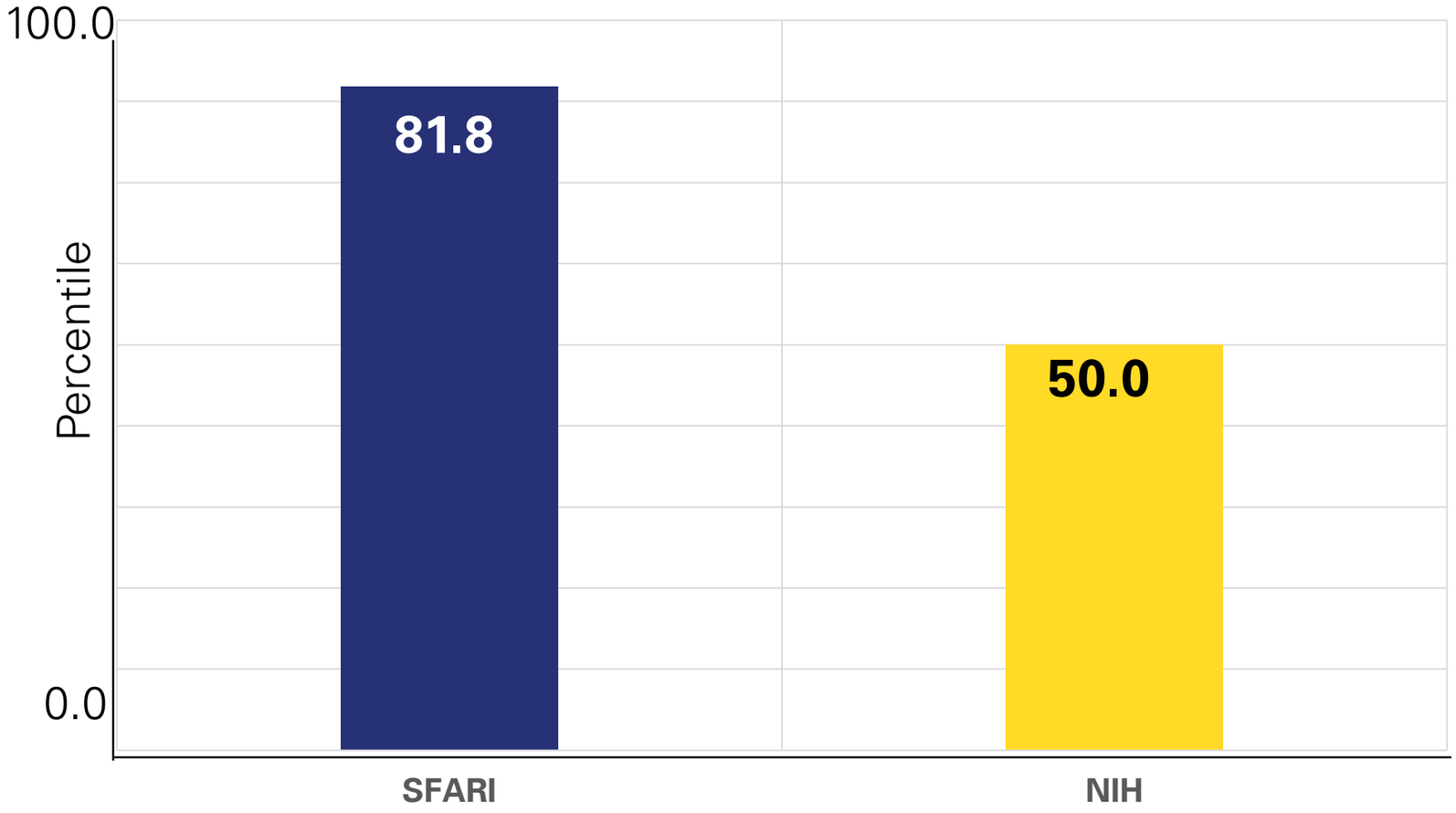
How many SFARI publications have an RCR >1.0



RCR 1.0 = NIH 50th percentile

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SFARI vs. NIH RCR

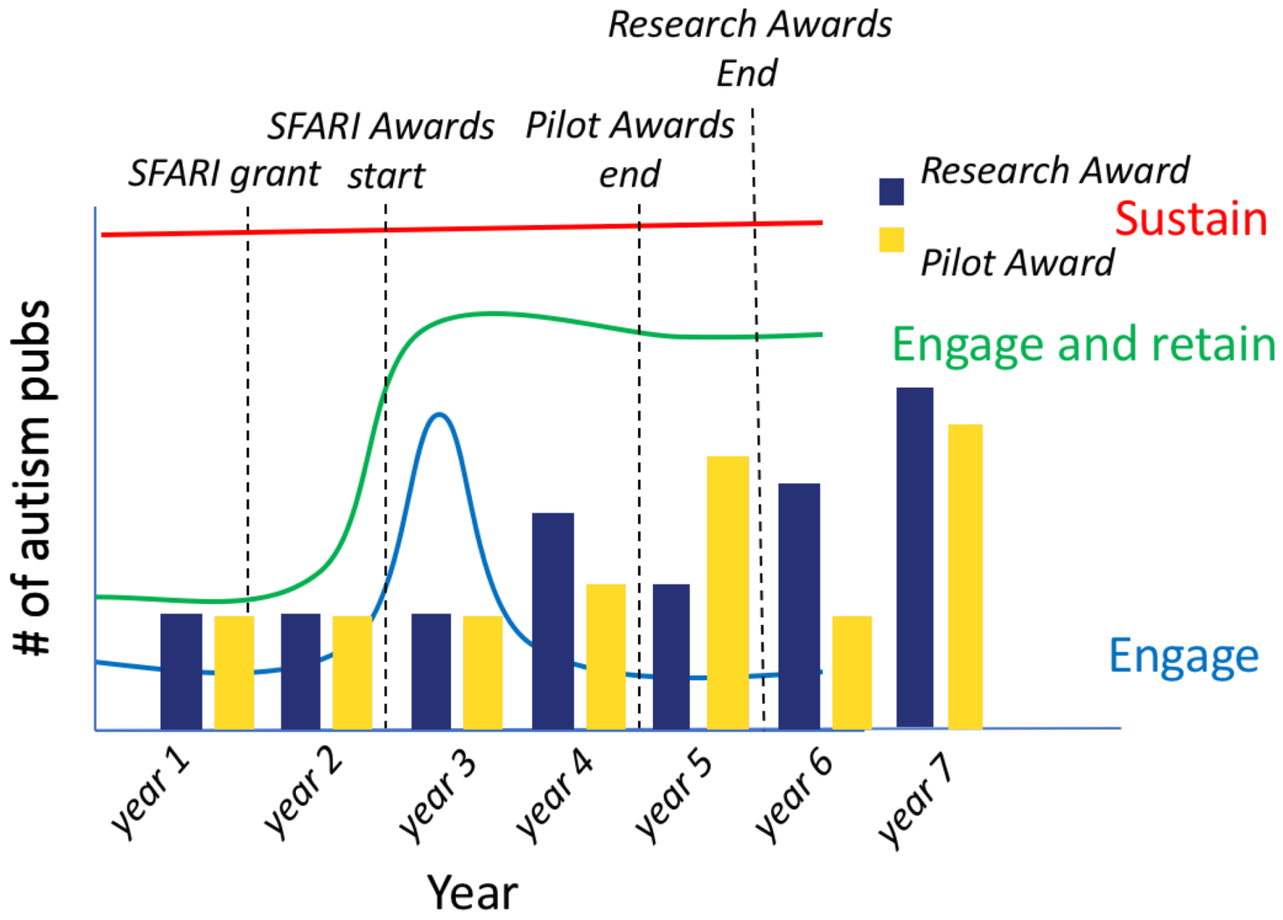
PERCENTILE	99.9	99	95	90	80	70	60	50	40	30	20	10	0
NIH RCR	38.00	13.11	5.72	3.81	2.39	1.72	1.3	1	0.76	0.56	0.56	0.38	0.20
SFARI RCR	72.63	33.8	14.32	10.21	5.79	4.19	3.24	2.56	1.9	1.47	1.05	0.63	0.03

SFARI RCR by award type

TYPE OF AWARD	TOTAL RCR	# OF PUBS	MEAN RCR
RESEARCH	1460.78	302	4.84
PILOT	478.35	109	4.39
EXPLORER	200.45	75	2.67
TARGETED RFA	65.24	15	4.35

Publication Trajectories (in progress)

Stickiness Factor: Do people brought into field by SFARI stay in the field?



- Pubmed: publications by SFARI investigators from 2002-2018
- Keyword "ASD" or "Autism"
- Plot # publications per year, per investigator
- Plot average number of publications 2 years pre and 5 years post SFARI funding by funding mechanism and year

Engagement and retention

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Assessment of Impact of Scientific Resources

- SFARI Research Cohorts
- SFARI Data resources
- Web portals: SFARIGene, Platforms for Visualization and Integration of Genomic Data

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SFARI Research Cohorts

Simons Simplex Collection
(SSC)

~10,000 individuals

Simons SearchLight
(VIP)

~1,500 individuals

SPARK

Igniting autism research
Improving lives

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SSC Contribution to Autism Research

- Over 150 publications resulting from SSC data
- Researchers have been approved for over 500 requests for SSC resources
  - 280 biospecimen requests
  - 222 genetic data requests, including whole exome and whole genome data
    - Some requests included multiple datasets – Illumina data has been requested 186 times, Nimblegen177, whole genome pilot data 42
  - 14 external research teams have recruited SSC families into new studies
    - SSC sites have also included SSC families in new, local research with topics ranging from adult issues to imaging studies
- Impact locally at SSC institutions: "The SSC literally launched this clinic. We would not have received the administrative and grant support we have today without the solid foundation built using the SSC funding and training. The impact on careers and families' lives cannot be overstated."

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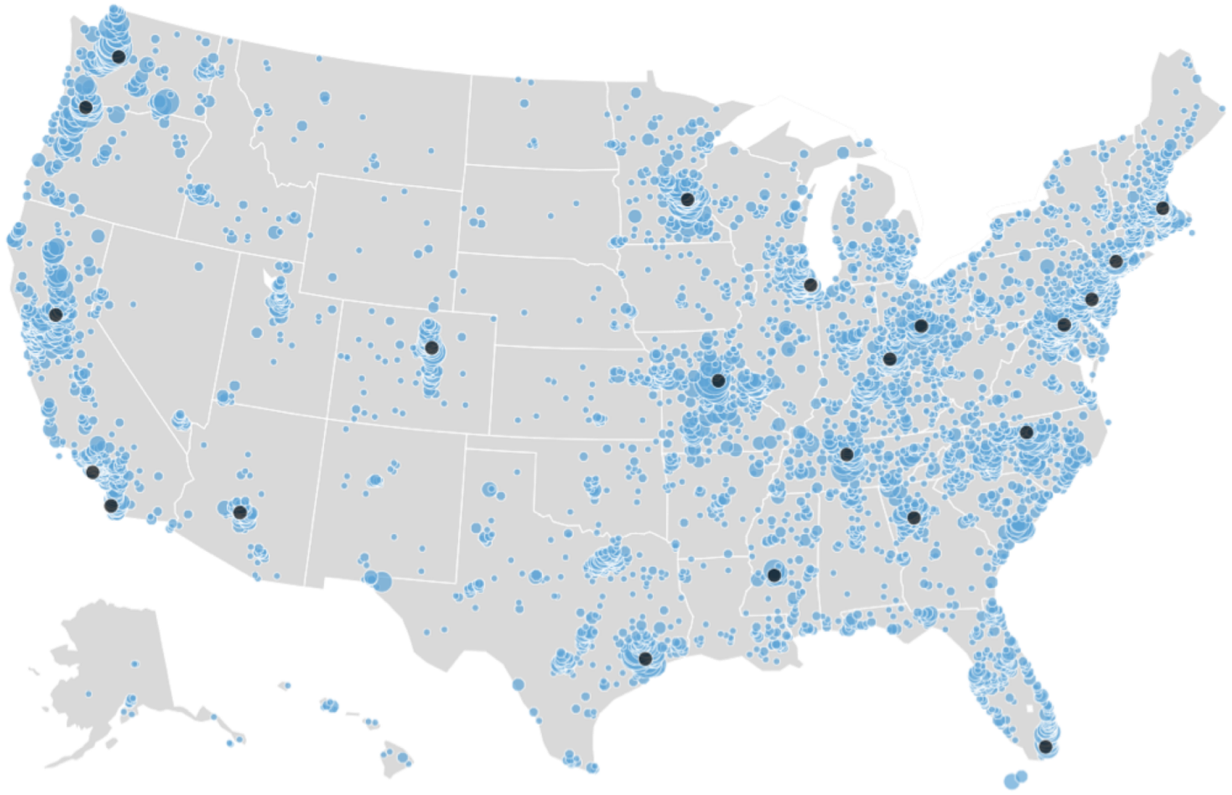
Simons Foundation Powering Autism Research through Knowledge

SPARK
Igniting autism research
Improving lives

https://sparkforautism.org

Recruit, engage, and retain 50,000 individuals with ASD and their biological family members to:

- identify causes of ASD
- enable genotype-driven research
- find better treatments to improve lives



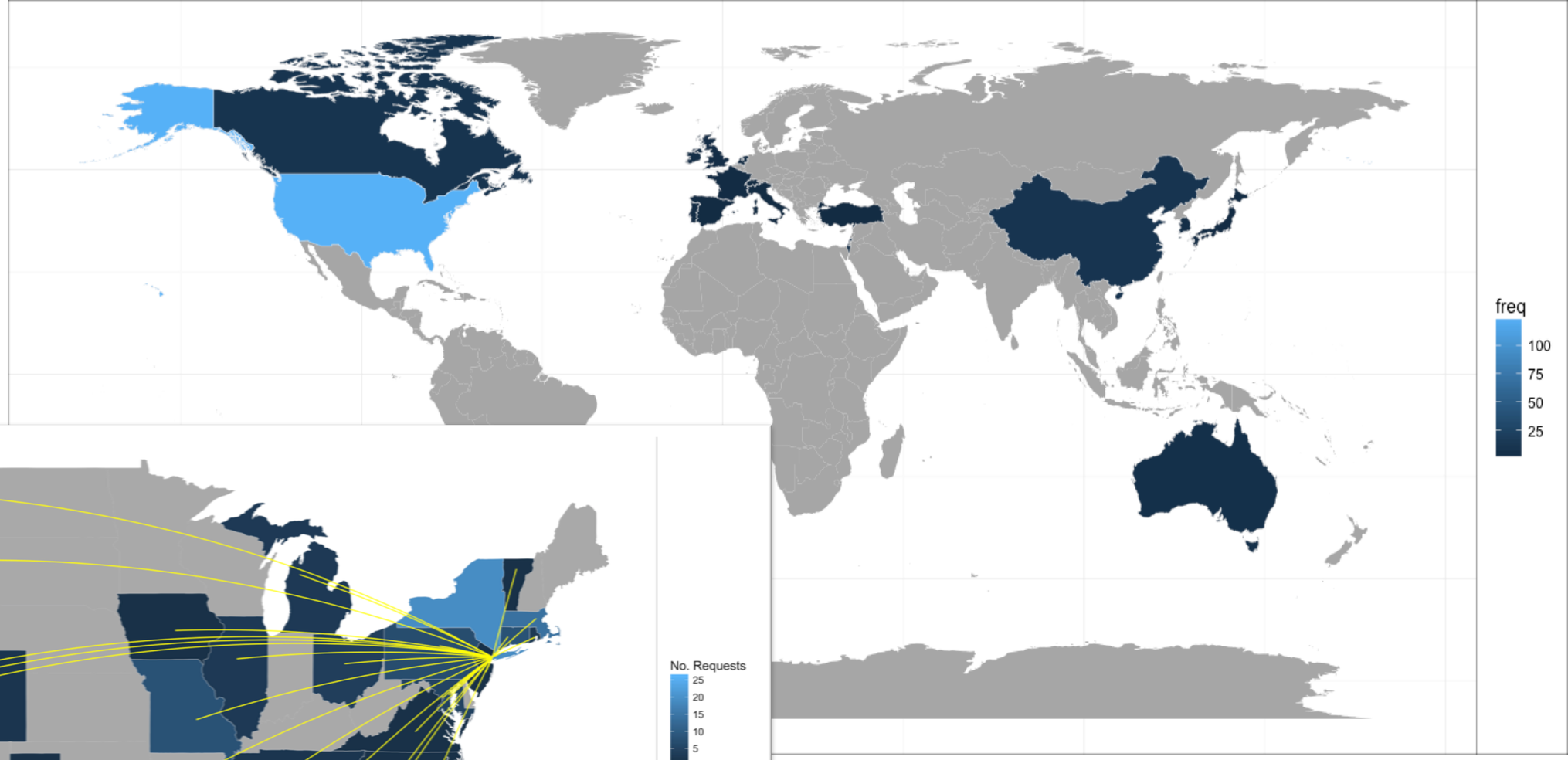
Participants
n= 140,869
Participants with ASD
n= 53,786
Completed trios
n= 14,035

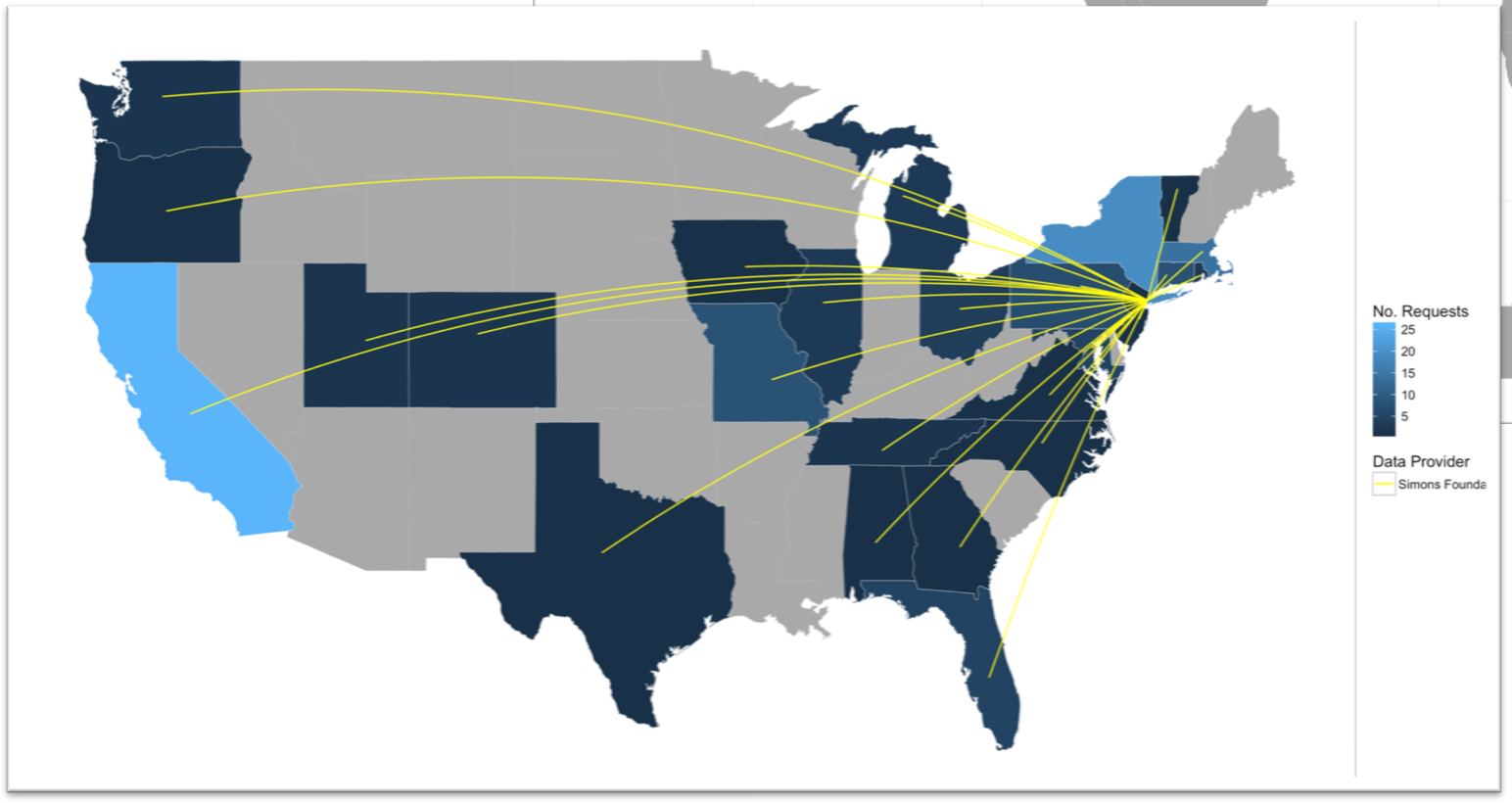
Participants invited to participate in at least 1 project
n >=26,000
Participates expressed interest to participate
n >=10,700

SFARI Data Resources

DATA SET	DATA SIZE	ACCESS	REFERENCES
SSC Whole Exome sequencing, 2014 ~10,000 samples,	120Tb	S3@AWS Flatiron Institute FNAL	Iossifov et al; (2014) Krumm et al, (2015)
SSC Whole Genome Data ~2000 samples	300Tb	S3@AWS Flatiron Institute FNAL	Turner et al, (2017)
SSC Whole Genome Data ~10,000 samples	830Tb	S3@AWS Flatiron Institute FNAL	September 2017
SPARK, Whole Exome sequencing. ~1500 samples	21Tb	S3@AWS Flatiron Institute FNAL	Feliciano et al, (2018)
SPARK, Whole Genome sequencing. ~1600 samples	200Tb	S3@AWS Flatiron Institute FNAL	October 2018
SPARK Whole Exome Data ~27,000 samples	200Tb	S3@AWS Flatiron Institute FNAL	October 2018

SFARI Data Requests





SFARI genomic data requests through **SFARIBase @ sfari.org**

SFARI Web Portals

- Platforms for Visualization and Integration of Genomic Data
- SFARIGene

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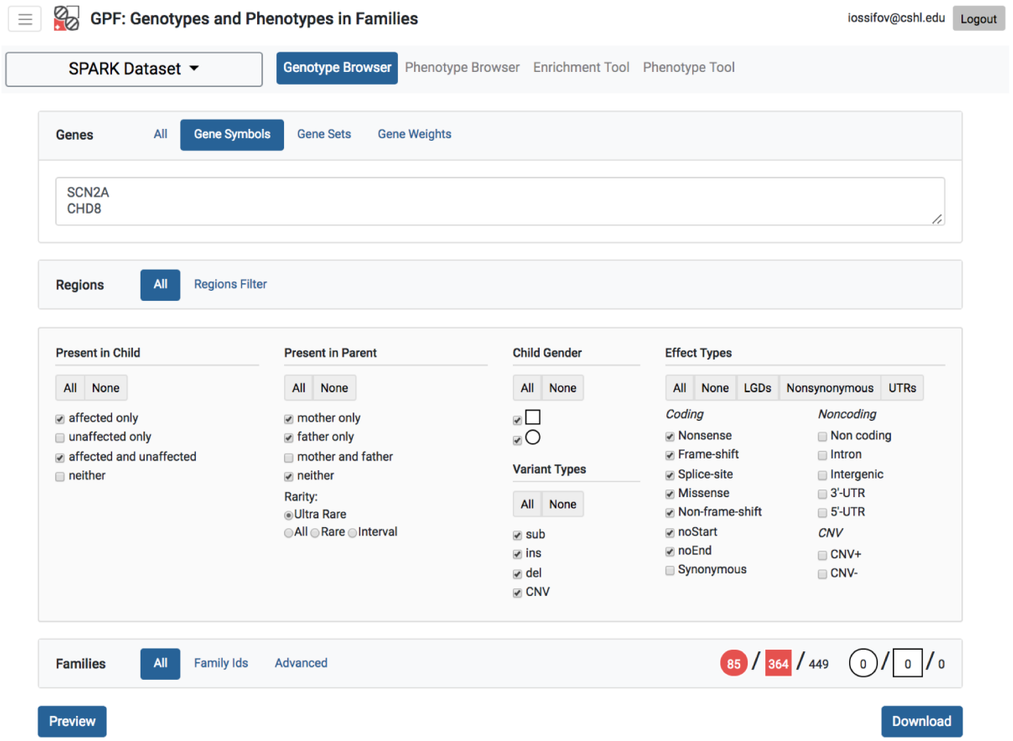
Genome and Phenotype Tool(GPF)

https://gpf.sfari.org/

Query



17 variants selected (17 shown)

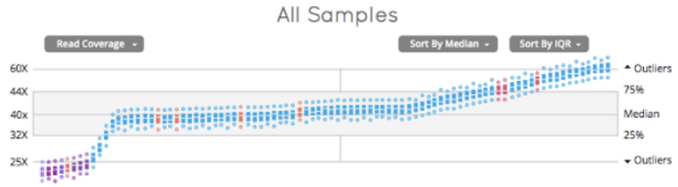
family		variant		genotype		effect		allele freq	SCQ Scores	
familyId / stdy		loc / var		ch / par		type / gene		SSC / EVS / E65	Summary / Final	
SF0033656	SPARK	2:166170524	sub(A->C)			missense	SCN2A		25.0	25.0
SF0037822	SPARK	2:166187917	sub(A->T)			nonsense	SCN2A		29.0	29.0
SF0003489	SPARK	14:21899097	sub(G->A)			nonsense	CHD8			
SF0018345	SPARK	2:166179722	sub(C->A)			missense	SCN2A	SSC 0.01%	18.0	18.0
SF0045449	SPARK	2:166179831	sub(G->A)			missense	SCN2A	E65 0.00%	35.0	35.0
SF0000213	SPARK	2:166223756	sub(A->G)			missense	SCN2A			
SF0037822	SPARK	2:166245784	sub(A->C)			missense	SCN2A	SSC 0.01% EVS 0.01% E65 0.02%	29.0	29.0
SF0008141	SPARK	2:166246036	sub(T>C)			missense	SCN2A	E65 0.00%	19.0	19.0
SF0000400	SPARK	14:21853996	sub(G->A)			missense	CHD8		25.0	25.0
SF0010732	SPARK	14:21854265	sub(C>T)			missense	CHD8	E65 0.05%	31.0	31.0
SF0041178	SPARK	14:21854319	sub(G->A)			missense	CHD8		14.0	14.0
SF0019186	SPARK	14:21860802	sub(G->A)			missense	CHD8		24.0	24.0
SF0025295	SPARK	14:21861685	sub(C->G)			missense	CHD8			
SF0042736	SPARK	14:21862057	sub(T>C)			missense	CHD8		20.0	20.0
SF0003386	SPARK	14:21899129	sub(G->A)			missense	CHD8		23.0	23.0
SF0004355	SPARK	14:21899391	sub(C->G)			missense	CHD8	E65 0.00%	32.0	32.0
SF0006219	SPARK	14:21899658	sub(T>C)			missense	CHD8	SSC 0.03% EVS 0.31% E65 0.11%	13.0	13.0

Features:

- SPARK Content:
  - De novo variants
  - Rare and common transmitted variants
  - Phenotypic data
- Integration:
  - SSC exome and whole-genome
  - VIP
- Query: Interface
  - By gene
  - By set of genes (i.e. by pathway)
  - By predicted variant effect (i.e. LGDs)
  - By variant frequency
  - By transmission pattern (i.e. de novo or transmitted from mother)
  - By phenotypic properties (i.e. affected children with SCQ score larger than 20)
- Analysis tools:
  - Enrichment of de novo variant in a given gene set.

SFARI-IOBIO Data Federation Project

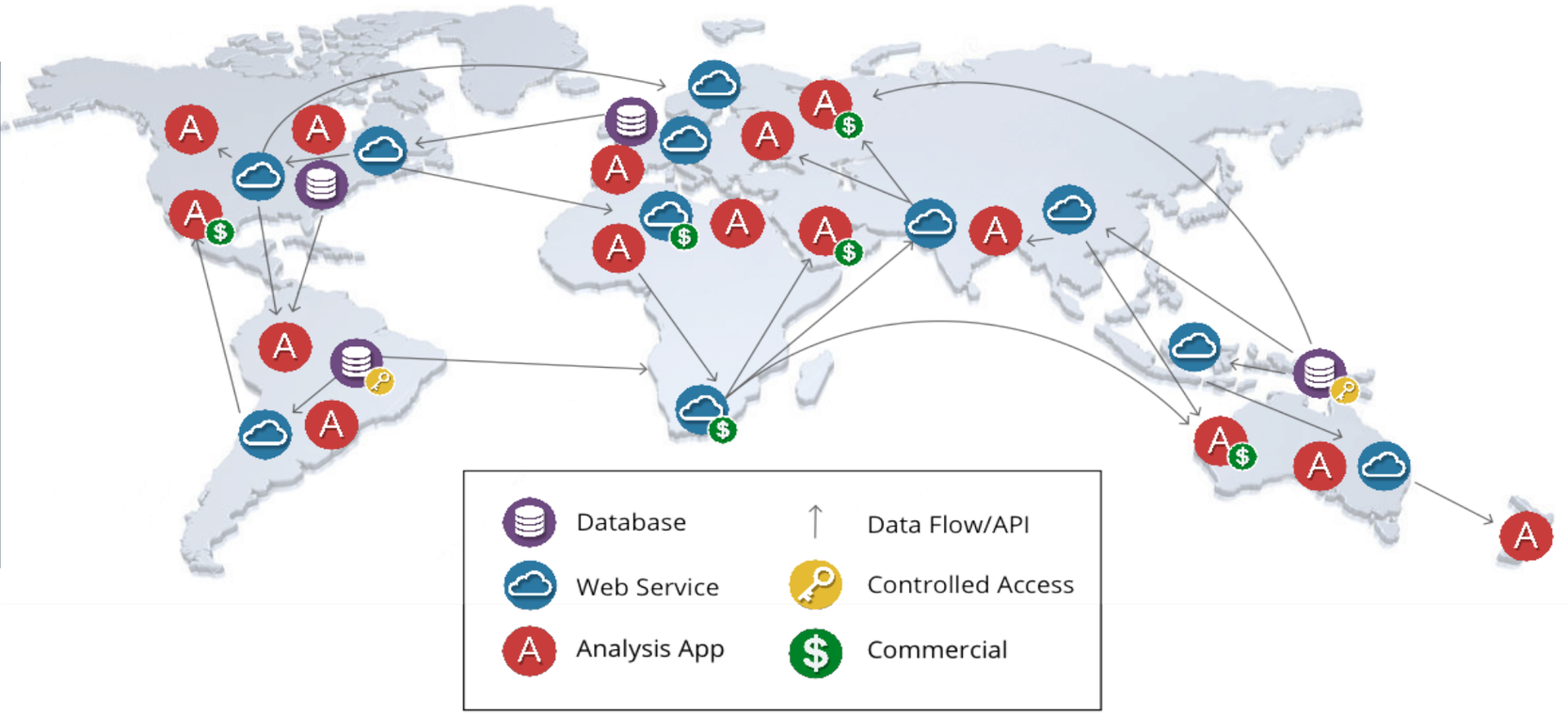
bam.iobio: http://bam.iobio.io
vcf.iobio: http://vcf.iobio.io
gene.iobio: http://gene.iobio.io



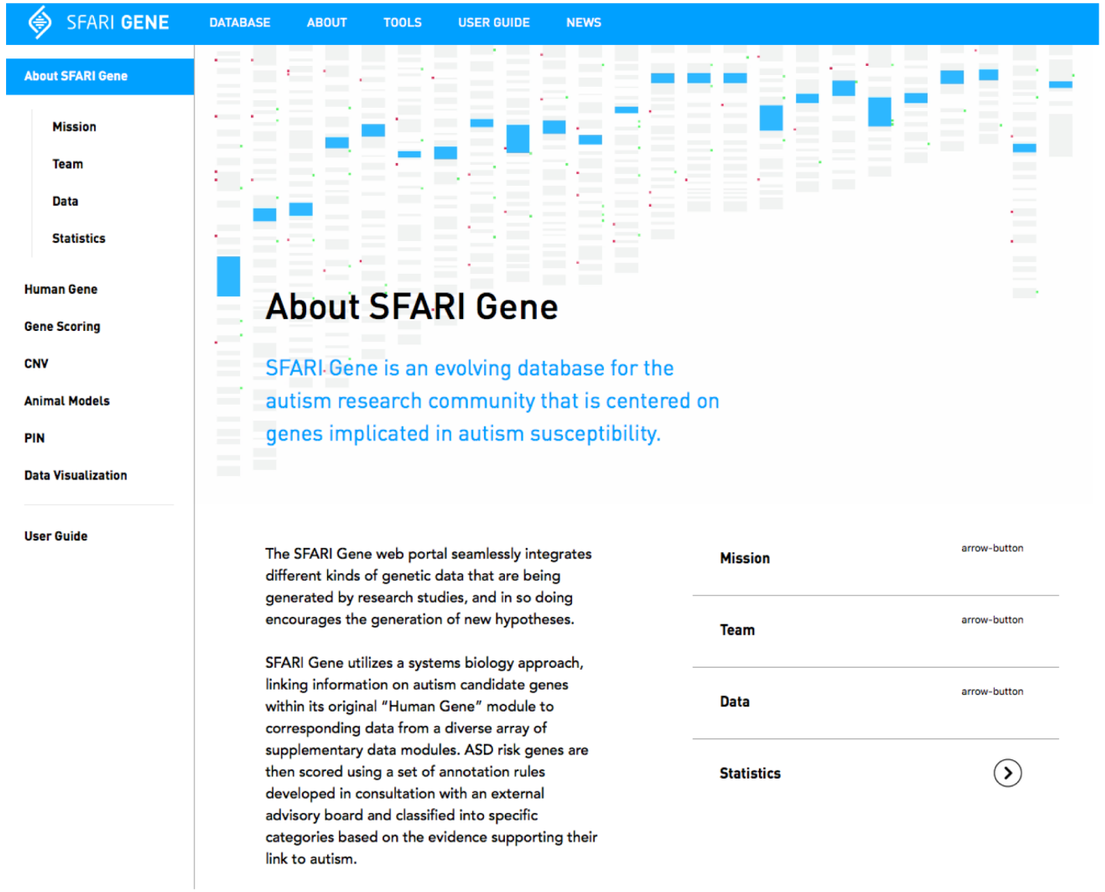
Data Hub
register + find databases
hub.iobio/data

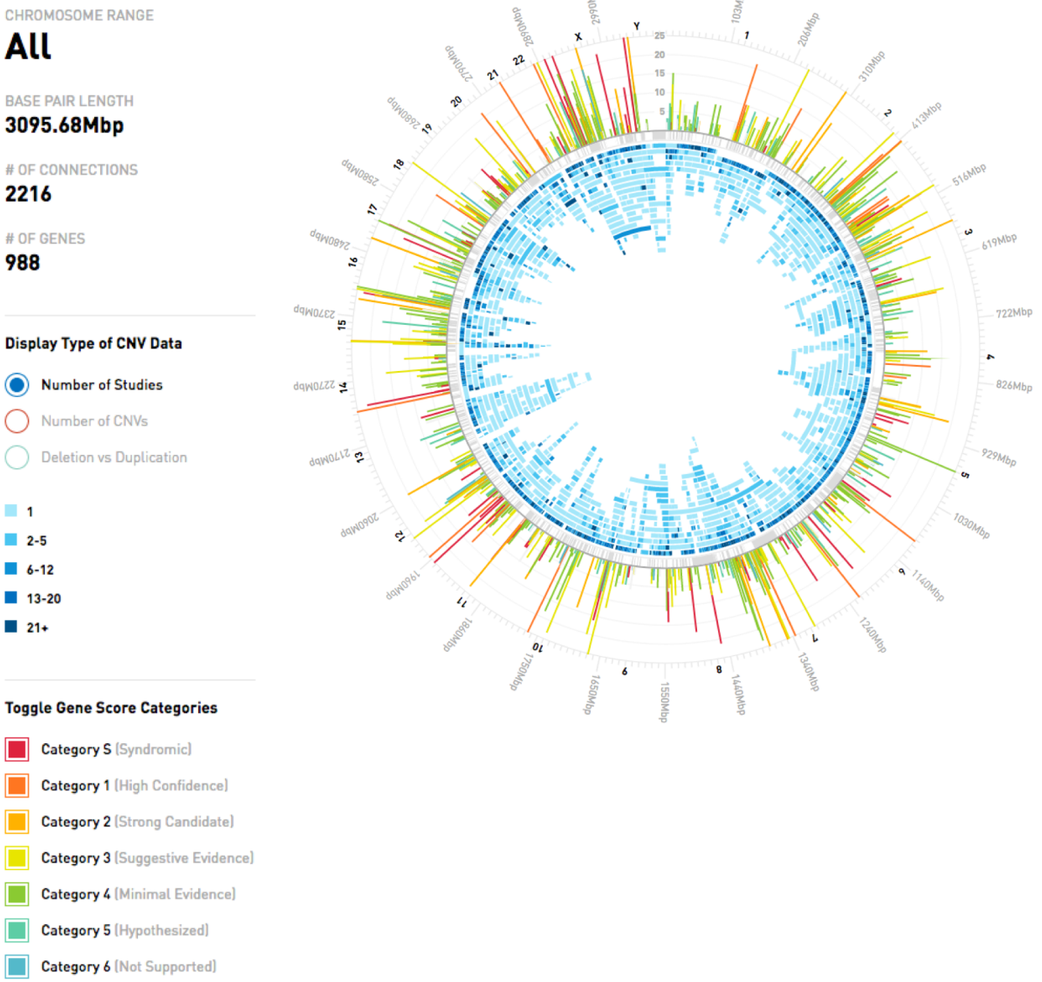
Service Hub
register + publish + find services
hub.iobio/services

App Hub
register + find apps
hub.iobio/apps



SFARI Gene





https://gene.sfari.org

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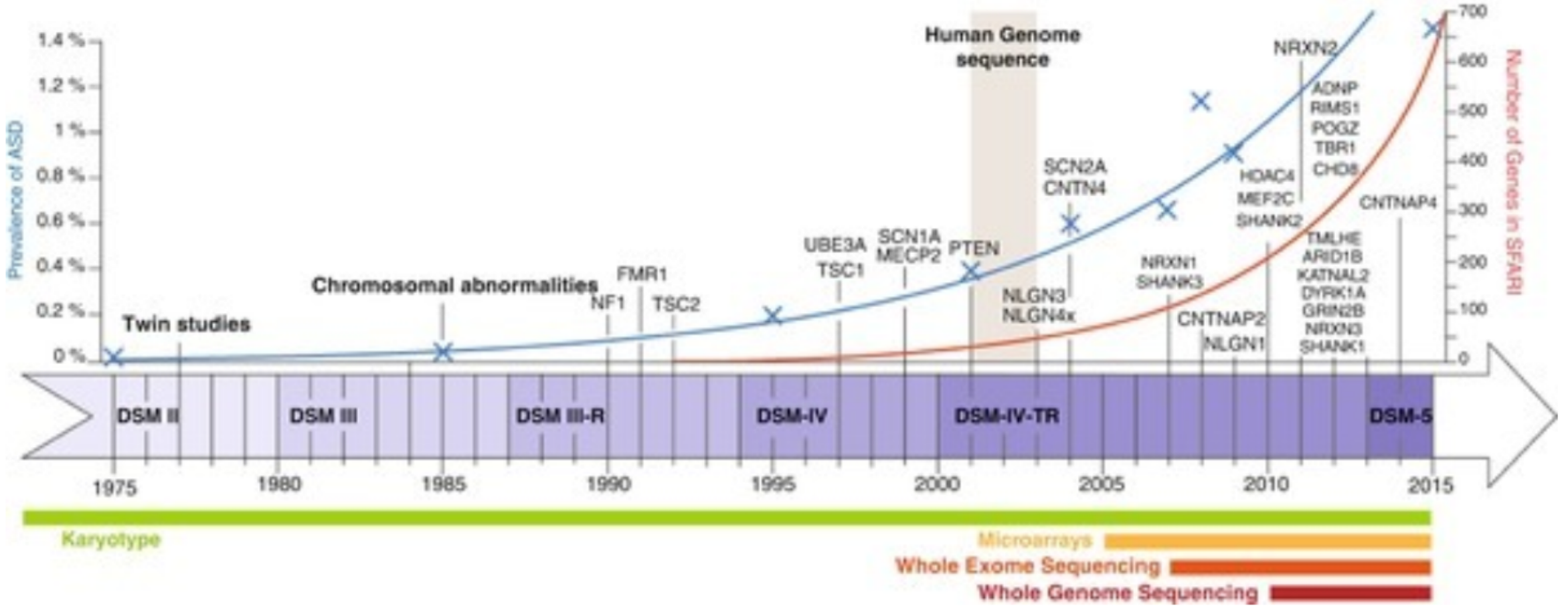
The History of Genetics of Autism through SFARI Gene



Huguet, Benabou, and Bourgeron, 2016

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Lessons Learned and Recommendations

- Metadata Collection and Visualization
- Data Sharing Policy: results of the funded studies should be deposited to responsible and accessible Data Archive

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