The Xia-Gibbs Syndrome Registry: A Valuable Resource for Researchers and the Community

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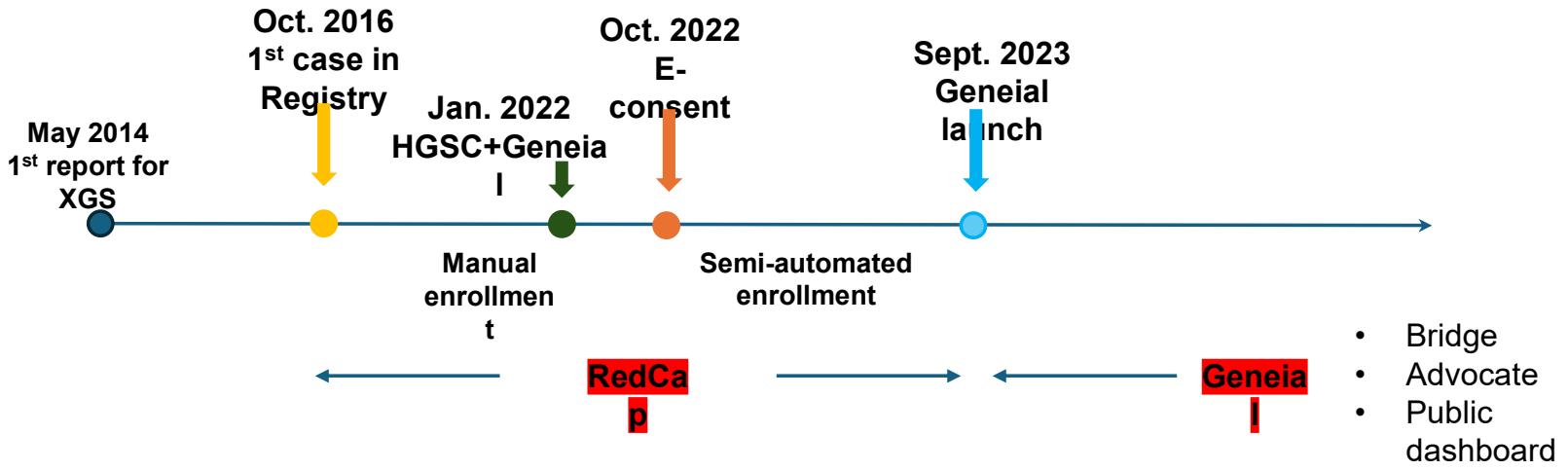
Xia-Gibbs Syndrome (XGS) and XGS Registry

Xia-Gibbs Syndrome (XGS): a phenotypically heterogeneous neurodevelopmental disorder (NDD) caused by mutations in the AT-Hook DNA-Binding Motif-Containing 1 (AHDC1) gene

XGS Registry: a collection of phenotype and genotype information about XGS individuals for the systematic research studies under HIPAA compliance

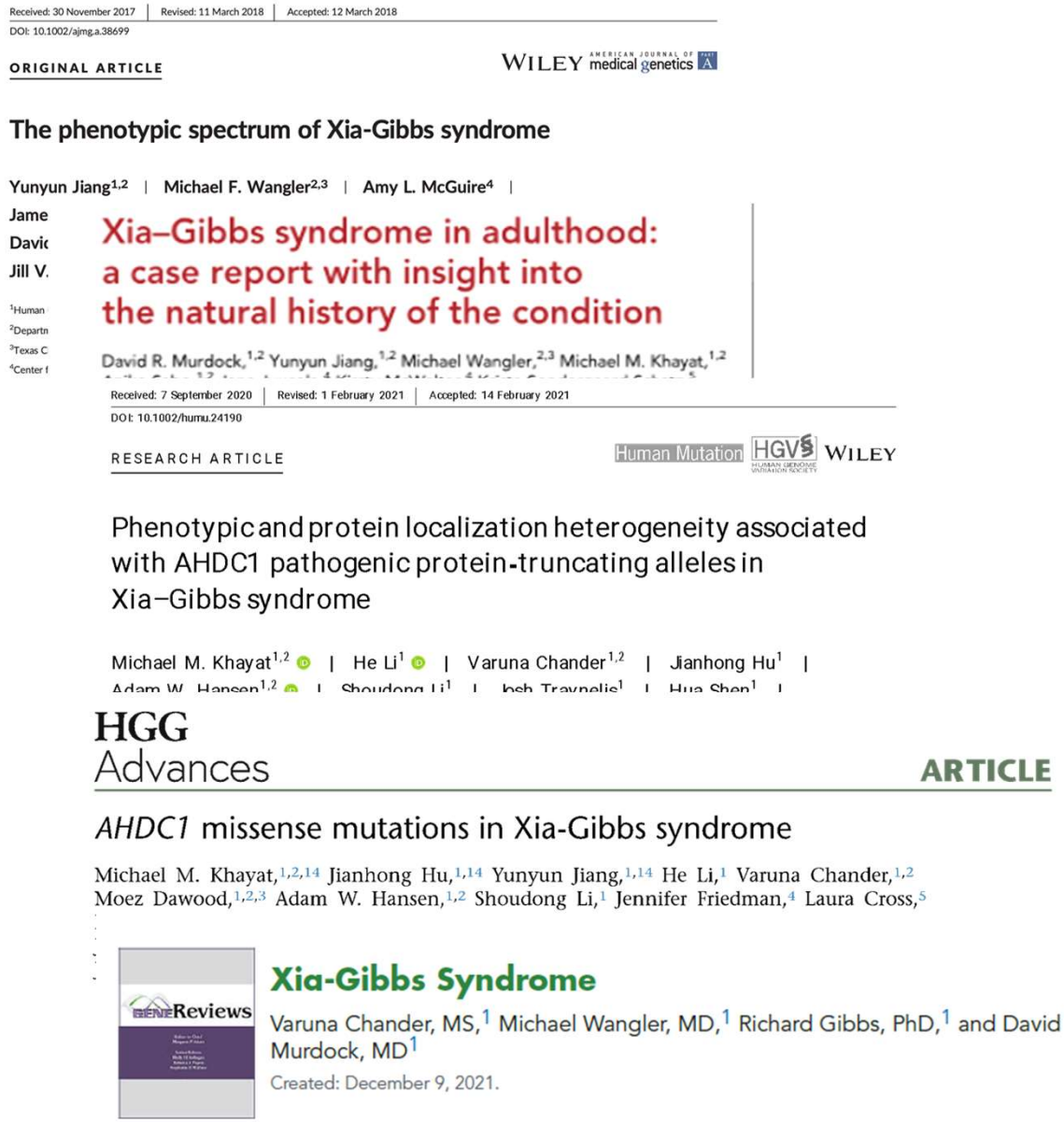
- General information
- Clinical information (medical history, phenotypes, medication et al)
- Genetic variant data

Timeline of the XGS Registry:



Why the XGS Registry is important?

- The largest centralized database for XGS individuals
- Recruitment of XGS families to build the community
- A foundation for XGS research
- Enabling collaboration among researchers, health providers, and XGS families
- The Registry may provide phenotypic information to the healthcare community



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ORIGINAL ARTICLE

WILEY AMERICAN JOURNAL OF medical genetics A

The phenotypic spectrum of Xia-Gibbs syndrome

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Xia–Gibbs syndrome in adulthood: a case report with insight into the natural history of the condition

David R. Murdock,[1,2] Yunyun Jiang,[1,2] Michael Wangler,[2,3] Michael M. Khayat,[1,2]

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RESEARCH ARTICLE

Human Mutation HGVS HUMAN GENOME VARIATION SOCIETY WILEY

Phenotypic and protein localization heterogeneity associated with AHDC1 pathogenic protein-truncating alleles in Xia–Gibbs syndrome

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Adam W. Hansen[1,2] | Shoudong Li[1] | Josh Travnelis[1] | Hua Shen[1] |

HGG Advances ARTICLE

AHDC1 missense mutations in Xia-Gibbs syndrome

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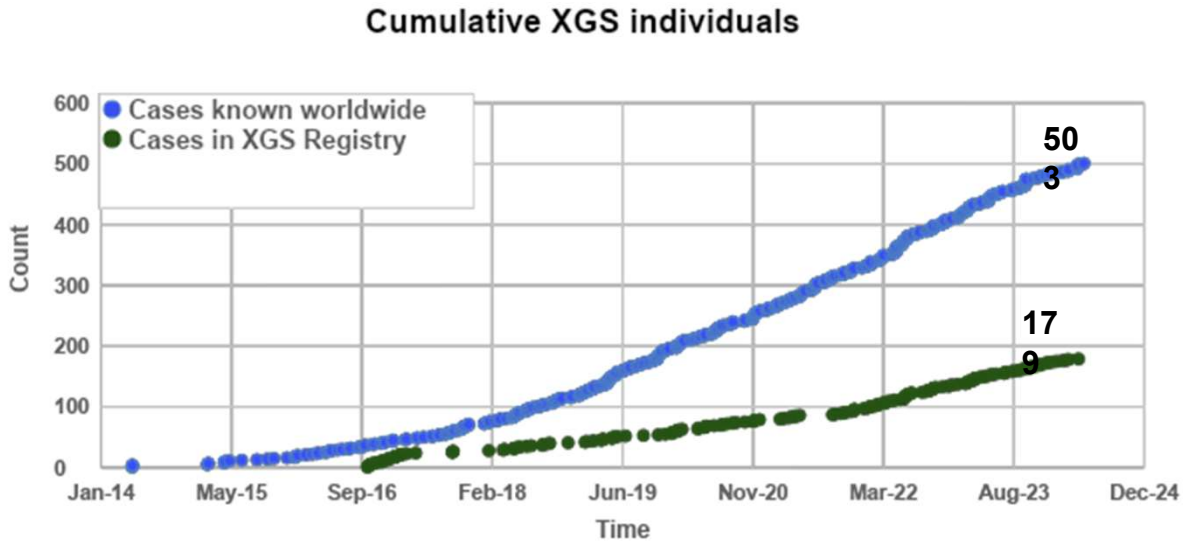
Moez Dawood,[1,2,3] Adam W. Hansen,[1,2] Shoudong Li,[1] Jennifer Friedman,[4] Laura Cross,[5]

Xia-Gibbs Syndrome

Varuna Chander, MS,[1] Michael Wangler, MD,[1] Richard Gibbs, PhD,[1] and David Murdock, MD[1]

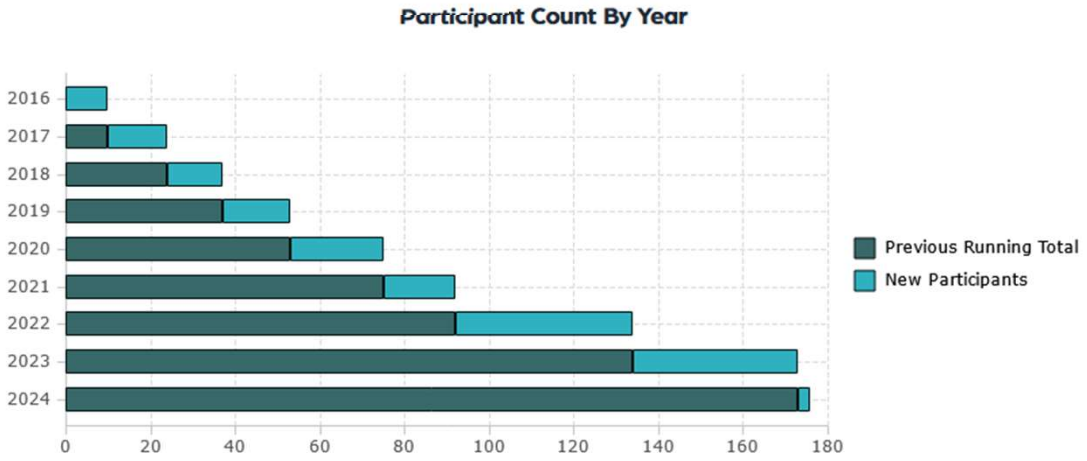
Created: December 9, 2021.

Enrollment of XGS Individuals in the XGS Registry

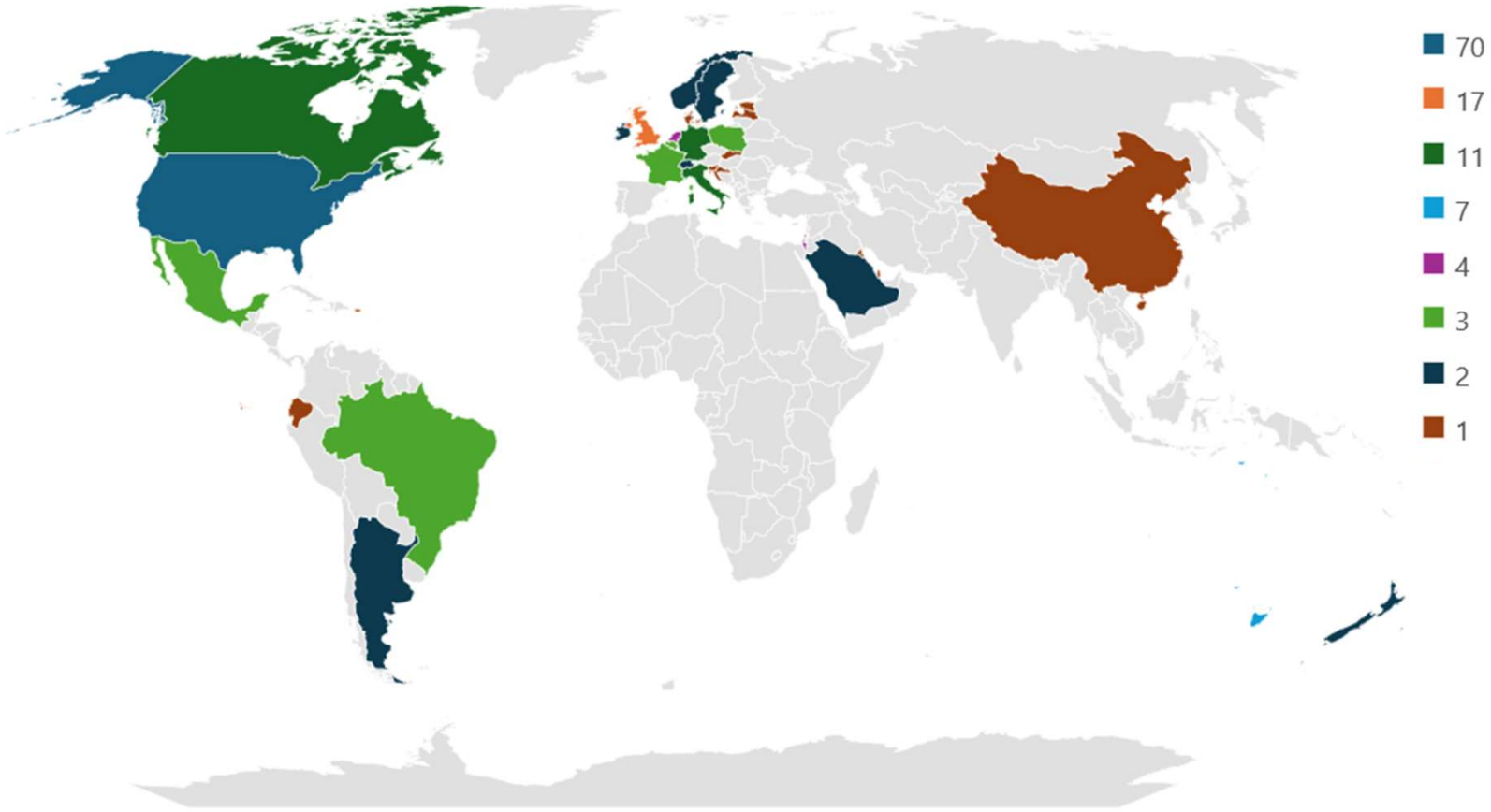


Sources to know the XGS cases:

- **XGS Society**
- Social media
- Clinician direct contact
- Family direct contact
- Publication



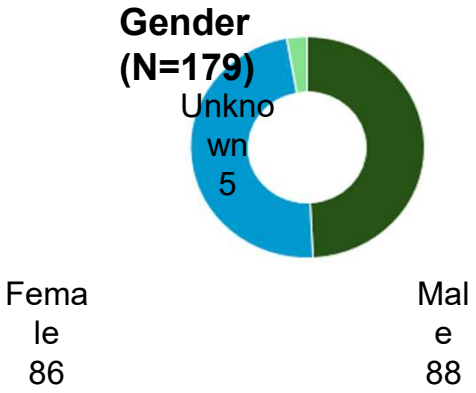
XGS Individuals Distribution Worldwide (33 Countries)

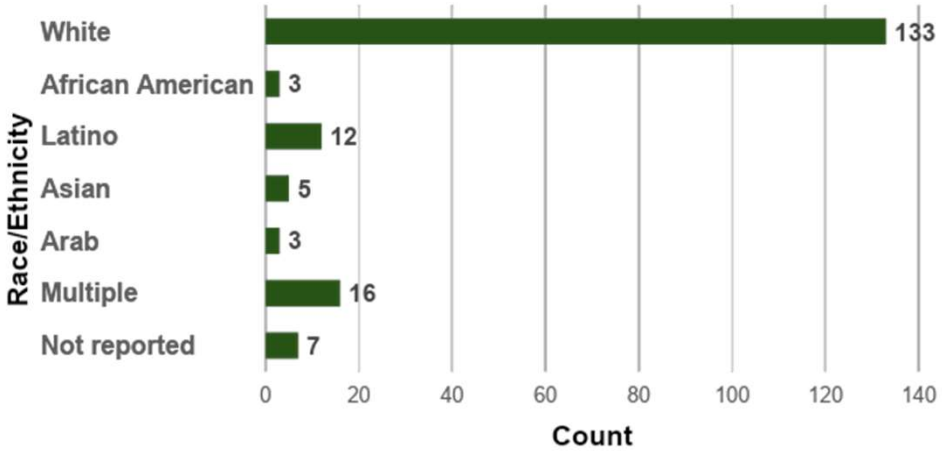


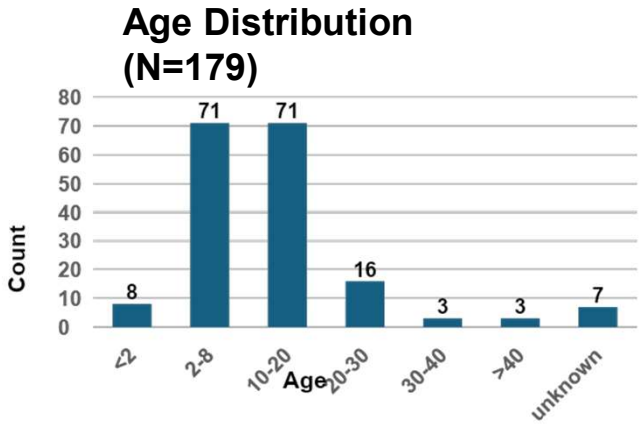
Total 179 cases

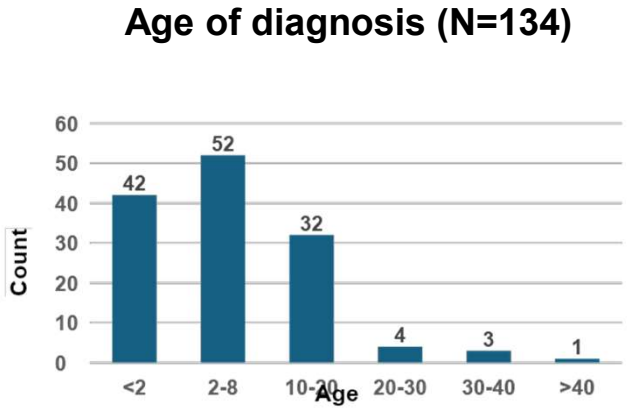
Case #	Country
70	United States
18	United Kingdom
11	Canada, Germany, Italy
7	Australia
4	Netherlands, Israel
3	Belgium, France, Poland, Brazil, Mexico
2	Norway, Sweden, Saudi Arabia, Argentina, New Zealand, Switzerland
1	Denmark, Qatar, Estonia, Singapore, Puerto Rico, Slovakia, China, Kuwait, Swizerland, Latvia, Croatia, Slovenia, Ecuador

Demographic Data from Registry

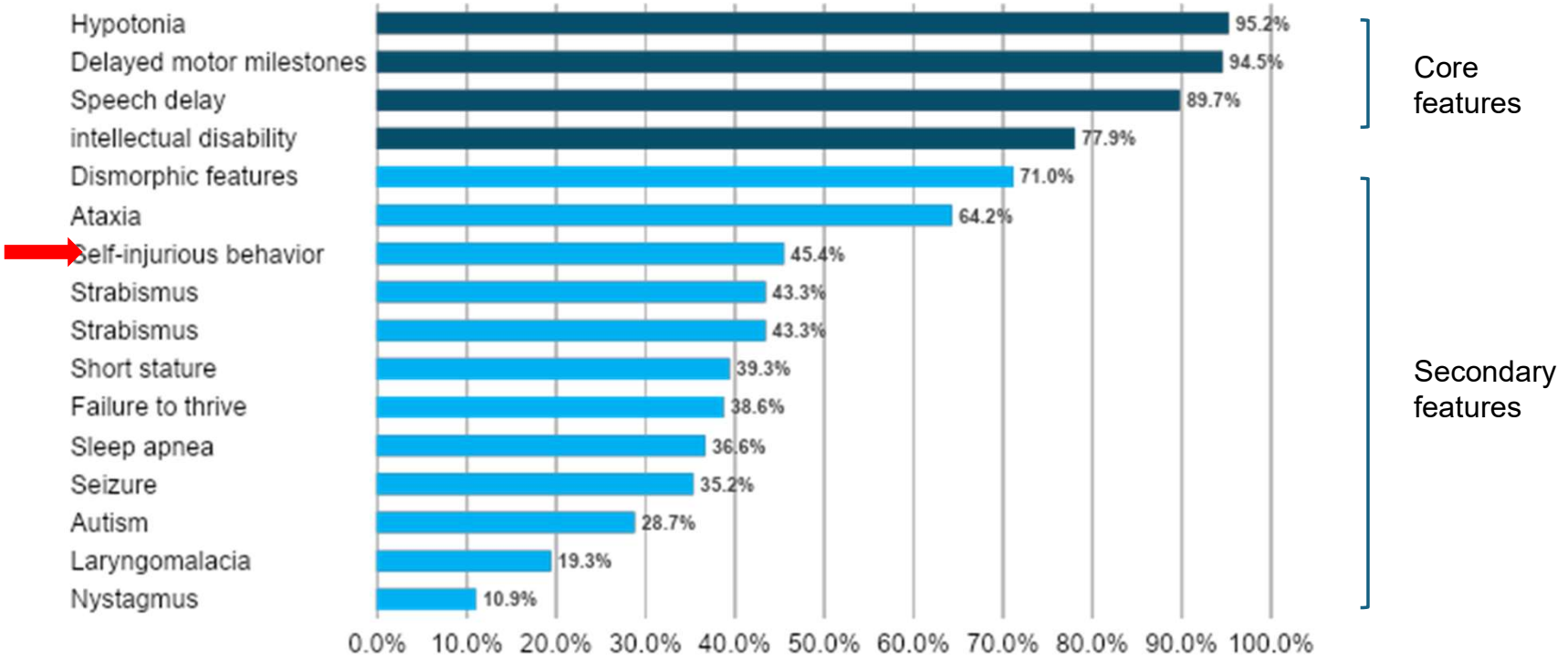








XGS Individual Phenotype Analysis



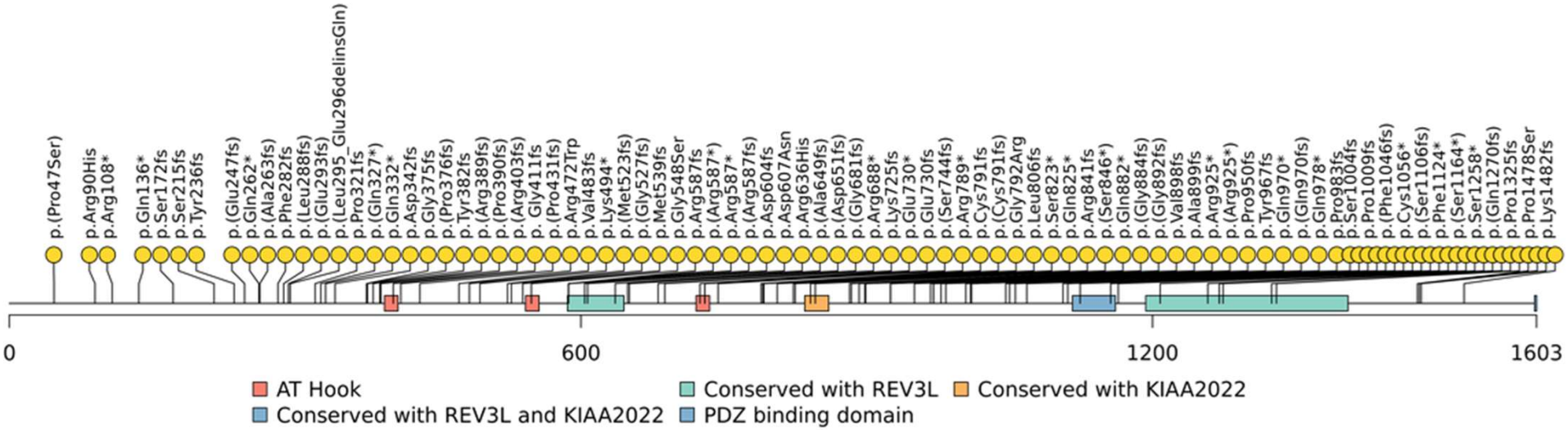
Headbanging and Self-Injury Behavior Survey

- Launched in Sept. 2023 at Geneial platform
- To survey if headbang occurred, onset, frequency, medication, time occurrence et al
- 15 participated in the survey. 7 individuals are affected

onset age	0.3 - 5 yo	
Frequency	Daily	57.1%
	Very often	14.3%
	Occasionally	28.6%
Medication	No	100%
Time occurrence	Awake	85.7%
	Both awake and asleep	14.3%

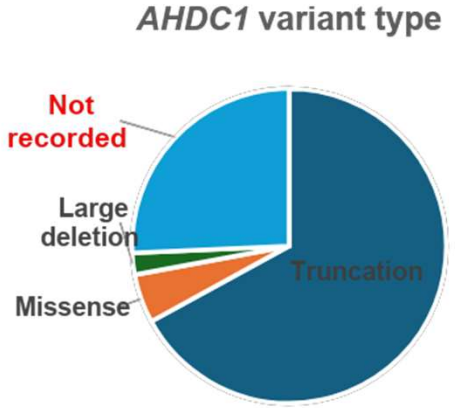
Improvement method:
Redirection; Try to identify and resolve the cause of distress; Offering food, juice; Attempting to comfort; Interact with patient, call to do a task, call name seeking for attention for interaction or play

AHDC1 Protein Map and AHDC1 Variants from XGS Individuals



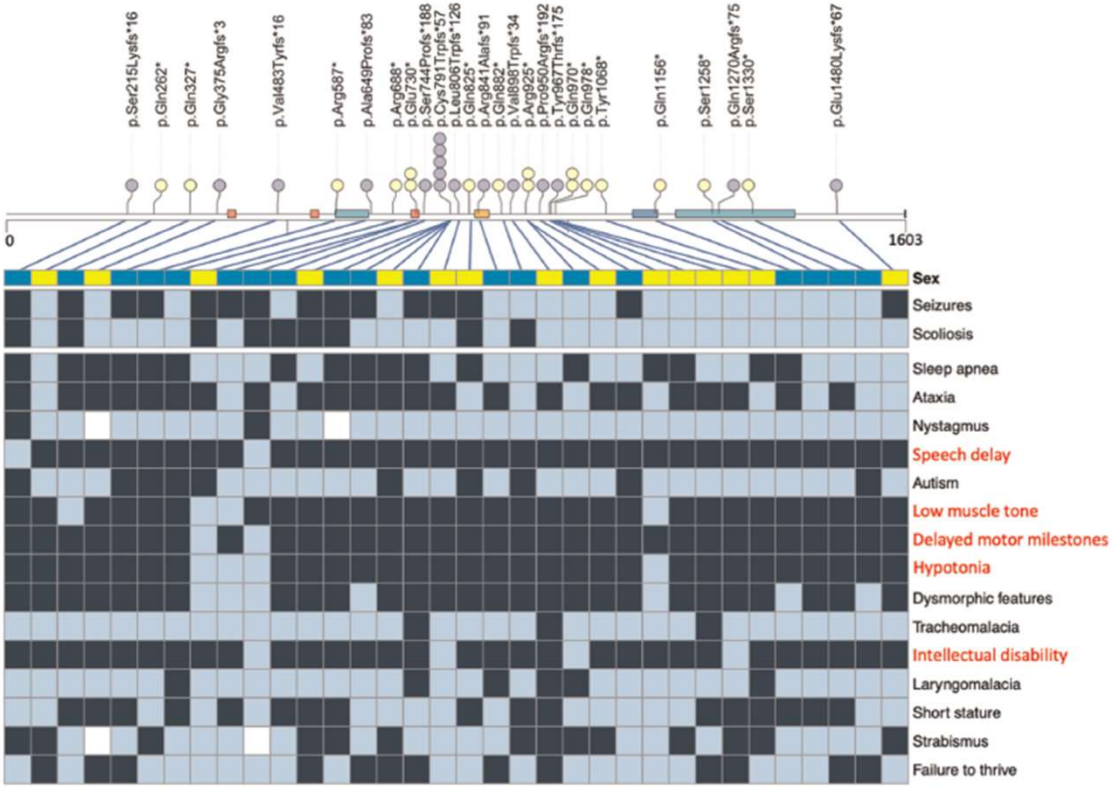
Types of genetic mutations identified in XGS individuals:

- Truncation (insertion, deletion, substitution)
- Missense (substitution)
- Large deletions

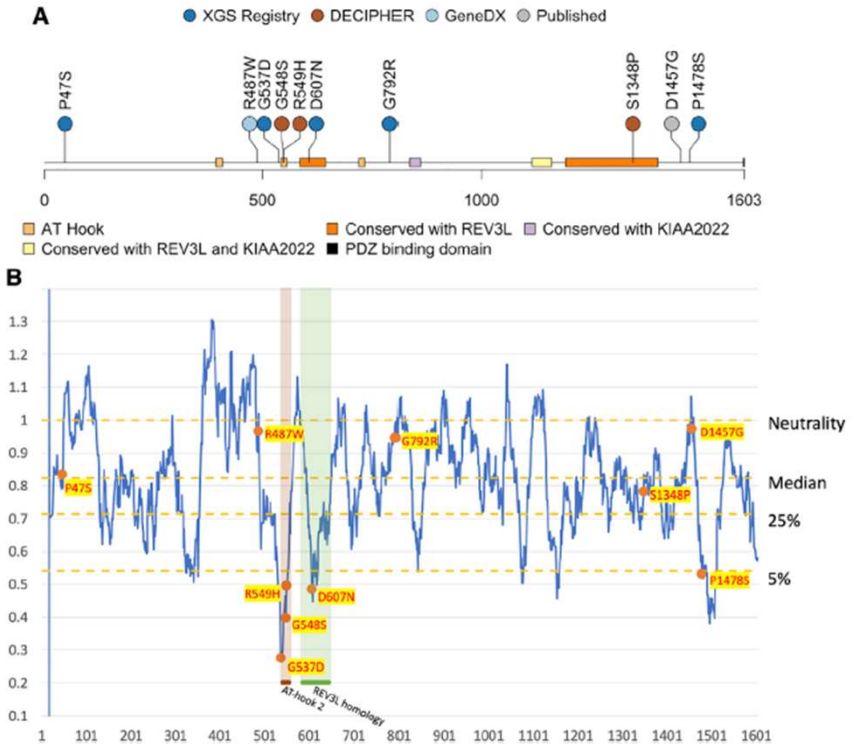


Genetic Variation is Important to Help to Understand the Function of AHDC1 Protein

- Analysis of the localization of truncation mutations vs patient phenotypes



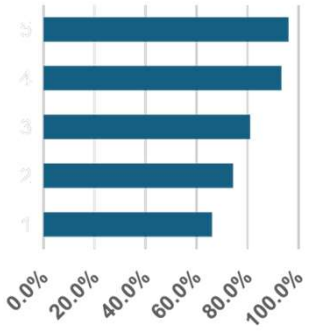
- Analysis of the localization of missense mutations vs mutation tolerance



Michael Khayat et. al, Human Mutation, 2021
Michael Khayat et. al, HGG Advances, 2021

Registry Module Completion Status

Order	Enrollment Procedure	Number of Completion	Completion Rate
1	Account creation	179	
2	Demographics	172	96.1%
3	Consent	167	93.3%
4	Clinical Surveys	145	81.0%
5	Genetic variant data	133	74.3%
6	MCHART	113	66.1%
Headbanging Survey		15	8.4%



Complete dataset in the registry is essential to ensure the reliability and validity of the data collected to avoid bias!

How We may Improve the Quality of the Registry Data

Good-quality registries help to support research programs and healthcare community

XGS families:

- Participate in the Registry
- Provide complete and accurate data

Researchers:

- Standardizing data collection
- A system to update the data for patient over the time for longitudinal study
- Separation of validated and non-validated data
- From registry data to wet lab research to study the function of AHDC1 protein

Future goals

- Access of the de-identified data to outside researchers
- Transfer the data ownership to XGS Society
- Development of gene-targeted approaches for treatment

Acknowledgements

- XGS individuals and families who participated in the Registry
- XGS Society Funding

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