

## Introduction

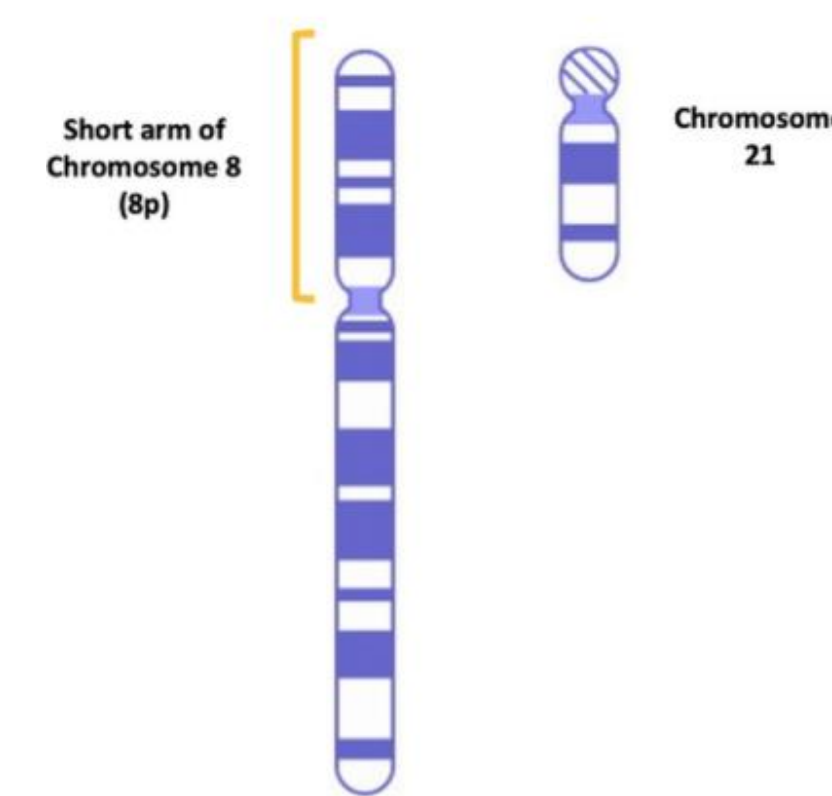
Chromosomal Disorders are a disproportionately under-researched area of genetics, with around 16 million people worldwide suffering from some chromosomal disorders. Each of these disorders has widely different causes and symptoms. Chromosome 8p disorders are a rare subset of chromosomal disorders affecting ~1 in 10,000 children.

Chromosome 8p disorders specifically involves mutations on the p arm of chromosome 8.

- Three of the most common mutations are deletions, duplications, or inverted duplication deletion (Inv Dup Del) ("8p Genetics", 2023)
- Each of the mutation is unique across individuals, leading to each disorder presenting differently phenotypically. Often these mutations lead to intellectual and developmental disorders.

Common Comorbidities with chromosome 8p disorder

- Autism, epilepsy, sleep disorder, congenital heart disease, intellectual disabilities, sensory processing disorders, digestive issues, and hypotonia/hypertonia (Vibert et al., 2022).



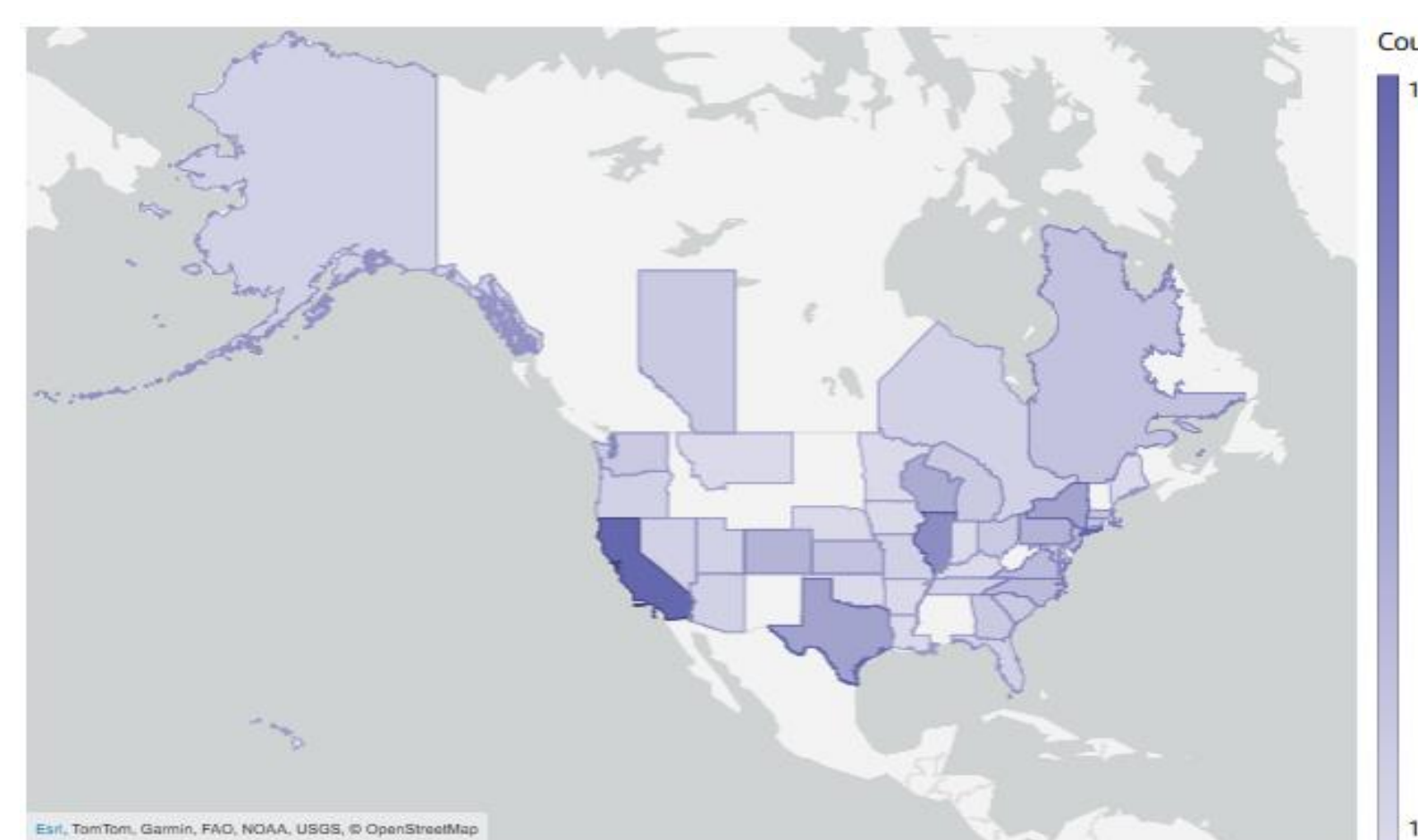
**Figure 1.** Visualization of chromosome 8 compared to chromosome 21.

### Current Project

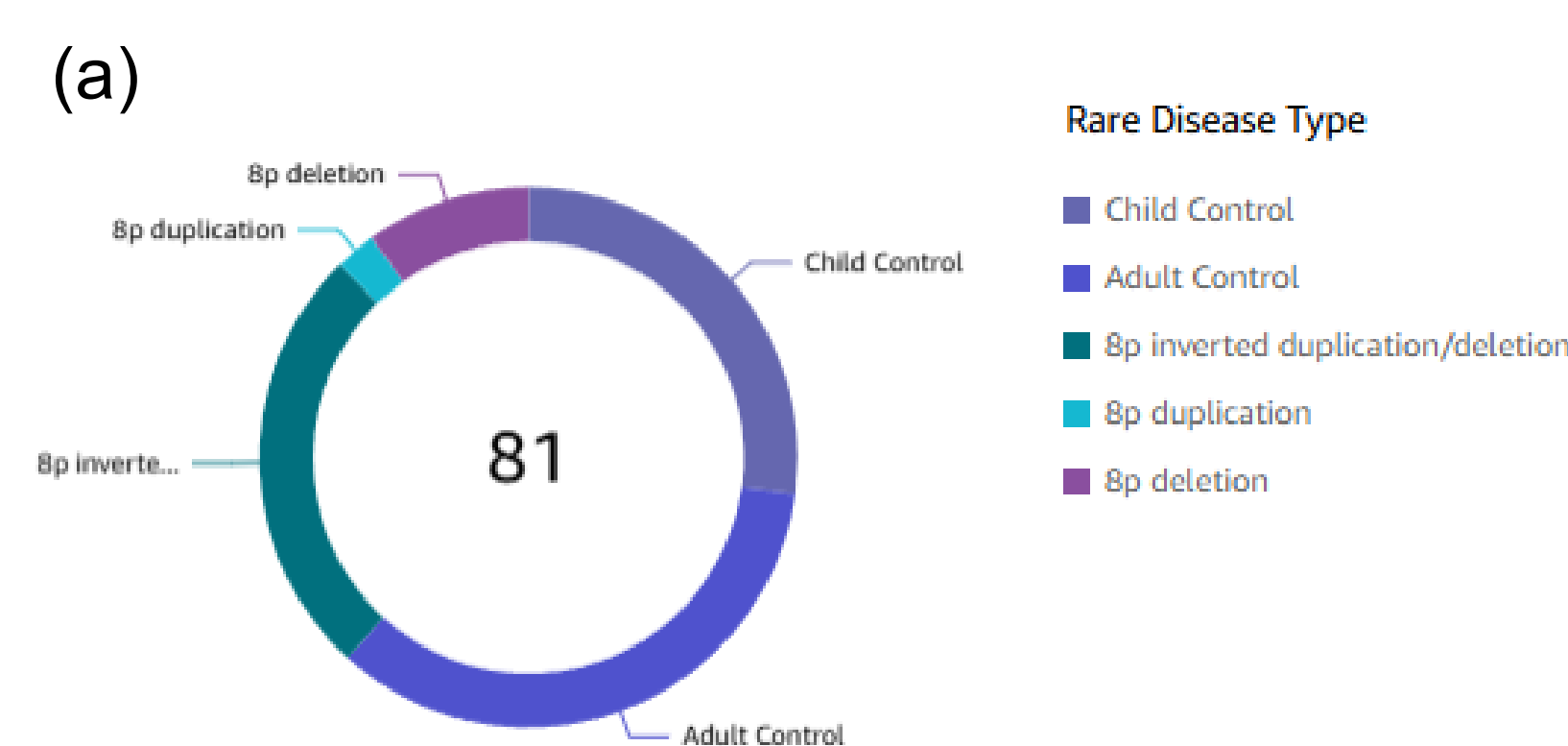
In collaboration with the Project 8p Foundation, a non-profit organization focused on understanding these relationships, we developed interactive dashboards in Amazon QuickSight to integrate and visualize large-scale genotypic and clinical data. These tools enable doctors, patients, and researchers to explore complex relationships across multiple datasets, facilitating deeper interpretation of the disorder. By presenting data in an accessible and interactive format, these dashboards can highlight patterns and potential targets for future research and clinical intervention. Ultimately, this approach aims to improve understanding of 8p rearrangements and guide more effective treatment strategies for affected individuals.

## Participants

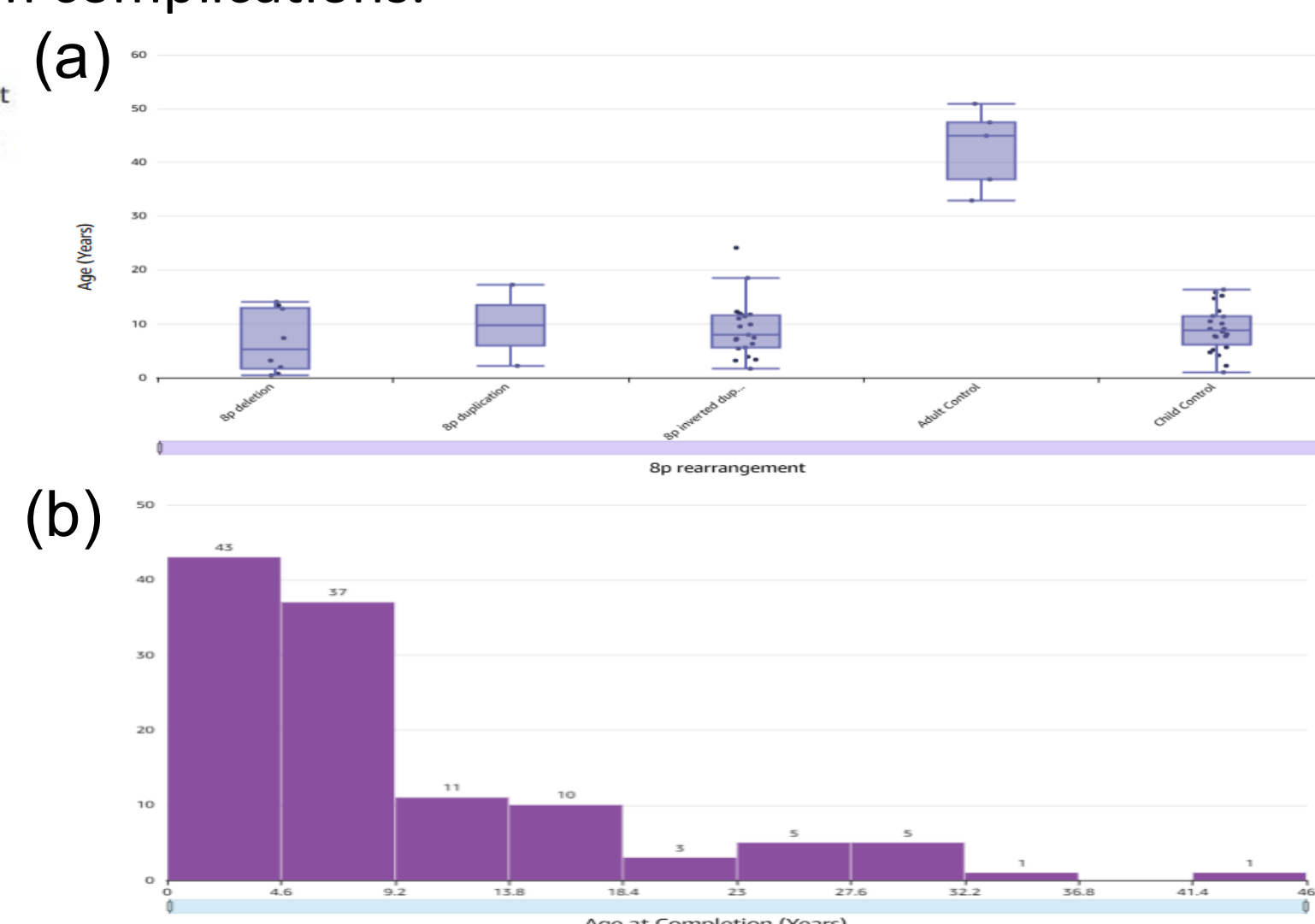
All participants for each analysis were sourced from the Chromosome 8p Natural History Study. The Mitochondrial Dashboard integrates mitochondrial measures with developmental milestones (e.g., walking, first words). The Genotype-Phenotype Dashboard investigates which genes are present or modified in individuals with a variety of organ-system complications.



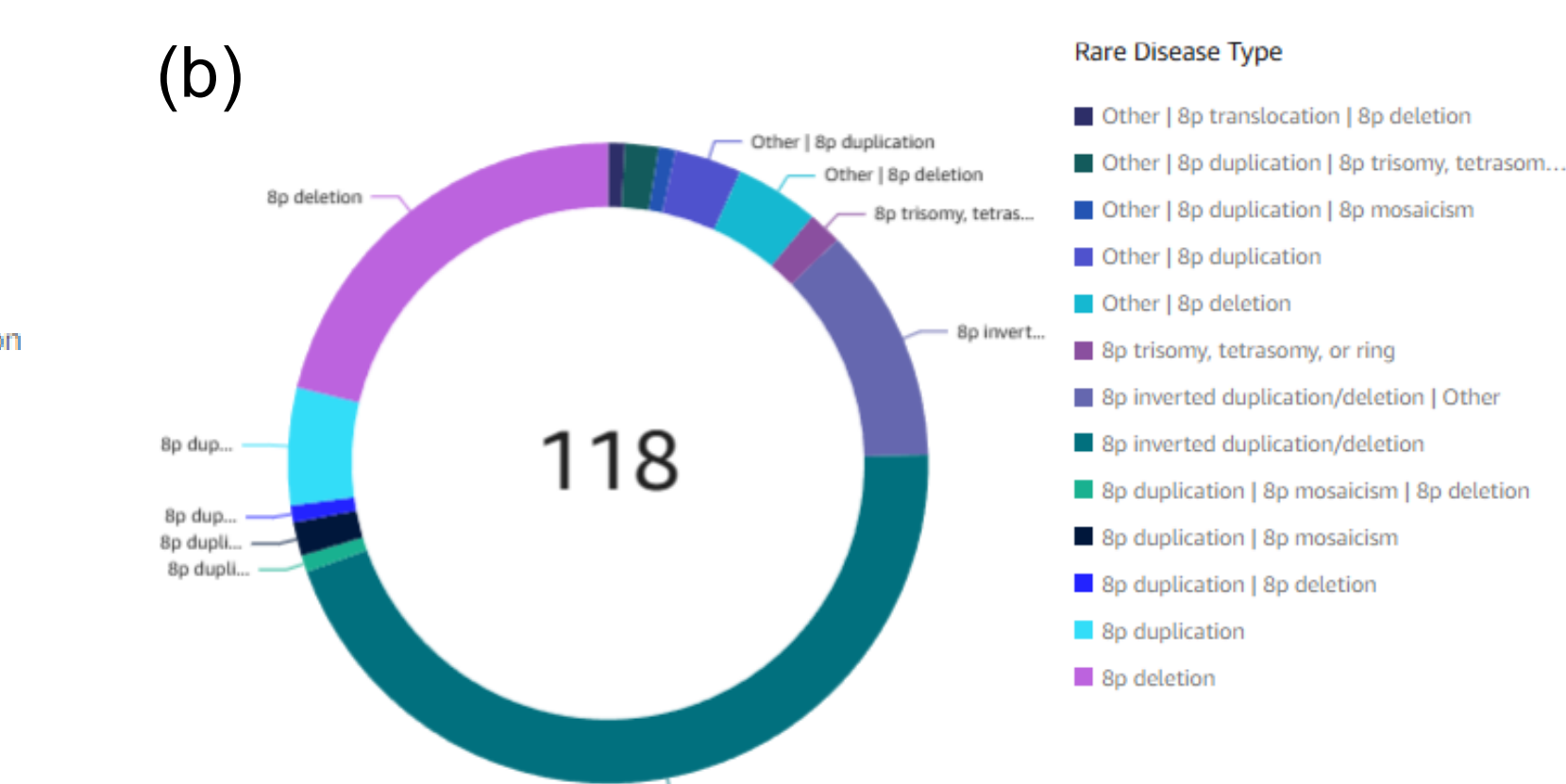
**Figure 2.** Count of 8p families by states and providences



**Figure 4.** Breakdown of rare disease type and controls in the (a) mitochondrial analysis and (b) genotype-phenotype analysis.



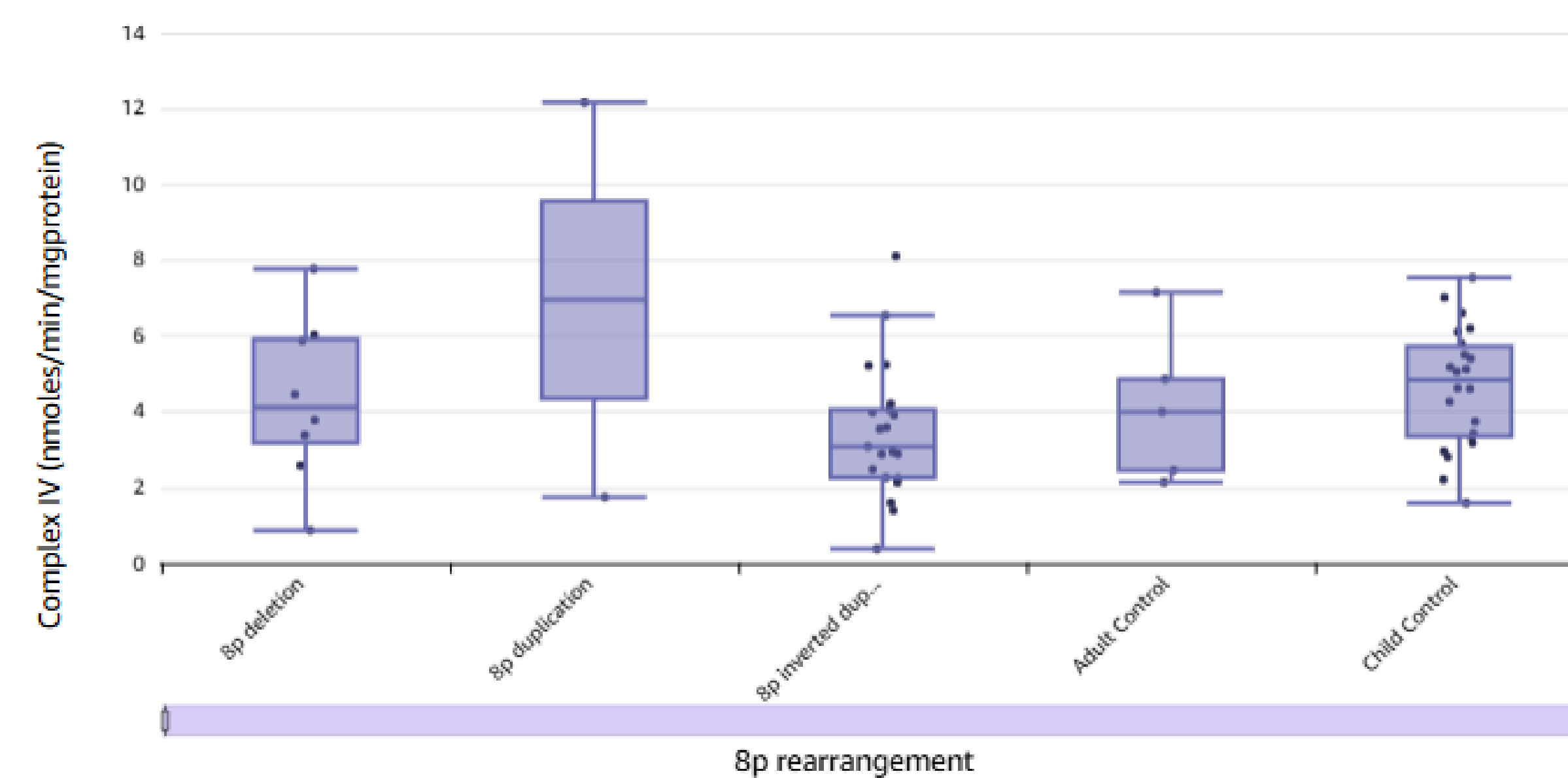
**Figure 3.** (a) age ranges for 8p Heroes and controls (mito data) (b) ages of 8p Heroes when survey was completed (geno-pheno data).



## Mitochondrial Dashboard

### Mitochondrial Analysis

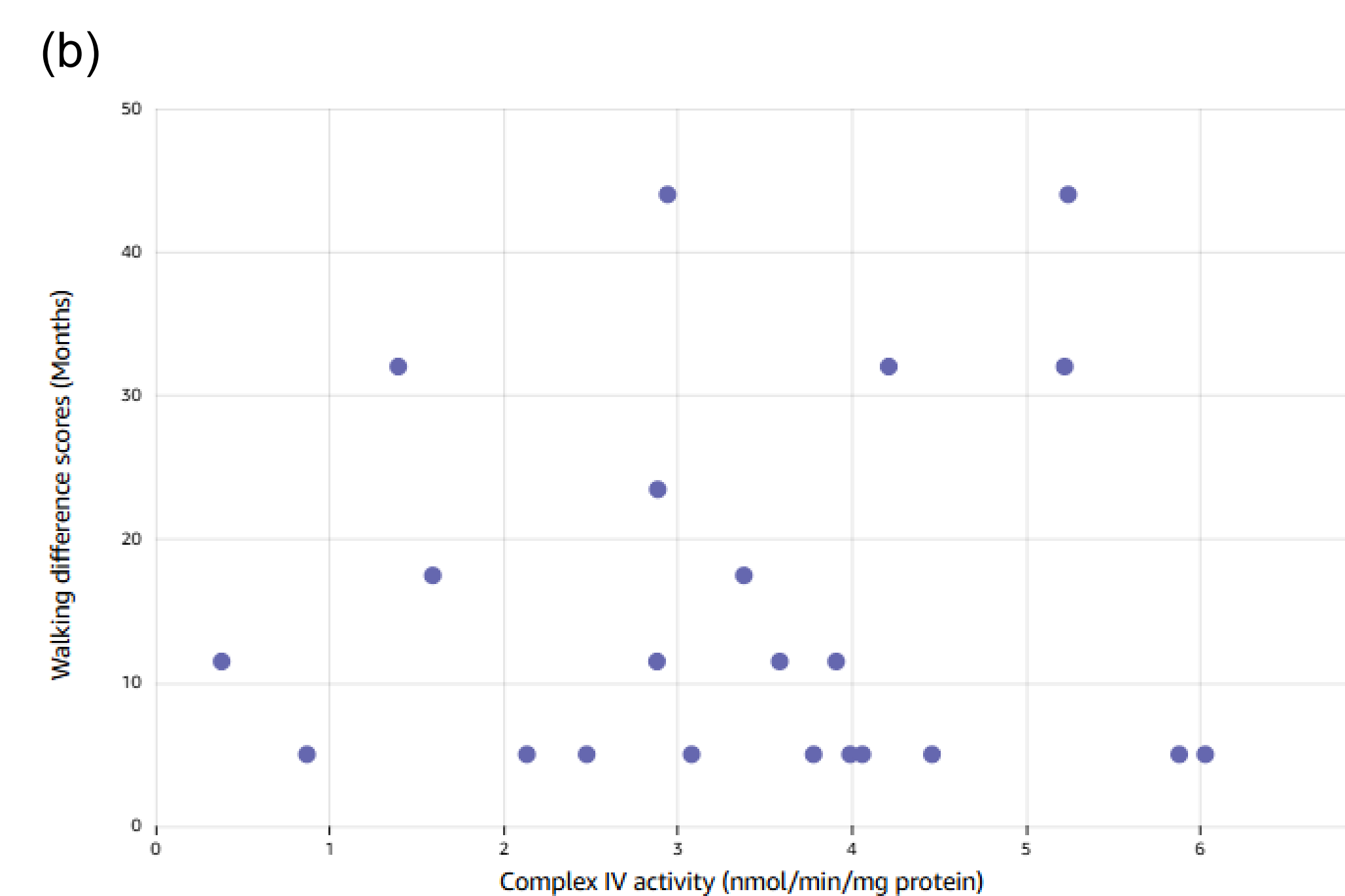
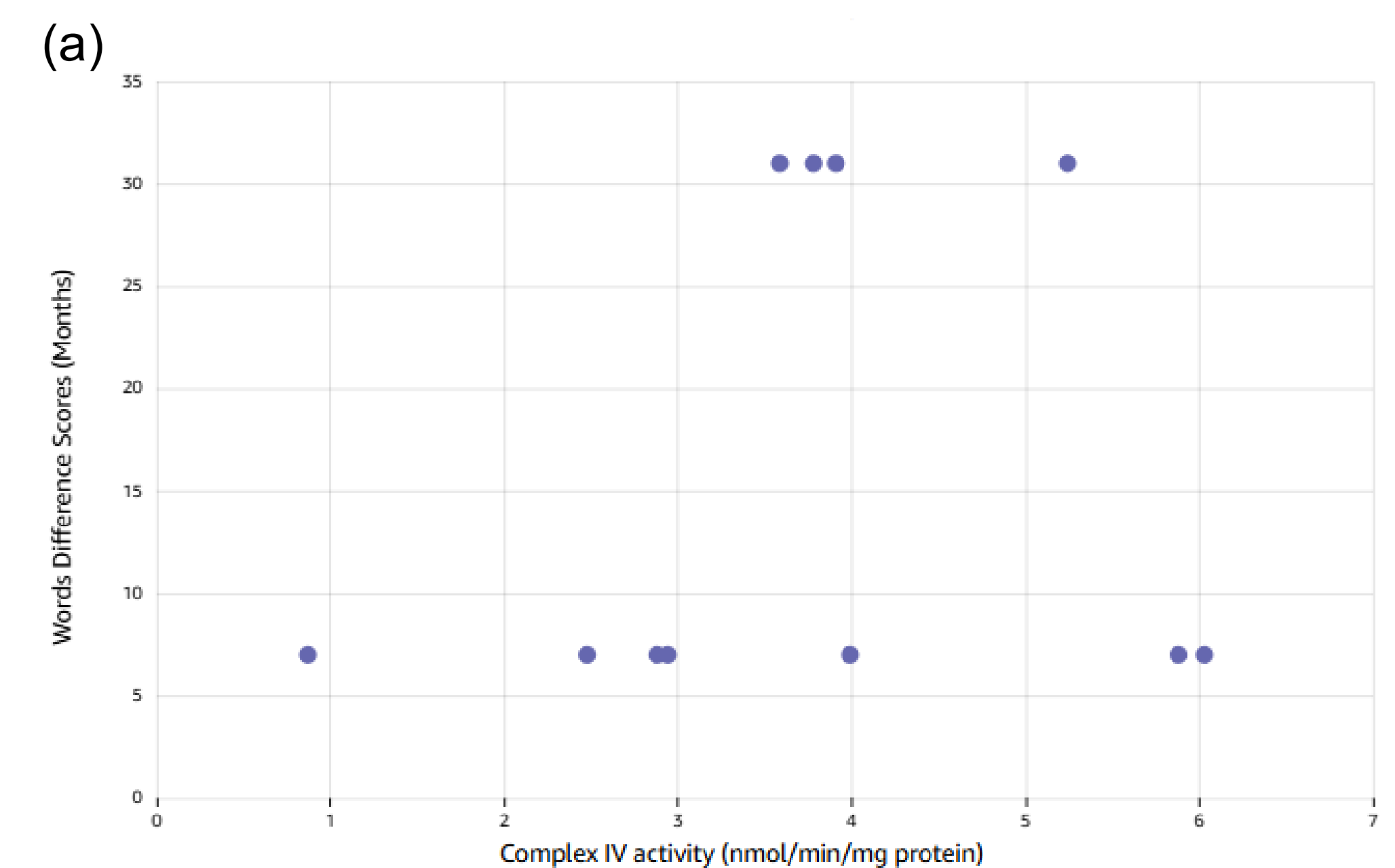
Through the Natural History Study, many different mitochondrial biomarkers were collected from 8p Heroes as well as family members (to serve as controls). By examining mitochondrial biomarkers, we can assess mitochondrial health and therefore gain insight into overall health.



**Figure 5.** Visualization of complex IV, the final enzyme in ETC, across the most common 8p mutation, child controls, and adult controls.

### Development Milestones

Using a separate survey, we collected data on when 8p heroes reached key developmental milestones, including speaking and walking. Difference scores were calculated relative to national averages for typically developing children. By comparing these milestone deviations with mitochondrial health, we can better understand how the condition impacts overall quality of life.

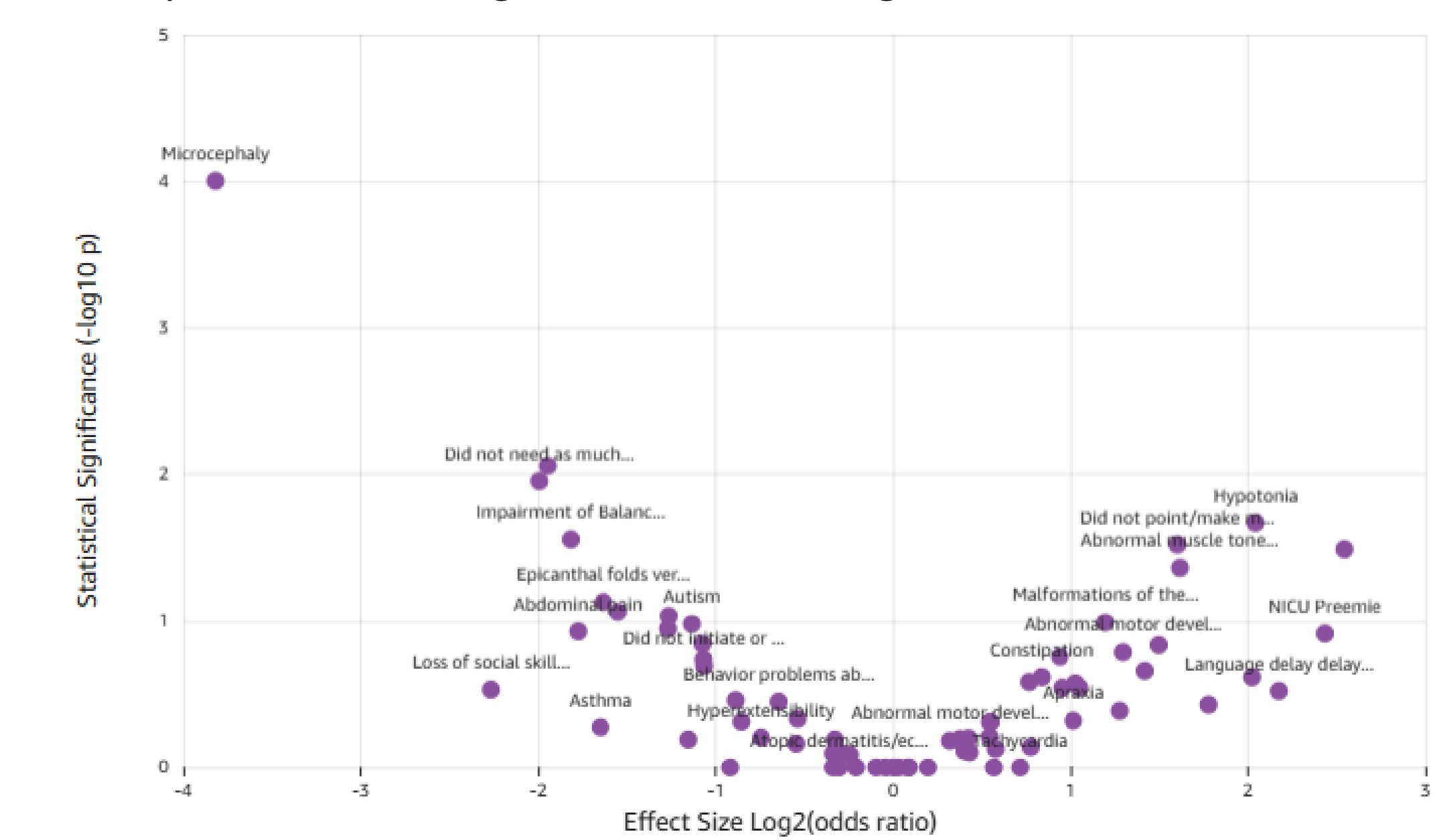


**Figure 6.** Scatterplots showing relationships between complex IV activity with (a) age of first words difference score (b) age of walking difference scores.

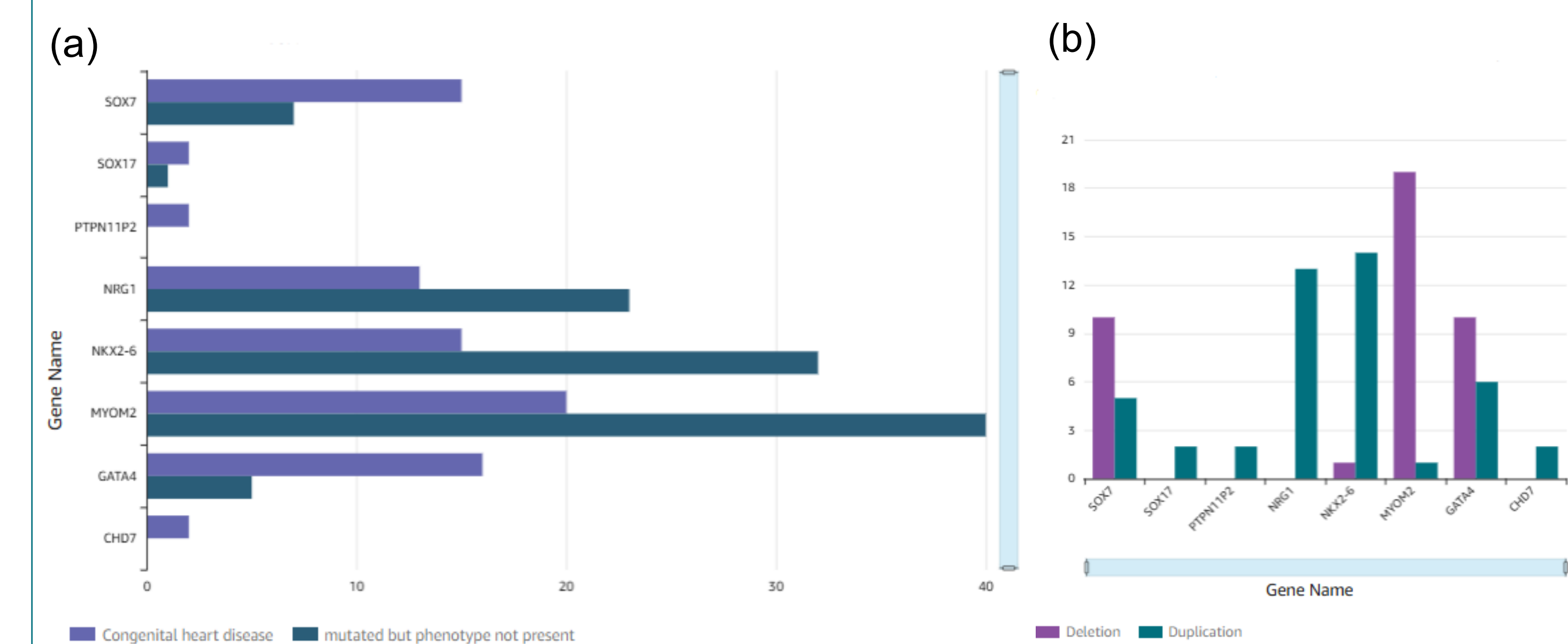
## Genotype-Phenotype Dashboard

### Genotype-Phenotype Analysis

Another component of the Natural History Study collected genotype data from 8p heroes, identifying which genes were deleted, duplicated, or involved in Inv Dup Del rearrangements. Because individuals often present with multi-system developmental differences, a complementary survey captured organ system outcomes. Integrating these genetic and clinical data is critical for identifying meaningful genotype-phenotype relationships and advancing our understanding of the condition.



**Figure 7.** Volcano plot of symptom prevalence in 8p Heroes with Inv Dup Del.



**Figure 8.** (a) Visualization of cases of congenital heart disease sorted by gene name. (b) The 8p Heroes that have congenital heart disease if the gene region was deleted or duplicated.

## Conclusions

The Natural History Study provides a rich, multidimensional dataset capturing the complexity of chromosome 8p disorders. We are creating dashboards in order to offer a structured, accessible way to interpret those data. By making patterns more visible, these tools can guide future research priorities and inform more targeted, data-driven clinical interventions.

## Acknowledgements

This project was supported by Project 8p Foundation. The data provided by the 8p Heroes was necessary for this project and future research on chromosome 8p disorders. Without the generous donations of biosamples and valuable time given by the 8p families, this and similar projects would not have been possible. All of us who work through the Natural History Study and the Project 8p Foundation are deep grateful to all of the 8p Heroes, caregivers, and families in the Project 8p community for their contributions. The dataset built by the 8p Heroes helps us understand this complex disease. We support Project 8p Foundation's patient-centric commitment to fostering impactful research, connecting scientific and clinical communities, and improving the lives of individuals with 8p-related disorders.

Finally, this project would not have been possible with the help and support from our fellow lab members: Tiana Bassett, Hannah Bushey, Chloe Haldeman, Indira Jaikaran, Jesslyn Lopez, Makenna Snyder, and Megan Spiegelberg, who have provided feedback and research to help make this project possible.

### References

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4. Vibert, R., Mignot, C., Keren, B., Chantot-Bastarud, S., Portnoi, M.-F., Nougès, M.-C., Moutard, M.-L., Faudet, A., Whalen, S., Haye, D., Garel, C., Chatron, N., Rossi, M., Vincent-Delorme, C., Boute, O., Delobel, B., Andrieux, J., Devillard, F., Coutton, C., ... Heide, S. (2022). Neurodevelopmental phenotype in 36 new patients with 8p inverted duplication-deletion: Genotype-phenotype correlation for anomalies of the corpus callosum. *Clinical Genetics*, 101(3), 307-316. <https://doi.org/10.1111/cge.14096>