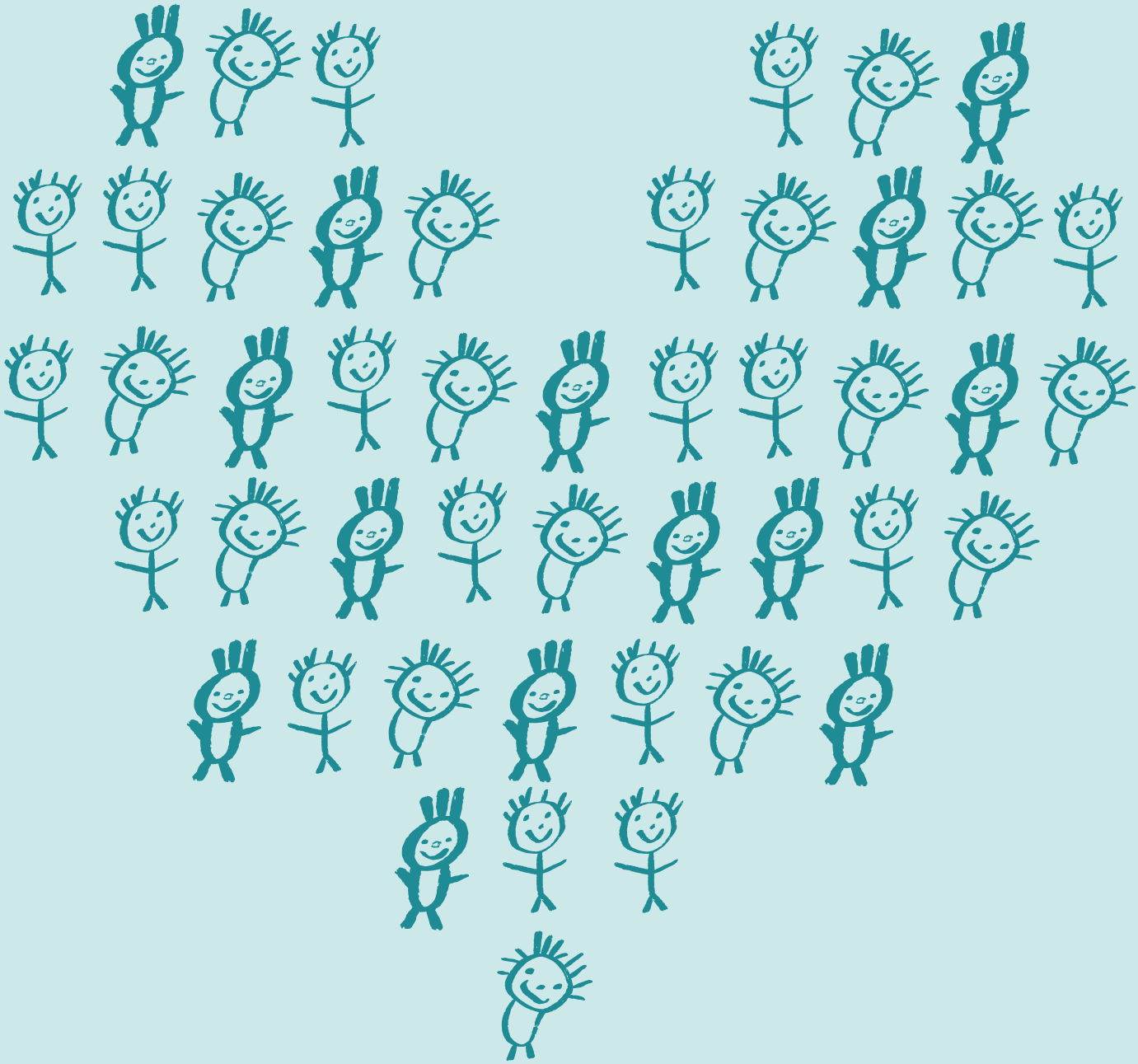
IMPACT REPORT 2023

AGO

In This Report

AGO



Message From The President

A Natural History Study is key to educating parents and medical providers, and developing rare disease treatments.

2023 marked our third year, during which we focused on expanding:

- Our collaboration with leading disease researchers to enhance our understanding of the condition (see pages 9 and 11),
- Our brand and team to all AGO genes (refer to pages 7, 9, and 12), and
- Our digital footprint (explore page 9).

The Natural History Study, initiated by Prof. Lessel, represents a significant advancement for Argonaute Syndromes. Parents often have limited knowledge about what to expect as their child ages and clinical care practices. Our patient group has successfully recruited a substantial number of participants, with initial results to be shared in 2024.

We extend our heartfelt gratitude to all supporters and donors for their solidarity and trust. With this generous support, we are able to undertake essential projects that unite families affected by Argonaute syndromes, expedite therapeutic development, and provide education.

With care, Nora

Co-founder and President of AGO Alliance

Who We Are

Our mission

Improve the lives of children and families impacted by Argonaute syndromes (AGO1 & AGO2 genes) by

1. finding and funding paths to treatment,
2. connecting families,
3. increasing awareness.

About us

AGO Alliance is a family-driven patient advocacy organization, established by Nora and Christoph in 2021 following their daughter's diagnosis. Its aim is to support individuals with Argonaute syndrome in achieving their potential.

Based in Switzerland, AGO Alliance collaborates with Transnational Giving Europe and the Rare Village Foundation.

Team

Nora
President

Christoph
Vice-President

Silvio
Treasurer

Aldona
Science Officer &
Parent Lead Poland

Naomi
Parent Lead USA

Antje
Parent Lead Germany

Ana
Parent Lead Spain

Ivan
Web & Graphic Support

Stefan
Design & Website

Aga
Communication

We have grown!

Advisory board

Prof. D. Lessel
University Hospital
Salzburg

Prof. H.J. Kreienkamp
University Medical Center
Hamburg-Eppendorf

Prof. G. Meister
University of
Regensburg

Prof. A. Piton
University Hospital
Strasbourg

Highlights 2023

Accelerate development of treatments

Connect families

Raise awareness & educate

Re-branded as AGO Alliance to cover all Argonaute genes.

- Aldona joined team as science officer and parent lead Poland.
- Ana founded sister organisation in Spain. “Lo hAGO posible contigo” - we make it possible with you

Re-launched website and added 6 languages: www.argnoautes.ngo

Facebook support group grew to >100 members

42 patient families were recruited to participate in the Natural HIstory Study initiated by Prof. Lessel.

Prof. Piton published a research paper on the effects of AGO1 mutations in worms with Profs. Ambros & Zinovyeva

Featured in the news:

- Nora participated in a panel in honour of Rare Disease Day.
- EJP RD highlighted our 2022 conference in an article

Families received Christmas gifts

Created a communication strategy

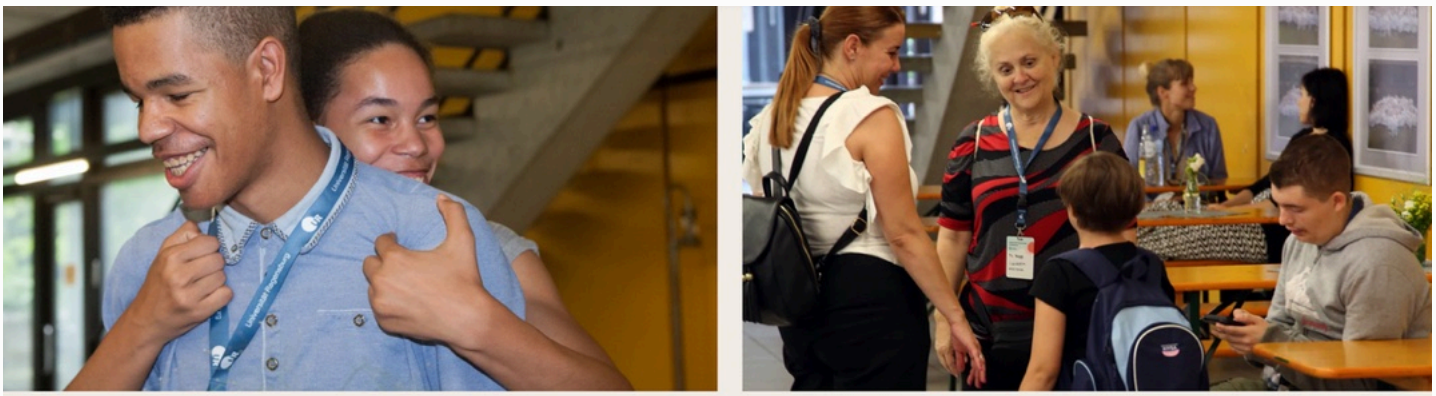
www.argonautes.ngo
3'460 users, 6'700 total
11'600 views, 26'000 total

6 newsletters

109 followers

Launched

EJP RD, which funded our 1st Argonaute Syndromes Conference in 2022, featured our event in an article about the Networking Support Scheme



EJP RD's Networking Support Scheme

> The EJP RD choose the Argonaute Syndromes conference for a journalistic article as we appreciated that a young patient organisation for a very unknown rare disease organised the first conference on AGO1- and AGO2-related syndromes in 2022. Furthermore, the EJP RD was excited about the excellent information on the outcomes of the conference on the website of AGO Alliance

Sonja van Weely
Networking Support Scheme Secretariat

Read full article

AGO

AGO1/2 Natural History Study led by Prof. Lessel

Help us gain a better understanding of AGO1-/ AGO2-related syndromes!

If your child has been diagnosed anywhere in the world, please take part.

You are part of the pathway to a cure

The information you provide will be used in **anonymous** form for scientific publications or presentations at scientific congresses.

Better understanding of disease is critical to developing care management guidelines, drugs and designing trials.

In case of questions:
o.ielesicheva@salk.at

A few words can say a lot about AGO Alliance

Empowering AGO families

We bring together families impacted by Argonaute syndromes for the best possible care of their children

Together for AGO children

As a united community we access resources and create transformative change for children with Argonaute syndromes, surpassing the impact of individual efforts alone

Transforming AGO children's futures

We partner with researchers to create a brighter future for children and families impacted by AGO gene disorders

Run by parents

By parents, for parents

Championing inclusion

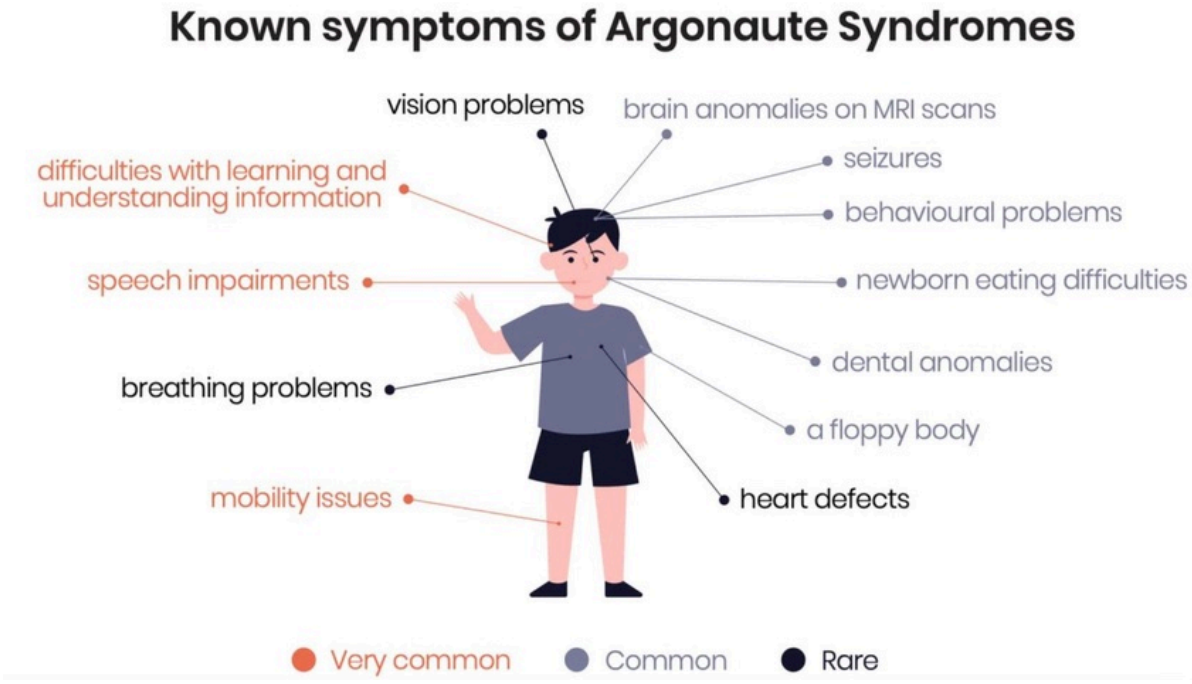
We believe that our children and families deserve a happy and inclusive life, just like all families

What are Argonaute syndromes?

Worldwide, ~100 people have been diagnosed with Argonaute syndromes

Changes to the AGO1 and AGO2 genes cause rare conditions with similar symptoms, AGO1-related syndrome and Lessel-Kreienkamp/LesKres syndrome respectively, that can collectively be referred to as Argonaute syndromes.

Argonaute syndromes are extremely rare. However, as these syndromes have only been recently discovered, as many as 1 in 16,000 children may be affected.

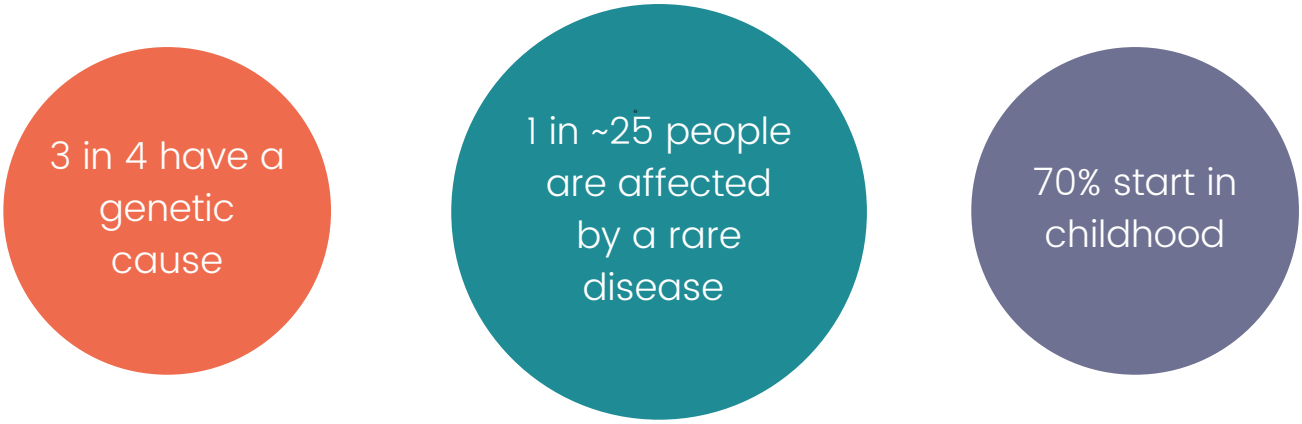


Lessel et al., Nature Comm 2020; Schalk et al., Journal Med Genet, 2021; Lopez-Rivera et al., Brain 2020

What is a rare disease?

Key facts

- In Europe, a disease is classified as rare when it affects fewer than 1 in 2,000 individuals.
- There are over 10,000 rare diseases identified.
- Only approximately 5-10% of these have at least one approved treatment available.



Consequently...

Research, early diagnosis, and suitable care present significant challenges, and a lack of awareness can result in misunderstanding and a sense of isolation.

> **"Only about 10% of rare diseases have an FDA-approved therapy. There is an urgent need for more research, and earlier and more accurate diagnoses of and interventions for these disorders"**
>
> - Anne Pariser, former Director of NIH NCATS Office of Rare Diseases Research

Sources: bag.admin.ch;
Wakap et al. European Journal of Human Genetics 2020
Haendel, M. et al. How many rare diseases are there? Nat. Rev. Drug Discov. 19, 77–78 (2020)

A Letter from Uxue, 5, Spain

Hello dear Argonaute friends,

My name is Uxue. I am from Navarra, a province located in the north of Spain. In am 5 years old. My mom had a normal pregnancy. When I was born, I couldn't breastfeed and mom had to use nipple shields and breast pumps. I was a very good girl, so good that I didn't cause any trouble, something that mom started to get worried about.

The first diagnosis was "Global developmental delay". We started with early attention therapies. When I was 2 years old I had an ear surgery (they placed drainage tubes). They did a hearing test and I couldn't hear well.

In addition, I had many otitis. My parents came to think that the problem was related to hearing and that with the surgery everything would be solved. After the surgery they checked my ears again and verified that my hearing was perfect although my evolution was still very stagnant. **The problem was not related to a lack of hearing.**

My parents thought with the ear surgery things would be solved.

They performed more medical tests to rule out any organic lesions: MRI, ECG in sleep, genetic tests... The results of these tests were normal. Meanwhile, in the kindergarten I was taken care by a fully dedicated caregiver (through government support). I needed her.

I didn't speak, I hardly understood orders, "I went my own way", everything I found on the floor I put it in my mouth...

The **second diagnosis was "Suspected Autism Spectrum Disorder (ASD)"**. The doctors did not classify me as a child with autism, but I did have autistic features. Due to this, they performed a "trio genome study" on mom, dad and myself. Usually in this study no altered gene comes out, that is, no disease is found.

My parents “hit the jackpot” when we received the results of the genetic study. They had found a de novo alteration in the **AGO1 gene,** specifically the variant **c.539_541delTCT p.Phe180del.** A very rare disease, with very few cases diagnosed in the world, **so few that the doctors told us that this disease had not yet been assigned with a name.**

> The doctor told us the disease is so rare, it has no name yet.

They told us that the disease caused intellectual disability, autistic traits, and epilepsy. They didn't know much more about this disease. We left the pediatric neurology clinic with an article on the disease, 3 pages in English, which we had to translate at home using Google translate. It was then when we realized that this disease caused the aforementioned symptoms, but also many more.

My evolution is very slow. I started walking when I was 26 months. I still don't say a single word, I'm not able to ask for water or food. The first epileptic attack was focal, at 3.5 years.

I am currently on medication for epilepsy, I have had more epileptic seizures at night. I am a very cheerful girl, but I need constant attention. I am totally dependent on other people to dress, bathe, eat... To this day I can bear having children around me, although “I do my own thing".

At the moment I go to a regular school, and to make this possible, a caregiver, Soraya, accompanies me throughout the school day. Not being able to communicate generates me a lot of frustration.
I receive several weekly therapies that are necessary so that time does not play against my evolution, and in order to be able to develop all my abilities to the maximum. I have a 1-year-old brother, who is not affected by this disease.

My parents found AGO Alliance recently, and it has helped them a lot. They have found a family in Florida whose daughter has the same mutation in AGO1. Being able to share information and learn more about this disease is amazing for them. For all these reasons I want to tell my story. And to make this disease more visible and find more people like me.

> Finding another family with the same mutation helped my parents a lot.

The future is uncertain, there is not enough understanding of the disease and effects vary significantly from one person to the next.

Our Partners

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Allianz Seltener Krankheiten – Schweiz
Alleanza Malattie Rare – Svizzera

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Foundation

Financial Report 2023
Balance Sheet

	31.12.2023 (in CHF)	31.12.2022 (in CHF)
Assets		
Liquid assets	44 045	32 140
Deferred income	373	14 360
Total assets	44 418	46 500
Liabilities		
Association assets	46 500	15 828
Profit/Loss	-2 082	30 372
Total liabilities	44 418	46 500

Financial Report 2023
Profit & Loss

	31.12.2023 (in CHF)	31.12.2022 (in CHF)
Revenue		
Patron contributions	0	33 847
Private donations	4 965	28 612
Legal entity donations	0	555
Total revenue	4 965	63 014
Expenses		
Project expenses incl. conference	4906	27 819
Salaries, Compensation	714	2 826
Bank fees, currency differencies	934	661
Memberships, Education, IT	494	432
Extraordinary expenses	0	604
Total expenses	7 048	32 342
Profit		
Profit (savings) / Loss	-2 082	30 672

We would like to thank the Swiss Re Foundation and Vanilla for their pro bono support.

In 2023 the board volunteered a total of 250 hours.

AGO Alliance is a non-profit organisation and pursues neither commercial nor self-help purposes. Our financial books are externally examined.

Hanna-Laura Mock
Hanna_Laura@hotmail.com
265 Cerro Street, CA-92024 Encinitas

INDEPENDENT AUDITOR'S REPORT

To the general meeting of AGO Alliance, Zurich

Report on the Financial Statements

I have audited the financial statements of AGO Alliance, which comprise the balance sheet as at December 31, 2023 and the statement of Profit & Loss for the year then ended.

My responsibility is to express an opinion on these financial statements based on my audit. I examined whether the balance sheet items were supported by evidence, invoices tie to journal entries on a sample basis and the accounting records are clear and understandable.

In my opinion, the accounting records and financial statements comply with Swiss law and the company's articles of incorporation.

I recommend that the financial statements submitted to you be approved with a loss of CHF 2'082.

San Diego, October 22, 2024

Hanna-Laura Mock

We Thank You For Your Support

Acknowledgements

Our heartfelt thanks to our supporters, donors, scientific advisors, and all those who worked hard behind the scenes. In particular, Stefan Kempf for our website.

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