20th October 2025

What are rare diseases?

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AGO Alliance Poland Foundation, president

Educational material for the "Youth for Rare Diseases" competition

Understand. Support. Change.

Understand rare diseases, support families and research, and together we will turn invisibility into hope.

Action. Generation. RespOnsibility. – for Rare Diseases

The aim of the campaign is to engage the young generation in activities promoting awareness, research and support for people with rare diseases.

#MISJAAGO

AGO Alliance Poland Foundation

This non-profit organization, run jointly by patients and scientists, was born out of love, determination, and the urgent need to develop treatments and help children with a rare disease - AGO syndrome.

RARE DISEASES ARE NOT THAT RARE.

>300 mln

people in the world live with a rare disease

These diseases differ in symptoms, but they share one thing in common: difficulty in diagnosis, a lack of treatment, and a limited number of specialists.

Therefore, collaboration between scientists, doctors, and families is essential to understand their causes and find effective treatments.

1 in 2 000

people have a rare disease

1 in 50 000

people have an ultra-rare disease

Most are genetic diseases that manifest in childhood, but some appear in adulthood.

Rare diseases include not only metabolic and neurological disorders, but also rare cancers..

The zebra is a symbol of rare diseases

> 10,000 rare diseases

5% has effective treatment

>2.5 million people in Poland live with rare diseases.

More than the inhabitants of Warsaw, Gdańsk and Kraków combined.

That's every 5th child in a pediatric hospital.

WHERE DO RARE DISEASES COME FROM?

Stories are written in our genes – not always happy ones.

MUTATIONS

Mutations are natural changes in our DNA that occur when cells copy genetic material.

Each of us has approximately 60–100 new mutations that our parents didn't have! Most of them don't change anything, some may be harmful, but occasionally one confers an advantage—and it's thanks to them that species evolve and adapt to the world.

ABOUT 20,000 GENES

Humans have approximately 20,000–21,000 genes, and even a slight change in one of them can lead to a rare disease. Although most genes function normally, sometimes a mutation disrupts their function or regulation. This demonstrates how precisely our bodies are programmed—and how crucial it is to understand DNA to develop effective gene therapies and medications to help people with rare diseases.

ONLY ABOUT 1–2% OF OUR DNA CONSISTS OF GENES, WHICH MAKE PROTEINS. THE REST ARE NON-CODING REGIONS THAT CONTROL GENE FUNCTION AND INFLUENCE DEVELOPMENT AND DISEASE.

ABOUT 80% OF RARE DISEASES HAVE A GENETIC BASIS

Mutations in DNA change the way a cell produces proteins, leading to their absence or malfunction.

Some changes are inherited from parents, while others appear randomly, even before a child is born.

THE REMAINING 20% OF RARE DISEASES HAVE A DIFFERENT CAUSE

The remaining 20% are diseases with other causes – for example, autoimmune, infectious, or environmental factors.
Some rare cancers also have a genetic component, which increases the risk of developing the disease.

THE PATH TO DIAGNOSIS – FROM MYSTERY TO NAME

"The hardest journey is the one to diagnosis."

The average time to a rare disease diagnosis is 5–7 years.

Patients go through many visits before they find someone who orders the appropriate tests.

Many of them have previously been misdiagnosed with conditions such as ADHD, autism, or metabolic disorders.

Modern diagnostics

A breakthrough has been brought by WES (exome sequencing) and WGS (genome sequencing) technologies, which allow for the decoding of a person's entire genetic material.

Thanks to them, mutations in genes previously unknown to science can be discovered.

Genetic diagnosis not only ends long-standing uncertainty but also opens the door to research and support.

WGS (Whole Genome Sequencing)

Developed earlier, between 2000 and 2010, as an extension of the Human Genome Project, WGS reads the entire genome—both genes and non-coding regions. It enables the discovery of new mutations and disease mechanisms, although it requires more data and is more expensive.

WES (Whole Exome Sequencing)

This technology examines only the DNA fragments that encode proteins—known as exons.
It is in these exons that most mutations responsible for genetic diseases are found.

With WES, scientists can read thousands of genes simultaneously and check if any of them contain an error that causes the disease.

HOW ARE DRUGS FOR RARE DISEASES DEVELOPED?

"From gene to reimbursement – a long but increasingly faster road."

Drug development is a multi-stage process that can take up to 15 years – although for rare diseases it is increasingly shortened by special regulations of the European Medical Agency (EMA) and the Federal Drug Administration (FDA).

1 PRECLINICAL STUDIES

Scientists are studying the mechanisms of the disease:
in cell cultures and animal models (e.g., fruit flies, fish, mice), they are testing the safety and effectiveness of potential substances.

2 CLINICAL TRIALS - CONDUCTED WITH THE PARTICIPATION OF PATIENTS

Phase I – safety,
Phase II – efficacy,
Phase III – confirmation of efficacy in a larger group.

3 REGISTRATION AND REIMBURSEMENT

After a positive assessment by the EMA, the drug is sent to national agencies (e.g. Health Technology Assessment (HTA) in Poland), which decide on financing.

For rare diseases, accelerated market authorization is possible if the drug has the potential to save lives.

Rare diseases benefit from shortened registration pathways.

HOW RARE DISEASE RESEARCH HAS HELPED MILLIONS OF PEOPLE

"Small diseases – great discoveries."

RARE DISEASE RESEARCH BENEFITS NOT ONLY A SMALL GROUP OF PATIENTS. IT OFTEN LEADS TO DISCOVERIES THAT HELP HUNDREDS OF THOUSANDS OF PEOPLE.

HUTCHINSON-GILFORD PROGERIA SYNDROME

Accelerated aging disease has taught scientists how to protect DNA and prevent cell damage. This provides a foundation for research into heart disease and aging.

Progeria Research Foundation

FAMILIAL HYPERCHOLESTEROLEMIA

Research on the LDLR and PCSK9 genes allowed the development of statins, today widely used in millions of people with high cholesterol.

V(ermissen et al, 2009)

RETINAL TUMORS (RETINOBLASTOMA)

Research on rare mutations in the RB1 gene has uncovered the mechanisms of cancer development and initiated oncogenetics, which has changed cancer diagnosis.

Children with Cancer UK

GASTROINTESTINAL STROMAL TUMORS

The discovery of a mutation in the KIT gene led to the development of imatinib – the first targeted drug in oncology, now also used in other cancers.

Zwrotnik raka

TREATMENT OF RARE DISEASES IN EUROPE AND POLAND

"Together we can do more – although we are still at the beginning of the journey."

EUROPE IS DEVELOPING COOPERATION NETWORKS:

ERN (EUROPEAN REFERENCE NETWORKS)
24 networks of specialist centres in 27 countries, including ERN-ITHACA for developmental diseases.

EURORDIS
a patient organisation based in Brussels, connecting over 1,000 organisations from across Europe.

ERDERA
a new initiative funding research into rare diseases across Europe.

While this is a huge step forward, many of these efforts are still in their infancy.

Europe and Poland still lack systematic government support, stable sources of research funding, and dedicated grant programs for rare diseases.

Most initiatives are developed thanks to the involvement of scientists and patient organizations.

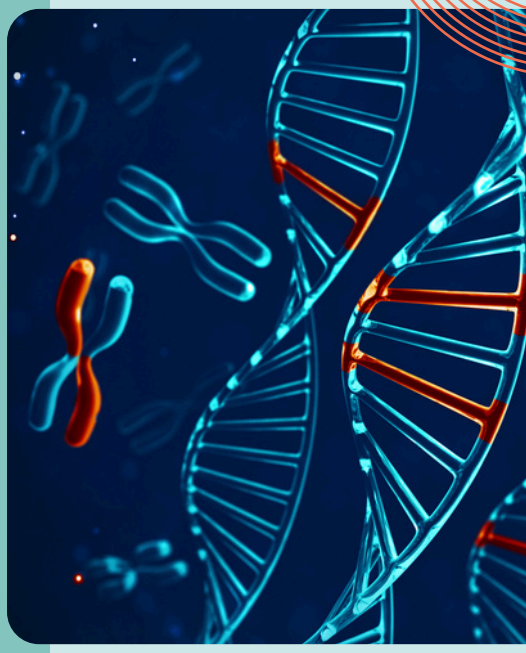
THERE ARE NO SYSTEMIC SOLUTIONS, BUT COOPERATION GIVES HOPE.

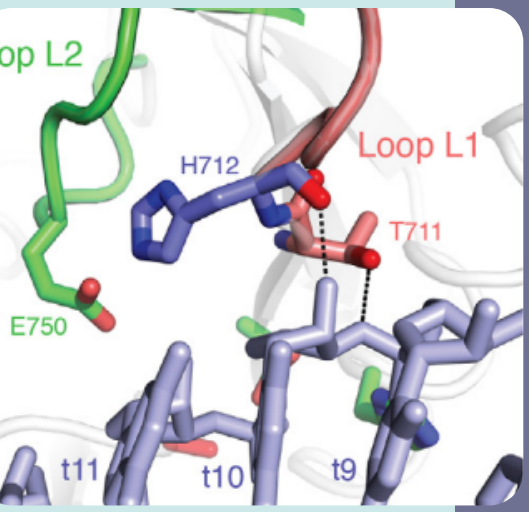
WHAT IS AGO SYNDROME?

"When a cell loses its filter, chaos ensues."

AGO syndrome (mutations in the AGO1 or AGO2 genes), also known as Argonaute syndrome, is an ultra-rare genetic disorder that affects development. Children with this syndrome often have:

- Delayed motor and speech development,
- Difficulties with learning and concentration,
- Hypersensitivity to stimuli,
- Autism spectrum symptoms,
- Sometimes epilepsy or sleep disorders,
- Autism,
- Eating problems





AGO proteins function in cells similar to a spam filter – they recognize and "silence" unnecessary RNA fragments that could disrupt the body's functioning.

When this filter fails, information chaos reigns within the neurons—similar to a computer with a faulty system. Additionally, muscles don't function as they should.

AS A RESULT, THE BRAIN DEVELOPS MORE SLOWLY AND THE PROCESSING OF STIMULI IS IMPAIRED.

IN AGO SYNDROME, THE RISC COMPLEX, WHICH CONTROLS WHICH GENES ARE TURNED ON OR OFF, DOES NOT FUNCTION PROPERLY.

HOW ARE RARE DISEASES AND AGO SYNDROME DIAGNOSED?

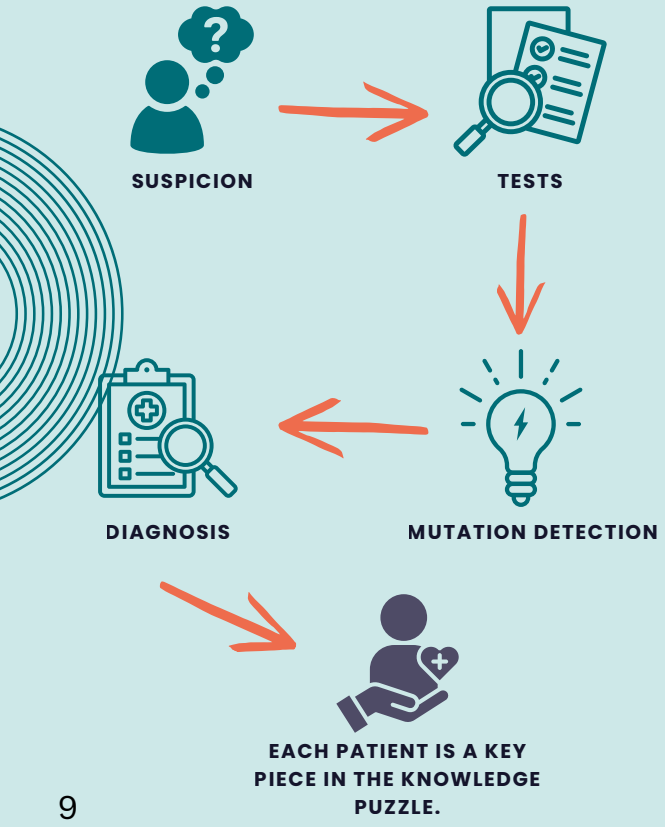
"Genome Sequencing – The Microscope of the 21st Century."

The diagnosis of AGO syndrome is only possible thanks to new generation genetic tests (WES, WGS).

Doctors suspect the disease when they observe communication disorders, below-normal speech development, learning difficulties, and abnormal EEG in a child.

Once a mutation in the AGO1 or AGO2 genes is detected, the diagnosis is confirmed.

Each new case brings unique data, allowing researchers to understand the diversity of symptoms and mechanisms.



""Albert's first symptoms—lack of eye contact and muscle weakness—appeared very early. Despite therapy, new symptoms continued to develop, until he was diagnosed with autism at 13 months old. However, we didn't want to stop there—we felt the answer lay deeper. After a series of genetic tests, including the expensive Trio-WES, we discovered the cause: a mutation in the AGO1 gene, described just a few months earlier. It was a difficult but groundbreaking moment—then we learned that with such a rare disease, parents must become experts."

Once a mutation in the AGO1 or AGO2 genes is detected, the diagnosis is confirmed.

Each new case brings unique data, thanks to which researchers understand the variety of symptoms and mechanisms.

Dad of Albert with AGO syndrome (mutation in the AGO1 gene)

HOW IS TREATMENT FOR RARE DISEASES DEVELOPING?

"From cell to human – strategies for new medicine."

The progress of scientific development is very dynamic and new translational approaches are constantly emerging that may contribute to the development of treatment.

Research into rare disease therapies requires multiple stages and models. In the AGO syndrome, we utilize:

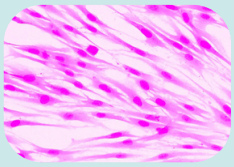
1. *Drosophila melanogaster* – fruit fly, ideal for genetic research.
2. *Caenorhabditis elegans* – nematode, a simple model for RNA research.
3. *Danio rerio* – zebra fish, a model of the development of nervous systems.
4. *Mus musculus* – mouse, a model of human disease.
5. Fibroblasts – skin cells collected from patients, used to study gene expression and AGO protein function and to create in vitro disease models.
6. iPSCs (induced pluripotent stem cells) – these can be differentiated into neurons; they allow the patient's brain development to be replicated in the laboratory and potential therapies to be tested.

D. melanogaster

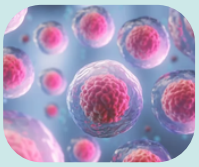
C. elegans

D. rerio

M. musculus



Fibroblasty



iPSC

BASED ON THIS, VARIOUS TREATMENT STRATEGIES ARE DEVELOPED. HERE ARE EXAMPLES FOR AGO SYNDROME:

REPURPOSING
testing known substances in new diseases.

ASO
RNA molecules that correct incorrect sequences.

SIRNA
mechanism of silencing harmful genes.

SMALL MOLECULES
chemical substances that affect the function of proteins.

GENE THERAPIES
introducing the correct copy of the gene or repairing the incorrect one.

Researchers need a range of model organisms to understand the genesis and mechanism of disease, to hypothesize, and to develop therapies that must be tested before being administered to patients.

In parallel, it is necessary to initiate a **Natural History Study** to determine how the disease, AGO syndrome, develops without treatment and how to measure the effects of future therapies when they are ready for testing.

RARE DISEASES FOR WHICH A CURE HAS BEEN FOUND

"Every success story started with a single mutation."

SMA (SPINAL MUSCULAR ATROPHY)

Zolgensma gene therapy and ASO therapy: Spinraza save thousands of children.


SMA

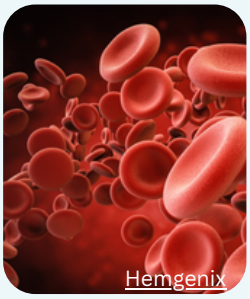

MPS

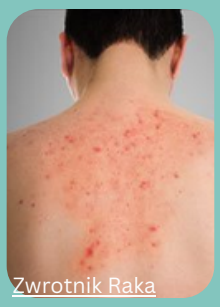
MUCOPOLYSACCHARIDOSIS (MPS I)

Aldurazyme enzyme therapy slows the disease.

HEMOPHILIA A/B

Hemgenix gene therapy eliminates the need for transfusions.


Hemgenix


Zwrotnik Raka

GAUCHER-FABRY DISEASE

Enzyme and small molecule therapies improve organ function.

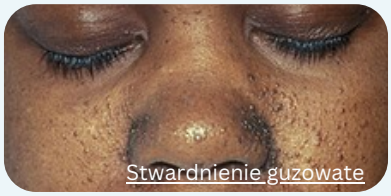
RETINAL DYSTROPHY (LUXTURNA)

gene therapy restores sight


EMA

TUBEROUS SCLEROSIS COMPLEX (TSC)

A rare disease that leads to the formation of tumors in the brain and other organs. Rapamycin (sirolimus) is a primarily immunosuppressive drug that limits tumor growth and seizures.


Stwardnienie guzowate

UNDERSTANDING A RARE DISEASE CAN CHANGE THE LIVES OF MILLIONS.

THE POWER OF PATIENTS – SCIENCE AND FAMILIES TOGETHER

"Rare doesn't mean lonely."

Patient families become part of the science.

They establish foundations, organize fundraisers and conferences connecting scientists with patients.

In the case of the AGO syndrome, an international network was established: AGO Alliance, AGO Alliance Poland and Asociacion de Sindromes AGO, bringing together families from over 30 countries.
Parents and patients are increasingly participating in scientific conferences, where they share their perspectives on living with the disease and their hopes for the development of treatment.

During patient-scientific conferences, research directions, cooperation and therapeutic priorities are discussed.

NOBEL PRIZE WITH A HEART – AMBASSADOR FOR RESEARCH ON AGO SYNDROME

Prof. Victor Ambrose

Professor Victor Ambrose is an outstanding molecular biologist from the USA, from UMAS Chan who received the Nobel Prize in 2024 together with Professor Gary Ravkun for the discovery of microRNAs – small RNA molecules that regulate gene activity.

This discovery revolutionized genetics and opened the way to the development of RNA therapies, i.e. those that act at the RNA level (e.g. ASO, siRNA, mRNA).

- Prof. Ambrose has been supporting the AGO community for years as:
- A scientific mentor and advisor to researchers working on the mechanisms of the AGO1 and AGO2 genes.
- A family ally – participating in patient-scientific conferences and connecting the world of science with patients.
- Ambassador of the AGO Alliance Poland mission – inspiring cooperation and the development of therapies for children with AGO syndrome.

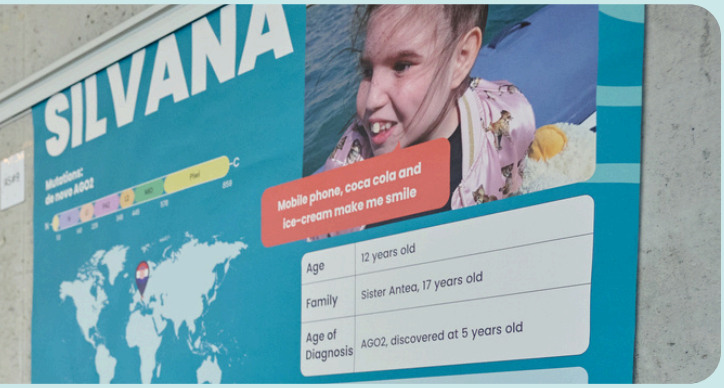
"IF YOU FAIL ONLY ONCE EVERY SIX MONTHS YOU ARE NOT MAKING MUCH PROGRESS, BUT IF YOU FAIL DAILY, YOU ARE LEARNING DAILY"

PATIENT ORGANIZATIONS – A NEW FORCE IN DRUG DEVELOPMENT

"From Patient to Partner – How Families Are Changing Science."

Patient organizations are now co-creating research: they establish patient registries, fund cell models, run educational campaigns, and support clinical trials.

In European projects, patients are increasingly setting the direction – helping to determine what is truly important for families.



In AGO syndrome, families became the initiators of drug research, connecting laboratories from around the world.

PATIENTS DON'T JUST WAIT - THEY ACT TOGETHER WITH SCIENCE.

FOUNDATION PARTNERS AND ADVISORS

LIVING AND CARING FOR A RARE DISEASE

"Behind every diagnosis there is a family."

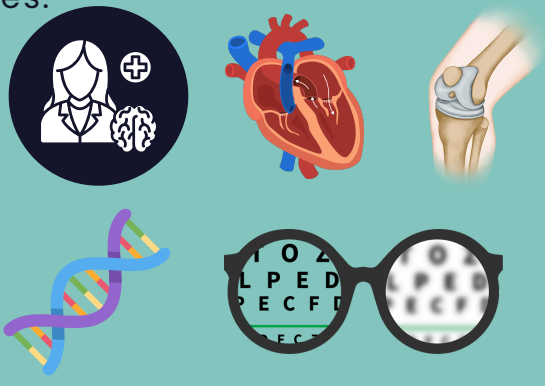
CARING FOR A PERSON WITH A DISABILITY RESULTING FROM A RARE DISEASE IS A DAILY CHALLENGE.

Parents and caregivers must juggle the roles of physiotherapists, teachers, translators, and advocates for their children.

They often lack access to therapy, rehabilitation, and psychological support.

People with rare diseases require multidisciplinary care from physicians. In AGO syndrome, this includes:

- psychiatrist,
- neurologist,
- geneticist,
- cardiologist,
- orthopedist,
- otolaryngologist,
- optician
- and others.



The support system in Poland is still fragmented, which is why foundations that organize camps, support groups and educational materials play a huge role.

CARING FOR THE SICK IS A DAILY ACT OF COURAGE, LOVE AND DETERMINATION.

HOW CAN YOU HELP?

"Everyone can be part of the change."

You can help in many ways:

- organizing events about rare diseases,
- supporting fundraising for research,
- sharing knowledge in the media,
- promoting understanding for patients and families.

AGO ALLIANCE POLAND GOALS:

- supporting research into therapies for AGO syndrome
- building a network of cooperation between scientists and families
- developing education about genetics, RNA and rare diseases
- organization of patient-scientific conferences in Poland and Europe
- creating a global patient registry

KNOWLEDGE, COOPERATION AND EMPATHY – THESE ARE THE FOUNDATIONS OF THE TREATMENT OF THE FUTURE.

AGO ALLIANCE POLAND

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