

Understanding HJMD – A Patient Information Guide

Hypotrichosis with Juvenile Macular Dystrophy

Introduction

This patient information guide is meant to encourage and support families affected by **HJMD**. We know how difficult it can be to understand such a diagnosis and to find the right balance between **information, hope, and reality**.

This document summarizes what is currently known about the condition, the reasons for different progressions, and what can be done to **protect the retina and maintain vision**.

What HJMD Is

HJMD is caused by changes (mutations) in the **CDH3 gene**.

This gene provides the blueprint for a protein called **P-cadherin**, which connects cells in the skin, hair roots,

and especially in the **retina** of the eye.

When this protein is missing or faulty, the cell connections become unstable — the retina becomes more sensitive to **light, oxygen, and metabolic stress**.

Over time, this leads to a slow functional decline of the central retina (macula), the part responsible for sharp central vision.

Why Hair Is Also Affected

The **CDH3 gene** plays a crucial role not only in the retina but also in **hair follicles**.

The P-cadherin protein ensures that cells in the hair roots adhere properly and communicate effectively.

When P-cadherin is missing, these connections weaken, and the hair may become **thin, fine, or sparse** — a condition known as **hypotrichosis**.

To stimulate hair growth, **minoxidil** (for example as foam or topical solution) can improve blood flow and cell metabolism in the hair roots.

It can extend the growth phase of existing hair and strengthen follicles, although it cannot change the underlying genetic cause.

Luis' Genetic Findings

In our son, two different changes in the **CDH3 gene** were identified:

1. **c.316_317delAA; p.Lys106Glufs*12** – an **early frameshift mutation**.
The genetic code shifts, and the protein construction stops after just 12 incorrect amino acids. This copy of the gene cannot produce a functional P-cadherin protein.
2. **c.1086G>A; p.Trp362*** – a **nonsense mutation** in the middle part of the gene.
Here, a premature stop signal appears.
The messenger RNA is usually degraded by the body (nonsense-mediated decay), preventing the production of a complete protein.

Both mutations are classified as **loss-of-function (LoF)** — meaning that normal P-cadherin is not produced.

Yet the course in Luis' case is **mild** – at age 16 he still retains about **90 % of his vision**.

This shows that the severity of HJMD is not determined by the gene defect alone, but by a **complex interaction of additional biological factors**.

Why Progression Differs So Much

Not all individuals with HJMD lose vision at the same rate.

The body is **more than just a single gene**.

In addition to the type of mutation, many other factors influence disease progression:

- **Efficiency of cellular repair mechanisms**
- **Antioxidant defense capacity** (vitamin C, E, lutein, zeaxanthin, taurine)
- **Activity of mRNA control systems (NMD)** – in some people, tiny amounts of protein still escape degradation
- **Retinal development before birth** – how well retinal cells connect during early development
- **Environmental factors:** light exposure, nutrition, sleep, physical activity, and stress

The **genetic mutation defines the framework**,

but within that framework each body reacts **individually – depending on its protective systems and environment**.

Why Cell Protection Matters

Even when the gene cannot produce complete P-cadherin, many retinal cells still function – they are simply more fragile.

The key is to **protect and relieve these cells** so they remain functional as long as possible.

The greatest threat to them is **oxidative stress** –

tiny, highly reactive molecules (“free radicals”) formed by light, oxygen, stress, or inflammation.

If these radicals accumulate, they damage cell membranes, proteins, and DNA.

Normally, **antioxidants** neutralize them — such as **vitamin C, E, lutein, zeaxanthin, zinc, copper, and taurine**.

If too few of these protective substances are present, the degeneration of retinal cells accelerates.

Key Protective Measures

- 🕶️ **Sunglasses with UV-400 or blue-light filter** – reduce harmful light exposure
- 🍬 **AREDS-2 nutrient formula** (e.g., Lutamax AREDS 2 or equivalent) – proven antioxidant protection
- 🐛 **Taurine** (500–1000 mg daily, pure supplement, caffeine-free) – stabilizes cell membranes, supports photoreceptors
- 🐟 **Omega-3 fatty acids (DHA, EPA)** – stabilize cell membranes and reduce inflammation
- 🍏 **Healthy diet, good sleep, and stress reduction** – support cellular balance

Even though energy drinks contain taurine, their caffeine and sugar content **increase oxidative stress** – they are **not suitable** for protection.

Nutritional Support According to AREDS-2

The **AREDS-2 formula**, developed by the *U.S. National Eye Institute*, showed that certain micronutrients can protect the retina and slow down vision loss.

Nutrient	Daily Dose	Function
Lutein	10 mg	Filters blue light, protects the macula
Zeaxanthin	2 mg	Enhances light protection
Vitamin C	500 mg	Neutralizes free radicals
Vitamin E	268 mg (400 IU)	Protects cell membranes
Zinc	25 mg	Supports retinal enzyme defense
Copper	2 mg	Balances zinc, antioxidant function

Regular Eye Check-ups

Eye examinations every **6–12 months** are recommended, including:

- **OCT (optical coherence tomography)**
- **Fundus photography**
- **Visual field testing**

These allow early detection and documentation of changes. Such data are also valuable for ongoing and future HJMD research.

Research and Future Outlook

Worldwide, researchers are exploring new treatment approaches, including:

- **Gene therapy** (replacement or reactivation of silent genes)
- **Retinal organoids** – miniature retina models used to test drugs
- **Stem-cell therapy** (replacing degenerated photoreceptors)
- **Molecule-based strategies** (imitating or stabilizing P-cadherin function)

These options are still under investigation, but they are important steps toward potential future therapies.

Living With HJMD

Despite the genetic limitation, many people with HJMD lead fulfilling lives. A stable daily routine, healthy nutrition, sufficient sleep, and regular physical activity are all important.

Careful handling of light exposure, screens, and stress supports not only the eyes but also overall wellbeing.

Family, friends, and sports can help shift focus away from the diagnosis and preserve a positive outlook on life.

Conclusion

HJMD is **more than a single gene defect** –

it represents an interplay between **genetics, cell biology, and environment**.

The mutation determines that P-cadherin is missing,

but the progression depends on how well the remaining cells are protected and supported.

The goal is not only to understand the gene,

but to create the **conditions that allow these cells to survive** –

through knowledge, care, and consistent protection.

Scientific References

- *Age-Related Eye Disease Study 2 (AREDS 2)* – National Eye Institute (USA), JAMA Ophthalmology 309(19): 2005–2015.
 - *Orphanet Journal of Rare Diseases (2023)* – CDH3-related disorders.
 - *European Journal of Human Genetics (2024)* – P-cadherin in hair and retinal development.
 - *NIH Genetics Home Reference / NCBI GeneReview* – CDH3 gene.
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Note

This **patient information** is intended to educate and connect affected families.

It does not replace professional medical advice or personalized consultation.
