# *NMNAT1* mutation causing retinitis pigmentosa

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## Introduction:

Retinal dystrophies (RD) is a group of blinding diseases that are characterized by clinical variability and pronounced genetic heterogeneity

Although the various forms of RD can be distinguished clinically, disease progression is difficult to predict and may vary even within the same family. Also, same mutation could induce different phenotypes.

**The aim** of this study was to identify the gene causing retinitis pigmentosa (RP) in a Tunisian family.

## Methods:

Two members of a consanguineous family With RP were clinically examined.

Patients underwent :

-BCVA,

-Slit lamp biomicroscopy,

-Fundus photography, and electrophysiology.

DNA sample from the index patient was subjected to whole exome sequencing (WES). Variants localized in homozygous regions Were validated by Sanger sequencing. Familial segregation was performed.

## Results:

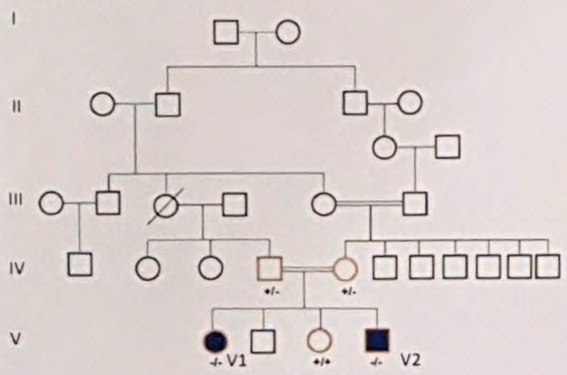



**Figure 1: Color** fundus photography of patient V.1 showing preserved posterior pole with peripheral retinal atrophy and spicule shaped pigment deposits.

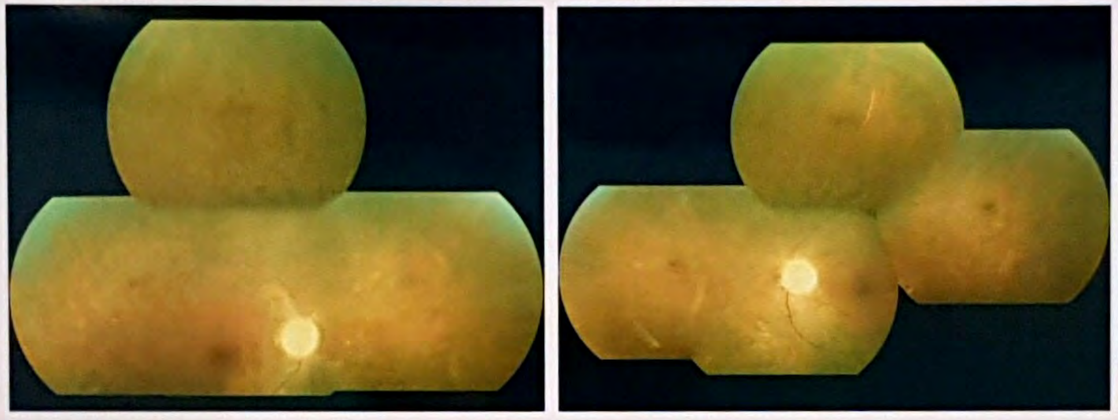
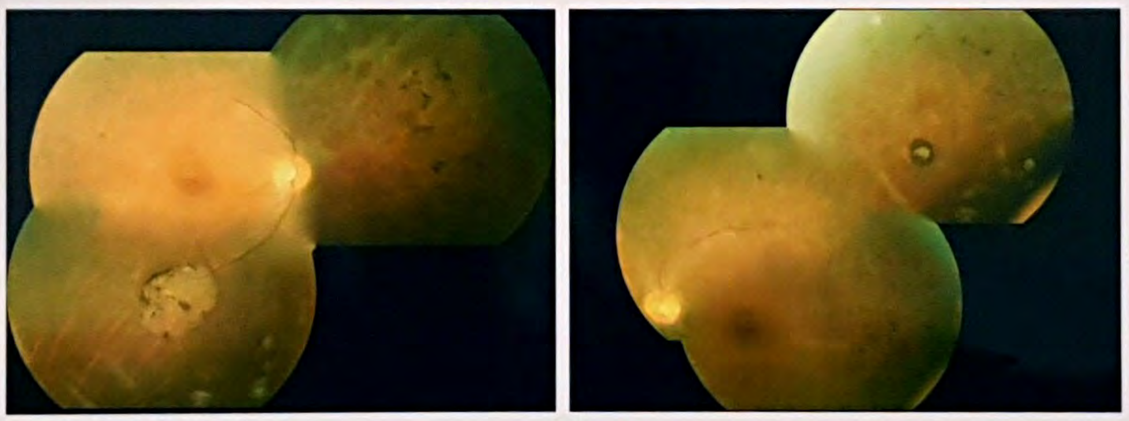


**Figure 2: Color** fundus photography of the brother V.2 showing same presentation



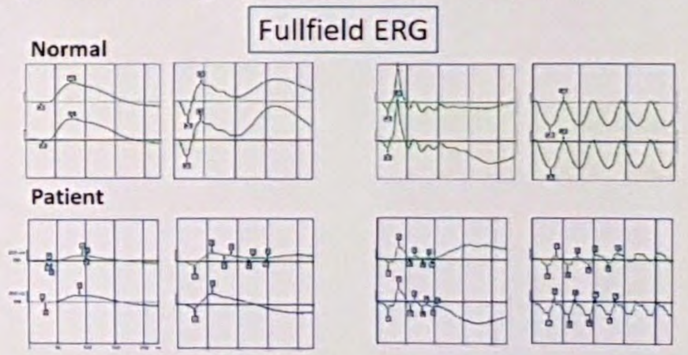
**References**
*Perrault I et al. Nat Genet. 2012 ; 44(9):975-7.
*Koenekoop RK et al. Nat Genet. 2012 ; 44(9):1035-9.

## Clinical results:

Affected patients had relatively preserved visual acuity until the third decade. On fundus examination, we found normal macular aspect with few bone spicule shaped pigment deposits and white dot deposits in the mid periphery.

| Patient | Gender | Age Years | Age of onset | Visual acuity RE | LE |
|---|---|---|---|---|---|
| V.1 | F | 23 | 5 | 5/10 | 5/10 |
| V.2 | M | 21 | 5 | 7/10 | 6/10 |

**Figure 3:** Fullfield-ERG of patient V.1 :altered scotopic responses with slightly altered photopic responses




## Genetic results:

The homozygous mutation NM_001297778.1: c.37G>A, p.A13T in the *NMNAT1*, segregated with the disease in this recessive RP family.

## Discussion and conclusions:

Unexpectedly, two probands in our family with RP had damaging missense mutation, **p.A13T in nicotinamide adenine dinucleotide (NAD) synthase gene *NMNAT1*.**

Such mutation have been identified in patients with Leber congenital amaurosis, although the variant is reported only in heterozygote form by the Exome Aggregation Consortium (ExAC) at an allele frequency of 0.0002.

Although the probands' phenotype is consistent with RP and the mutations are predicted to be deleterious, our patients showed preserved visual acuity and RP phenotype with few bone spicule shaped pigment deposits and white dot deposits in the mid periphery.

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