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Genomic and Clinical Assessment of Norrie Disease/ND

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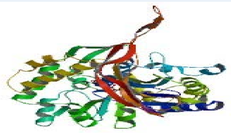


Abstract

***Purpose**: Discuss the clinical features of Norrie Disease, assess the pattern of genetic inheritance, highlight the genetic diagnosis and indicate treatment. The NDP gene with clinical diagnostic techniques are outlined.
***Methods**: Relevant comprehensive search using specific search terms used to look up appropriate literature in different databases. The next step was to assess the papers for further examination and the closely related articles were included in the poster. Genomic investigation was also performed in order to find updated data associated with *NDP* gene and Norrie disease.

Norrie Disease

*__Norrie Disease__ is a rare X-linked recessive disorder that affects males from birth. The primary feature is congenital blindness.

***Alternative names**

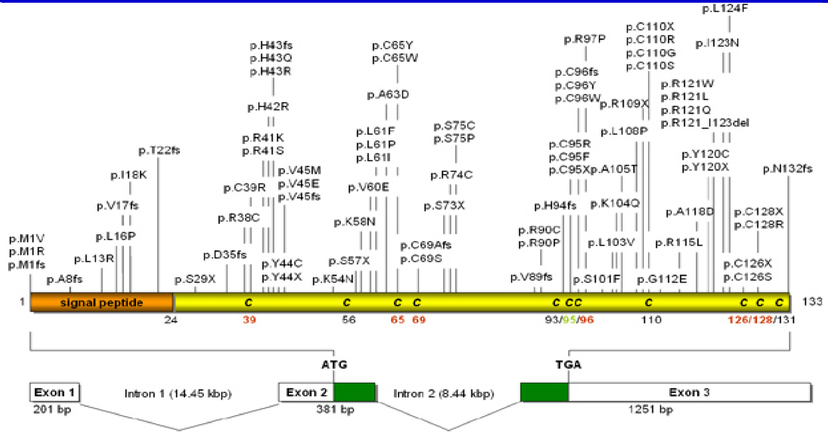
-Atrophia bulborum hereditaria

-Episkopi blindness

Ophthalmalogic Examination

*__Norrie Disease Pseudoglioma Gene__ located at **Xp11.3**

NDP Gene Mutation Map



Clinical Diagnosis

Diagnosis of ND includes a three generation pedigree, a thorough physical examination, B ultrasound scan, CT Brain and molecular genetic testing of *NDP* gene.

Genetic Testing

***Sequence analysis** of the entire coding region by GENETIX

-XLID NGS Panel by fulgent

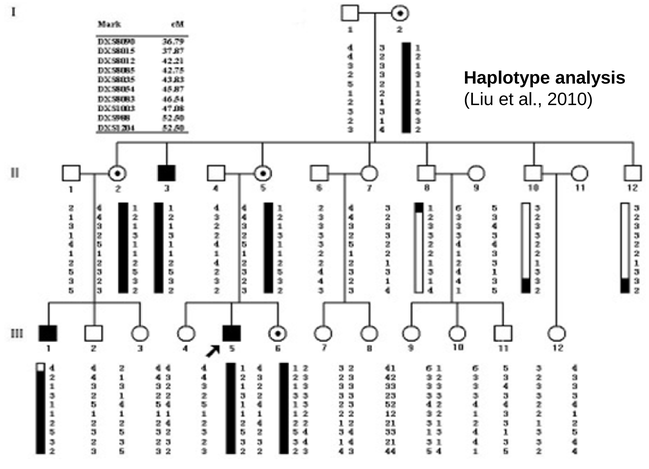
-Viteroretinopathy & Wagner Syndrome NGS Panel and eye disorder panel by fulgent

-Norrie disease (sequence analysis of NDP gene) by CGC Genetics

***Deletion and Duplication Analysis**

-Detects deletions and duplications that are not detected by sequence analysis.

-Performed by qPCR, real-time PCR, MLPA, or array CGH.



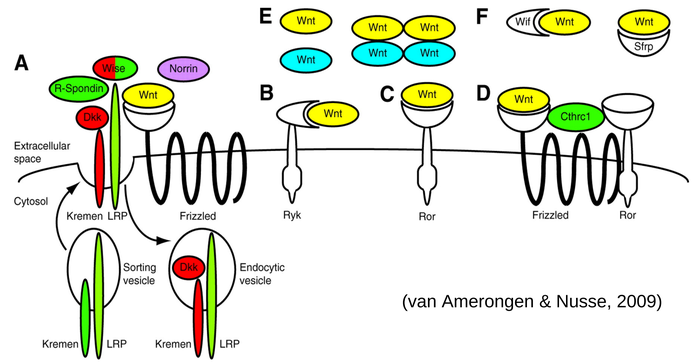
Haplotype analysis
(Liu et al., 2010)

***Linkage and Haplotype Analysis**

-Maximum LOD score for 17 microsatellite markers – 1.51 on Xq11.4

-Telomeric recombination event analysis between markers can be used to identify the disease gene locus

"Normal" Function of *NDP* Gene



(van Amerongen & Nusse, 2009)

*Without a mutation, the *NDP* gene codes for the norrin protein.

*Norrin activates the Wnt signaling pathway and plays a central role in retinal vascularization.(Nextprot)

Gene Interaction

TSPAN12	Regulator of cell surface receptor signal transduction
LRP5	Involved in the Wnt/beta catenin signaling pathway
LGALS8	lectin, galactoside-binding, soluble, 8
FZD4	Receptor for Wnt proteins
PPP1CA	Protein phosphatase 1 is essential for cell division
FZD8	Receptor for Wnt proteins
NDP	Activates the canonical Wnt signaling pathway

Treatment

*Incomplete retinal detachment and/or intraocular pressure may be treated with laser surgery.

* Hearing loss is treated with hearing aids or cochlear implants.

*Treatment for behavioral issues and cognitive impairment involves supportive interventions.

* Genetic counseling and prenatal diagnosis offered to carrier females considering pregnancy.

References available upon request