Genomic Unity® Case Study

Shifting the diagnostic paradigm with a whole genome platform

Overlapping 1bp and 7bp indels in *COL18A1* explain retinal symptoms in 11-year-old male

Clinical presentation

An 11-year-old male presented with retinal disorder symptoms including:

- Detached retina
- Bilateral high myopia
- Bilateral macular atrophy
- Fatty occipital cyst
- Secondary cataract
- Corneal scarring

Development and communication were normal.

Results and interpretation

Variantyx **Genomic Unity® Whole Genome Analysis** identified two overlapping small sequence changes in *COL18A1*: a likely pathogenic, maternally inherited 7bp deletion and a pathogenic, *de novo* 1bp deletion. Both are frameshift variants resulting in early termination of the protein.

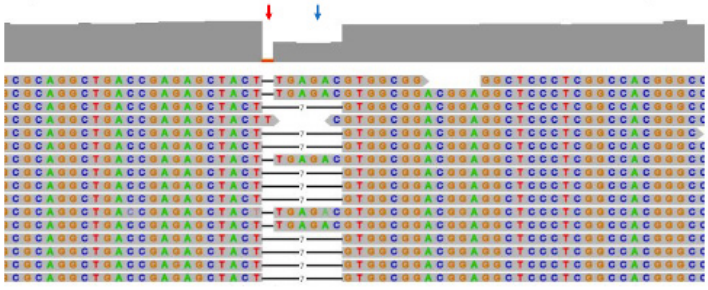
Diagnosis: Knobloch syndrome type 1

Previous genetic testing

An inherited retinal disorders panel was non-diagnostic.

Genomic Unity® Whole Genome Analysis was ordered because of its ability to identify all relevant variant types in a single test

The flanking GTG and GACG underlined sequences have the potential to shift and be misaligned, partially covering or masking both the 1bp and 7bp indel shown below



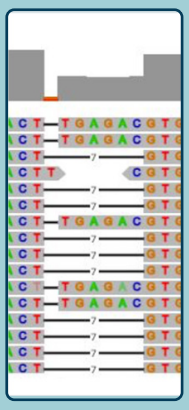
Variantyx

The Variantyx difference

Why were these overlapping indels identified by Genomic Unity® Whole Genome Analysis, and missed by a retinal disorders panel?

While small sequence changes are usually detectable by panel testing, there are features of these variants that likely complicated detection:

- The 1bp *de novo* deletion overlaps with the beginning of the 7bp maternally inherited deletion
- The nearby GTG and GAGC sequences (see red and blue underlined sequences in front page image) may have partially or completely masked the variants
- Even if some variants remained unmasked, there may have been too few remaining to detect



Variantyx genome analysis detects all major variant types in a single test including small sequence changes, structural variants, repeat expansions and mitochondrial variants. Robust alignment algorithms and trio testing facilitate variant detection and comparison.

Variantyx tests that would have identified this variant

Genomic Unity® Whole Genome Analysis | Genomic Unity® Exome Plus Analysis | Genomic Unity® Exome Analysis | Genomic Unity® Retinal Disorders Analysis

Bring the power of whole genome sequencing to your practice today.

To get started, contact your Clinical Sales Specialist and visit us online at variantyx.com.

Variantyx

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