## Case Study #3

### Angelman Syndrome

#### Patient and Clinical Presentation

Pediatrician ordered FirstStep\textsuperscript{Dx} for 5-year-old male with intellectual disability, ADHD, and excessive salivary secretions.

#### FirstStep\textsuperscript{Dx} Results

- Suggestive of uniparental disomy (UPD) of chromosome 15
- This indicates either Angelman or Prader-Willi syndrome depending on parent-of-origin of the UPD 15
- Lineagen confirmatory testing is consistent with Angelman syndrome

#### Angelman Syndrome Characteristics

- Developmental delay
- Lack of speech
- Seizures
- Walking and balance disorders/gait ataxia
- Apparent happy demeanor
- Abnormal EEG
- Incidence of 1 in 15,000 births

#### Management Changes

- Switched from intensive speech and language therapy to sign and picture communication
- Neurological evaluation ordered due to commonly occurring seizures in children with AS
- Informed individualized education program
- Management of sleep disturbances
- Evaluation and management of scoliosis

#### Case Study Summary

- UPD identified by FirstStep\textsuperscript{Dx} would have been missed by standard chromosome analysis or microarrays that lack SNP probes
- Speech therapy is contraindicated for AS – child is excelling in alternate communication methods
- Genetic counseling: The diagnosis accurately informed family planning decisions and helped the child qualify for a special education program in his school district

#### Long Continuous Stretch of Homozygosity

SNPs inherited from each parent are usually different, although some will be identical due to chance.

However, when many SNPs in a row are identical on each chromosome copy (called a long continuous stretch of homozygosity), it suggests that both regions of that chromosome were inherited from the same parent (uniparental disomy).

#### Long Continuous Stretch of Homozygosity Indicating UPD 15

Identical SNP probes on chromosome 15 indicate paternal uniparental disomy (UPD) – suggestive of Angelman syndrome.

Certain genes on 15q11.2 are only active on the chromosome inherited from the mother, while the same genes inherited from the father are methylated (turned off). When paternal UPD 15 occurs, all of these genes are methylated, leading to the features of Angelman syndrome.

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**FirstStep\textsuperscript{PLUS}**

For individuals with autism and other disorders of childhood development

2677 E Parleys Way
Salt Lake City, Utah 84109
www.lineagen.com

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