# Blueprint Genetics

## Blueprint Genetics Whole Genome Del/Dup (CNV) test

### TEST RESULT

The heterozygous microdeletion on 7q11.23 is classified as pathogenic.

### CLINICAL HISTORY

Patient is 8-year old boy who had surgery for supravalvular aortic stenosis at the age of 2. He was born as SGA at 38-week gestational age. His growth rate has been low, and height and weight are at -1.5-(-1.9) SD. His facial appearance is slightly dysmorphic. Family history is normal.

| POSITION | LENGTH | EVENT | COPY NUMBER | GENOTYPE | OVERLAPPING GENES | LINKS | CLASSI-FICATION |
|---|---|---|---|---|---|---|---|
| 7:72720001-74140000 | 1420 KB | DEL | 1 | HET | NSUN5;TRIM50;FKBP6;FZD9;BAZ1B;BCL7B;TBL2;MLXIPL;VPS37D;DNAJC30;WBSCR22;STX1A;ABHD11;CLDN3;CLDN4;WBSCR27;WBSCR28;ELN;LIMK1;EIF4H;LAT2;RFC2;CLIP2;GTF2IRD1;GTF2I | UCSC | Pathogenic |

### CLINICAL REPORT

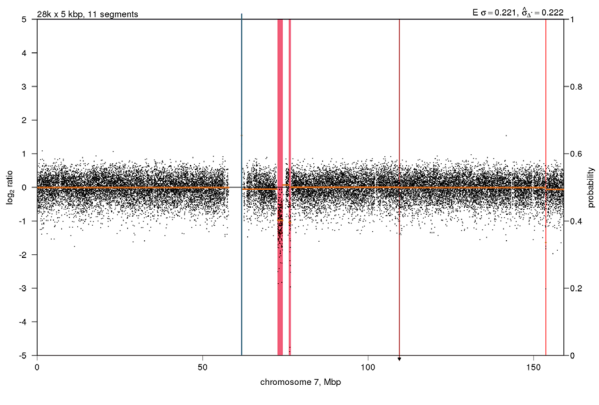
Blueprint Genetics Whole Genome Del/Dup (CNV) analysis detected a 1,42Mbp heterozygous deletion in chromosome 7 (chr7:72720001-74140000) encompassing the critical region associated with Williams syndrome.

Williams syndrome (WS, OMIM #194050) is generally a sporadic condition caused by de novo mutation. Rarely, in less than 5% of the cases, parent-to-child transmission is observed in autosomal dominant manner (PubMed: 26090456). Prenatal testing is possible but is rarely used because most cases occur in a single family member only; and no prenatal indicators exist for low-risk pregnancies. A study of WS patients in Norway reported a prevalence of 1:7,500 (PubMed: 12088082). Penetrance is 100% but expression of the phenotypic features is variable, and no single clinical feature is required to establish the diagnosis. WS is characterized by cardiovascular disease (e.g. supravalvar aortic stenosis, peripheral pulmonary stenosis and arteriopathy), distinctive faces, connective tissue abnormalities, intellectual disability (usually mild), a specific cognitive profile, unique personality characteristics and abnormalities in growth and endocrine function. Feeding difficulties often lead to failure to thrive in infancy. Clinical diagnostic criteria are available for WS but the mainstay for diagnosis is detection of the contiguous gene deletion of the Williams-Beuren syndrome critical region (WBSCR) that encompasses the elastin gene (ELN), among 28 other genes. Approximately 95% of WS patients have a deletion of 1.55 Mb and 5% of 1.84 Mb. Microdeletions larger than 1.84 Mb or smaller than 1.55 Mb are termed “atypical,” occurring in only 2% of cases, and often also associated with atypical clinical manifestations (PubMed: 12796854). A more severe phenotype with lower cognitive ability is observed in individuals with very large deletions (>2-4 Mb) (PubMed: 12838549 and 18565486). Individuals with WBSCR deletions that include the usual telomeric breakpoint (including GTF2I) have classic WS features, including intellectual disability (PubMed: 10644452 and 12920091). Those with short WBSCR deletions, not involving deletion of GTF2I, including some individuals with short de novo deletions and families with “SVAS plus”, do not have intellectual disability but often demonstrate the WS cognitive profile (PubMed: 14556246). Comprehensive medical follow-up is recommended for WS patients (GeneReviews).

### CONCLUSION

Considering the current literature and well-established role of the identified microdeletion on 7q11.23 as a disease causing mutation, we classify it as pathogenic. Genetic counseling for the family is recommended.

**Chromosom 7 - Copy number profile for Patient sample**




**Chromosom 7 - Copy number profile for Control sample**