

How to Read Your Genetic Report

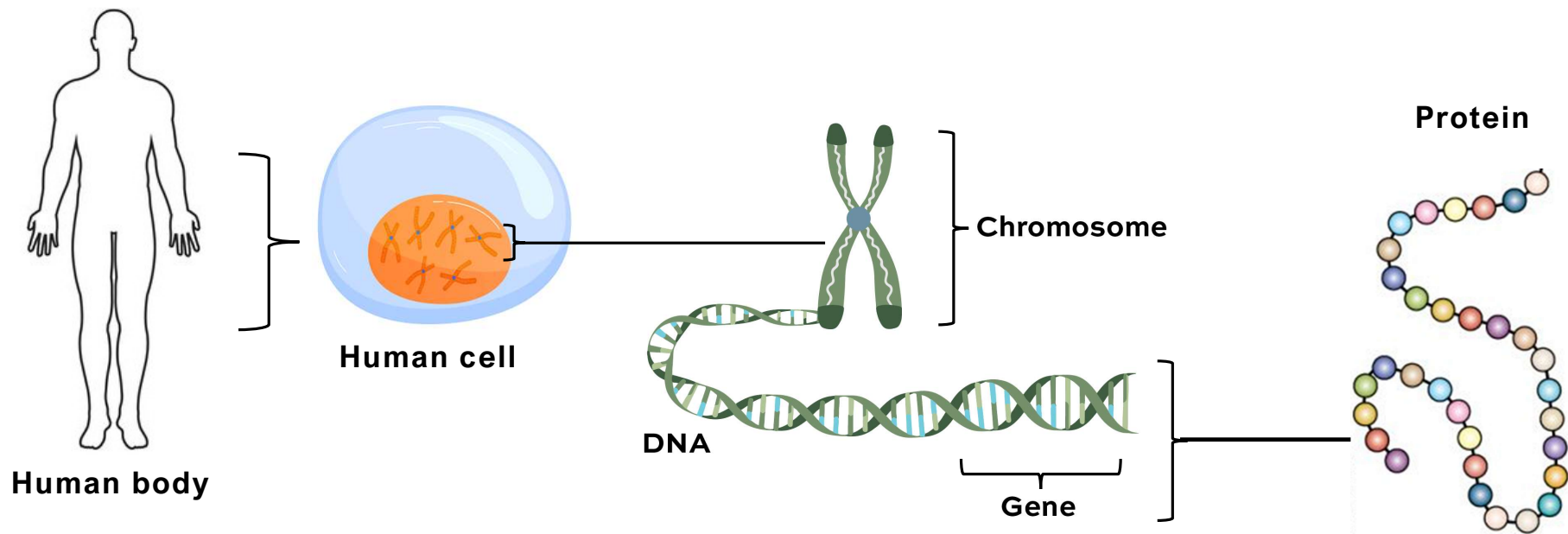
Erin McRoy, MS, CGC
September 16th, 2026



Agenda

- Basics of Genetics
- Components of a Report
- Types of Results
- Genotype vs Phenotype
- Your Report Goes Beyond You

Basics of Genetics

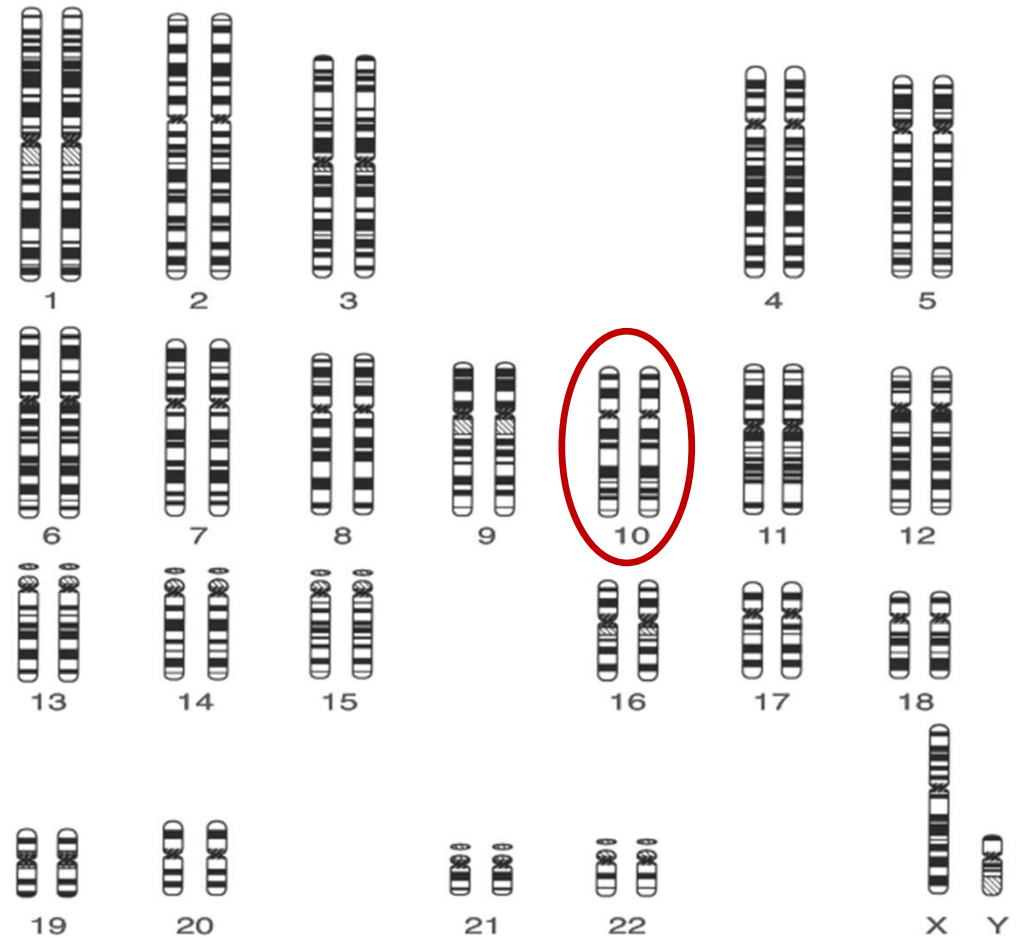


Basics of Genetics

- The gene associated with DeSanto-Shinawi syndrome is WAC and it is located on chromosome 10
- Variant = the specific change or alteration in the genetic code
 - Also called a “mutation”
 - There can be many different types of mutations associated with DESSH



Basics of Genetics



Basics of Genetics

- I often hear things like “my child tested positive for the gene for DeSanto-Shinawi syndrome” or “I tested negative for the gene”
 - We all have the WAC gene (2 copies: one from mom, one from dad)
 - The difference is what versions of the gene we have
 - DeSanto-Shinawi syndrome = having a non-working or altered version of the WAC gene due to a variant/mutation



Components of a Report

- DESSH can be diagnosed by a few different types of genetic tests
 - Panel: select number of genes are tested related to a particular set of symptoms
 - Whole exome or genome sequencing: all 20,000 genes are tested
 - Chromosomal Microarray: larger deletions or duplications of genetic material



Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
- Population Frequency
- Classification

Components of a Report

- Gene/Transcript
 - Specific region of the genetic code and its location
- Variant
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
- Population Frequency
- Classification

Components of a Report

- Gene/Transcript
- Variant
 - The change within the gene/chromosome and subsequent impact on the protein
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
- Population Frequency
- Classification

Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
 - Is the variant present in one or both copies of a gene
 - Do we know if the variant was inherited from a parent
- Disease/Condition
- Inheritance Pattern
- Population Frequency
- Classification

Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
- Disease/Condition
 - Associated diseases due to changes within that gene
- Inheritance Pattern
- Population Frequency
- Classification

Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
 - How a condition is passed down in families
- Population Frequency
- Classification

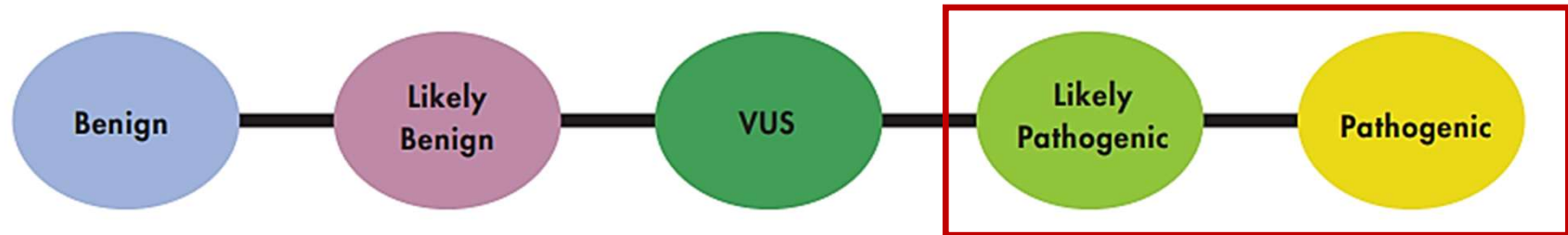
Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
- Population Frequency
 - How often we see this gene variant in healthy people of the general population
- Classification

Components of a Report

- Gene/Transcript
- Variant
- Zygosity/Inheritance
- Disease/Condition
- Inheritance Pattern
- Population Frequency
- Classification
 - Benign, Likely Benign, VUS, Likely Pathogenic, Pathogenic

Components of a Report



Components of a Report

Gene, Transcript	Variant Details	Zygosity (inheritance)	Disease and inheritance pattern	Population frequency*	Classification
WAC NM_016628.5	c.1405del p.Ile469Serfs*16 ClinVar ID: N/A	Heterozygous (De Novo)	DeSanto-Shinawi syndrome Autosomal dominant MIM#616708	N/A	Pathogenic

- WAC is the name of the gene
- NM_016628.5 is the location of the gene in the genetic code

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- c.1405del is the change in the gene/DNA
- p.Ile469Serfs* is the change in the protein
- ClinVar ID provides more information on the specific variant

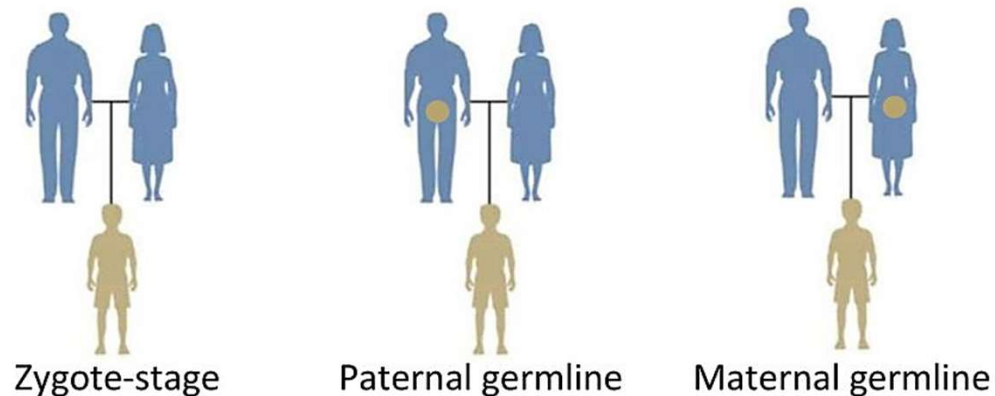
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- Heterozygous means the variant is present on only one copy of the WAC gene
- De Novo means this variant was not inherited from either parent, it is brand new in the patient

Components of a Report

De novo mutations



- Risk of recurrence would be considered <1%.
- The reason why there is some residual risk of recurrence is due to a rare phenomenon called “gonadal mosaicism”.
- This is when a parent carries a genetic change, but it is limited to a small cluster of their egg or sperm cells.

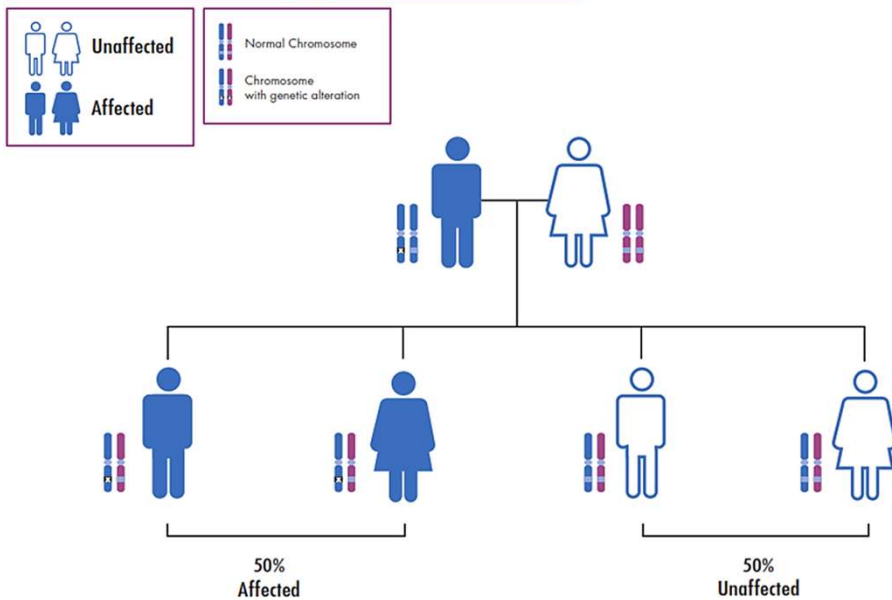
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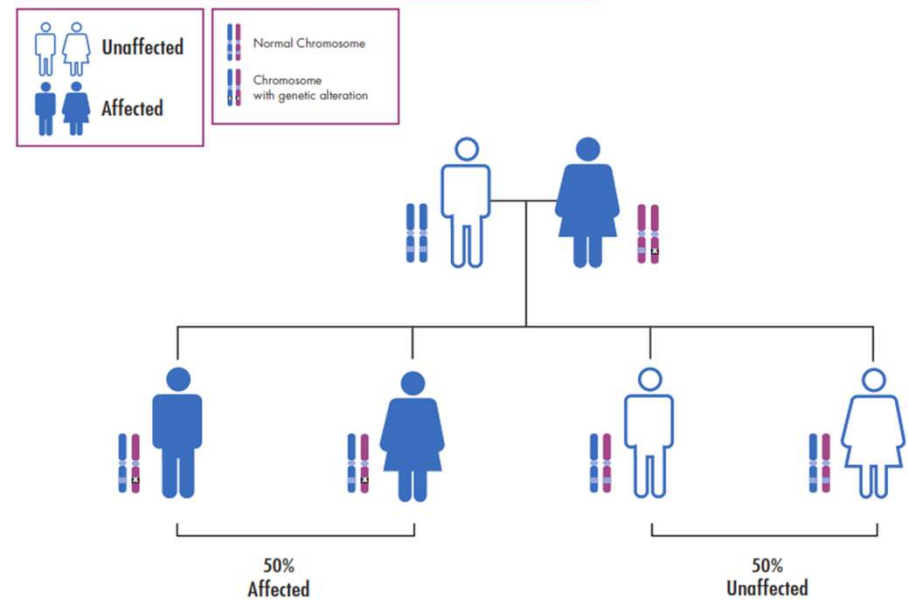
- DeSanto-Shinawi syndrome is the genetic condition that is caused by changes in this gene
- Autosomal dominant is the inheritance pattern
- MIM# is the database entry for information about DeSanto-Shinawi syndrome

Components of a Report

Autosomal Dominant Segregation, Affected Father



Autosomal Dominant Segregation, Affected Mother



Components of a Report

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There is no data on how common this variant is in the general population data (indicates it is rare)

Components of a Report

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There is enough data/evidence to say this variant disrupts the gene and protein and is associated with disease

Components of a Report

CNV	TYPE	SIZE	INHERITANCE	CLASSIFICATION	CONDITION
seq[GRCh38] 10p12.1(chr10:28499287_28610012x1)	Deletion	~110.72 kb	Unknown (not maternal)	Pathogenic	WAC deletion syndrome (Autosomal Dominant)



- This variant is a deletion within chromosome 10 that includes part of the *WAC* gene
- seq[GRCh38] 10p12.1(chr10:28499287_28610012x1) tells us the coordinates of the deletion in the chromosome
- ~110.72 kb tells us the size of the deletion

Components of a Report

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Only the mother provided a sample to use in comparison, and she was not found to carry the mutation. We do not know if this deletion was inherited from the patient's father or is brand new in the patient.

Types of Results

CAUSATIVE VARIANTS IN DISEASE GENES ASSOCIATED WITH REPORTED PHENOTYPE:						
Gene	Disease	Mode of Inheritance	Variant	Zygosity	Inherited From	Classification
WAC	Desanto-Shinawi syndrome	Autosomal Dominant	c.451 C>T p.R151X	Heterozygous	Unknown	Pathogenic Variant

Position 451

...ATGCGATCGAT**C**ACAACCTGTGGAT...



...ATGCGATCGAT**T**ACAACCTGTGGAT...

Nonsense Mutations end the instructions too soon

THE CAR WAS RED. → THE CAR. _____

Types of Results

Gene	Disease	Mode of Inheritance	Variant	Zygosity	Inherited From	Classification
WAC	DeSanto-Shinawi Syndrome	Autosomal Dominant	c.255_256delAG p.R85SfsX2	Heterozygous	De Novo	Pathogenic Variant

Position 255_256

...ATGCGATCGAT**AG**CAACCTGTGGAT...



...ATGCGATCGAT__CAACCTGTGGAT...

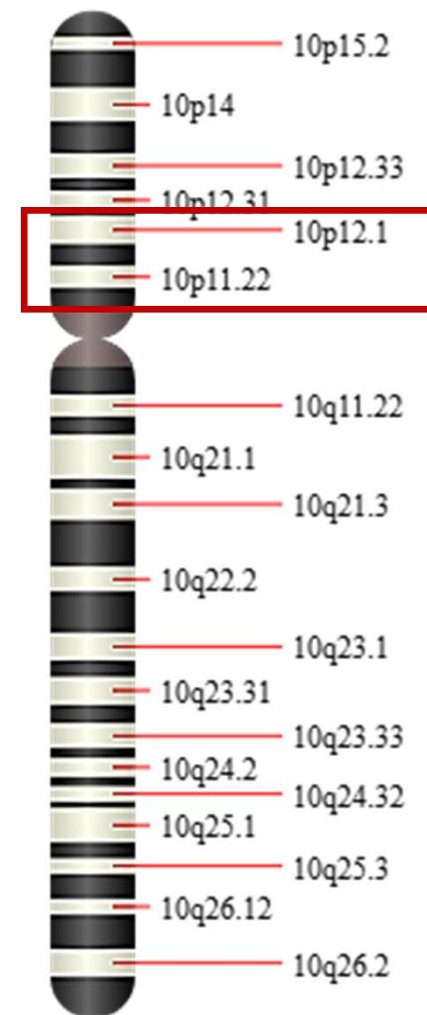
Deletion Mutations change the meaning by subtracting words or letters

THE CAR WAS RED. → THE __ WAS RED.
→ THE _AR WAS RED.

Types of Results

- 10p12.1p11.23(26,961,513_30,519,006)x1
- Some patients may have a larger deletion (mutation) identified on their genetic report
- These patients may have different/more severe symptoms because other genes may be missing in addition to the WAC gene
- May also be referred to as 10p12p11 deletion syndrome

Chromosome 10

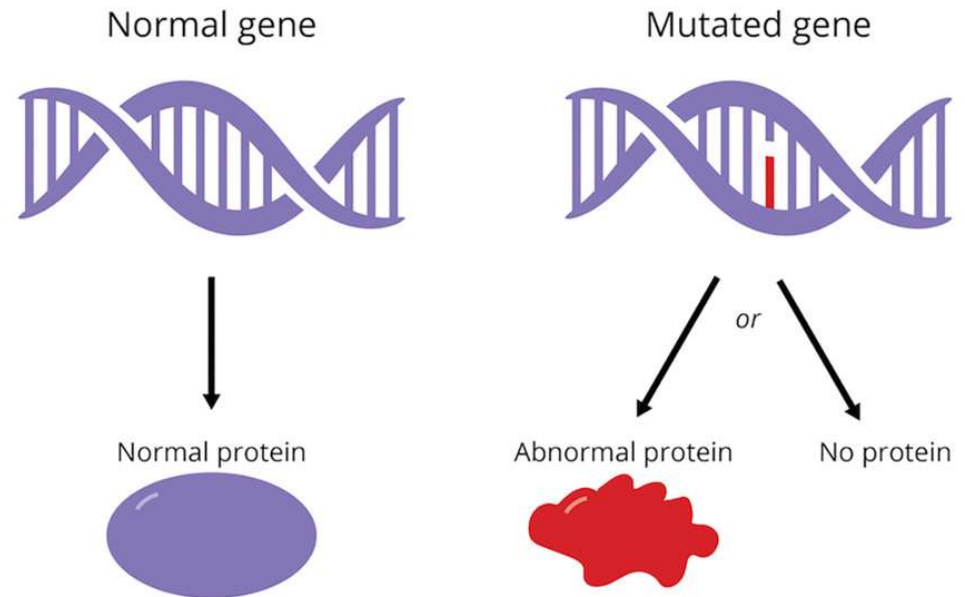


16 genes: WAC, MPP7, ARMC4, MKX, BAMBI, LYZL1, SVIL, IFRX, PDSS1, ACBD5, RAD18, ANKRD26, MASTL, ABI1, YME1L1, PTCHD3, JCAD

Genotype vs Phenotype

Different mutations in a gene can have different effects on the protein

- Type of mutation
- Where in the gene it occurs



Genotype vs Phenotype

Not everyone with the DeSanto-Shinawi syndrome shows all the same symptoms/features

- Different impacts of a specific mutation/variant on the protein's function
- Other genetic modifiers in the DNA/mutations in other genes and regions
- Non-genetic factors (environment, pregnancy exposures/complications, etc.)

Your Report Goes Beyond You

- New mutations in “hotspots” in the WAC gene are being discovered
- Research is being done to see if certain symptoms are more commonly seen with certain mutations
 - Databases and patient registries
 - Aim is to provide more tailored information for patients and families about what to expect and care management
- Research can also lead to new treatments and therapies for DESSH



References



- Rare Chromosome Disorder Support Group. (2016). 10p proximal deletions from 10p11 & 10p12. Unique: Understanding Rare Chromosome and Gene Disorders. Retrieved September 15, 2026, from <https://rarechromo.org/disorder-guides/>
- Greenwood Genetic Center. (2020). *Genetic Counseling Aids* (7th ed.).