Variant Nomenclature

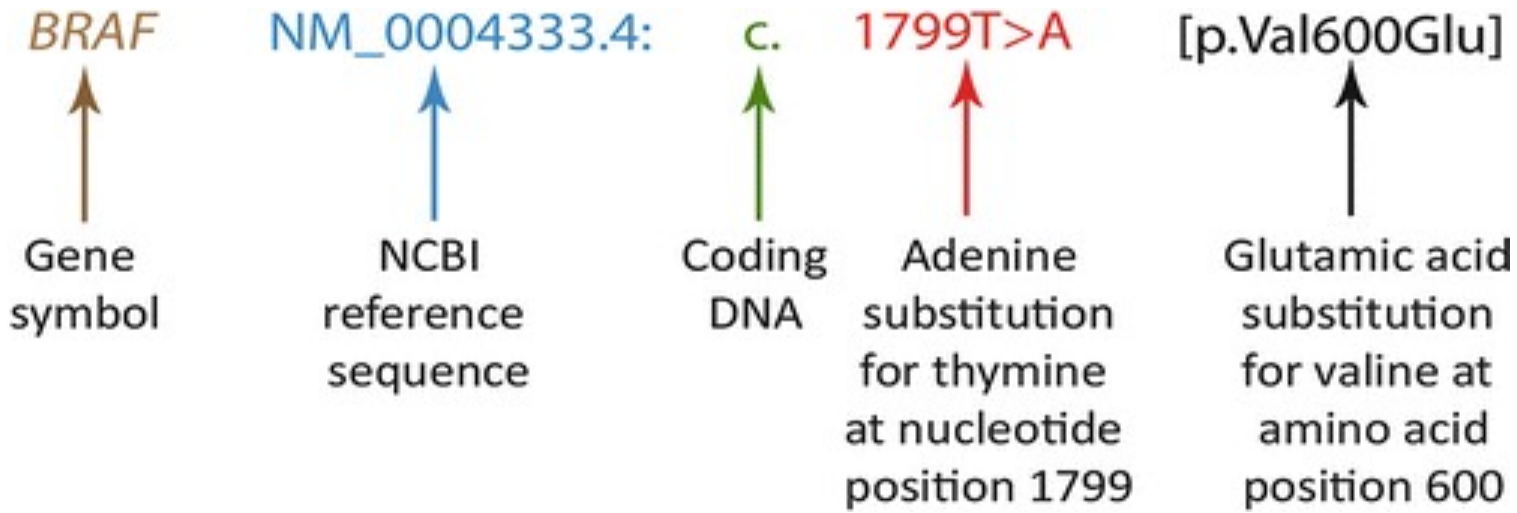
Sep 3, 2022

Objectives

By the end of the session, the students should be able to:

1. Describe the components of standard variant nomenclature
2. Explain the abbreviations in variant nomenclature
3. Recognize type of mutation from its molecular name

Standard variant nomenclature



Sequence Variant Nomenclature

http://varnomen.hgvs.org/

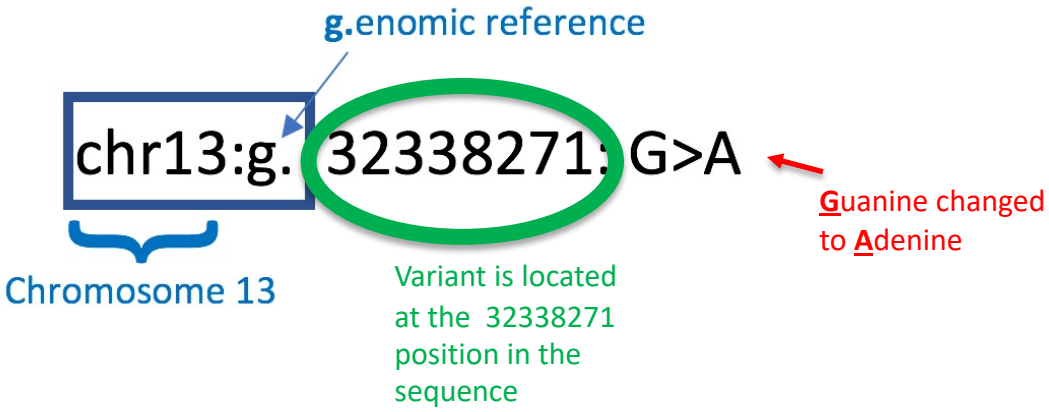
Letter Prefix.

- a **letter prefix** is mandatory to indicate the type of reference sequence used. Accepted prefixes are;
  - "**c.**" for a coding DNA reference sequence
  - "**g.**" for a linear genomic reference sequence
  - "**m.**" for a mitochondrial DNA reference sequence
  - "**n.**" for a non-coding DNA reference sequence
  - "**p.**" for a protein reference sequence
  - "**r.**" for an RNA reference sequence (transcript)

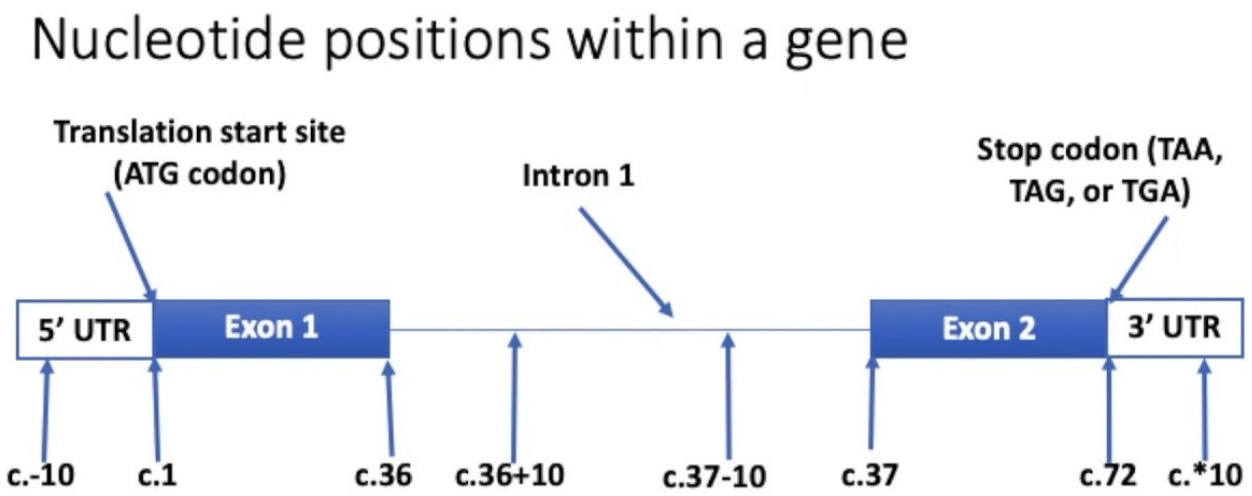
Numbering

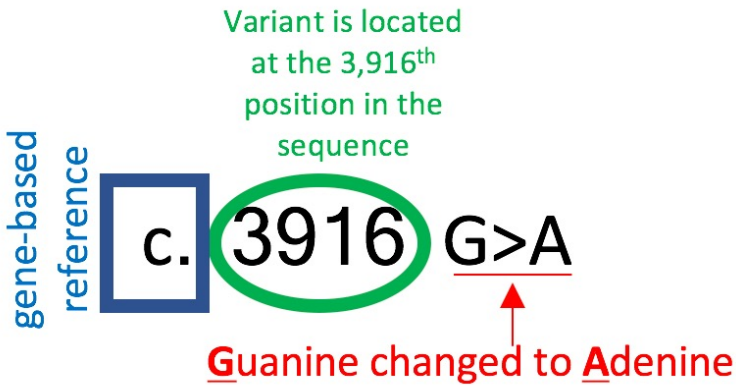
- Genomic reference sequence nucleotide numbering is g.1, g.2, g.3, …, etc. from the first to the last nucleotide of the reference sequence.

Example:

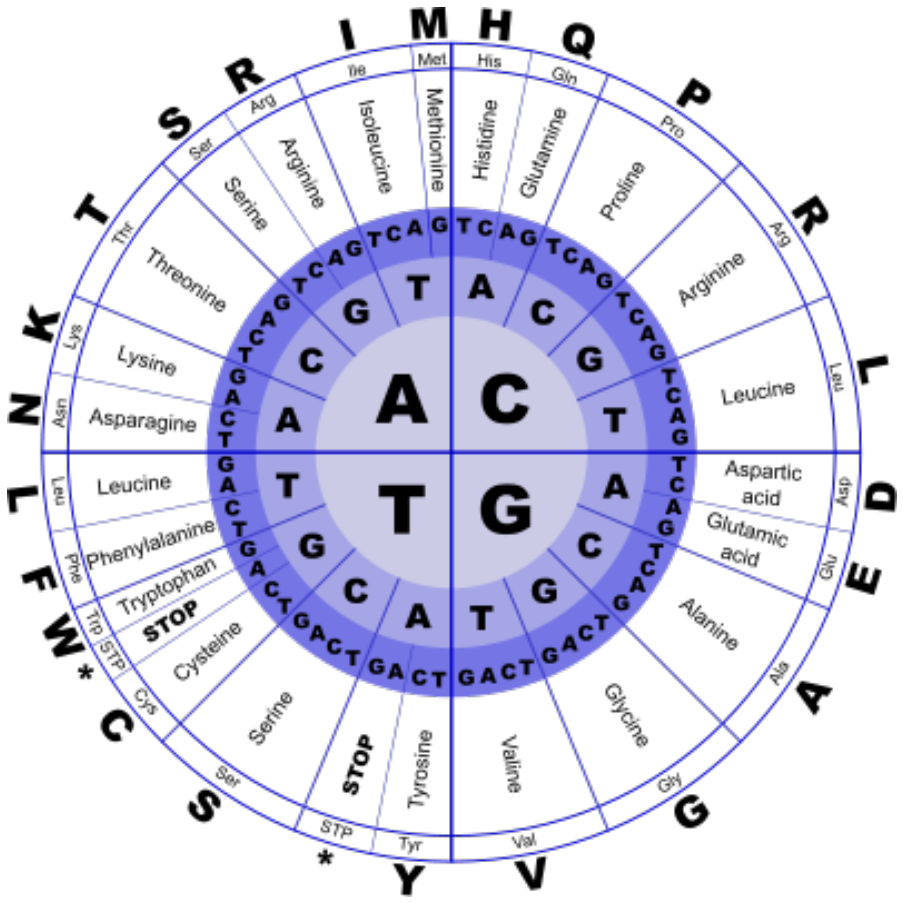


Coding DNA reference sequences (c.):





Letters



Amino acid	Three letter symbol	One letter symbol*
Alanine	Ala	A
Arginine	Arg	R
Asparagine	Asn	N
Aspartic acid	Asp	D
Cysteine	Cys	C
Glutamic acid	Glu	E
Glutamine	Gln	Q
Glycine	Gly	G
Histidine	His	H
Isoleucine	Ile	I
Leucine	Leu	L
Lysine	Lys	K
Methionine	Met	M
Phenylalanine	Phe	F
Proline	Pro	P
Serine	Ser	S
Threonine	Thr	T
Tryptophan	Trp	W
Tyrosine	Tyr	Y
Valine	Val	V

No need to memorize this!

Gene symbols

- Find the gene name and related genetic disorder in OMIM database:

https://omim.org/

Example: BRAF gene

If entered in OMIM , disease name and mode inheritance will be shown

*164757

Table of Contents

Alternative titles; symbols

V-RAF MURINE SARCOMA VIRAL ONCOGENE HOMOLOG B1
ONCOGENE BRAF
BRAF1
RAFB1

Other entities represented in this entry:

BRAF/AKAP9 FUSION GENE, INCLUDED
BRAF/KIAA1549 FUSION GENE, INCLUDED

HGNC Approved Gene Symbol: BRAF

Cytogenetic location: 7q34 *Genomic coordinates (GRCh38): 7:140,713,328-140,924,929* (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype Clinical Synopses	Phenotype MIM number	Inheritance	Phenotype mapping key
7q34	Adenocarcinoma of lung, somatic	211980		3
	Cardiofaciocutaneous syndrome	115150	AD	3
	Colorectal cancer, somatic	114500		3
	LEOPARD syndrome 3	613707	AD	3
	Melanoma, malignant, somatic	155600		3
	Nonsmall cell lung cancer, somatic	211980		3
	Noonan syndrome 7	613706	AD	3

PheneGene Graphics

External Links
Genome
DNA
Protein
Gene Info
Clinical Resources
Variation
ClinVar
DECIPHER
gnomAD
GWAS Catalog
GWAS Central
HGMD
NHLBI EVS
PharmgKB
Animal Models
Cellular Pathways

What is type of mutation?

	Name of mutation
A	c.482G>A; p.R117H
B	c.1756G>T; p.G542X
C	c.16_17delAG; p.Ser6ProfsX2

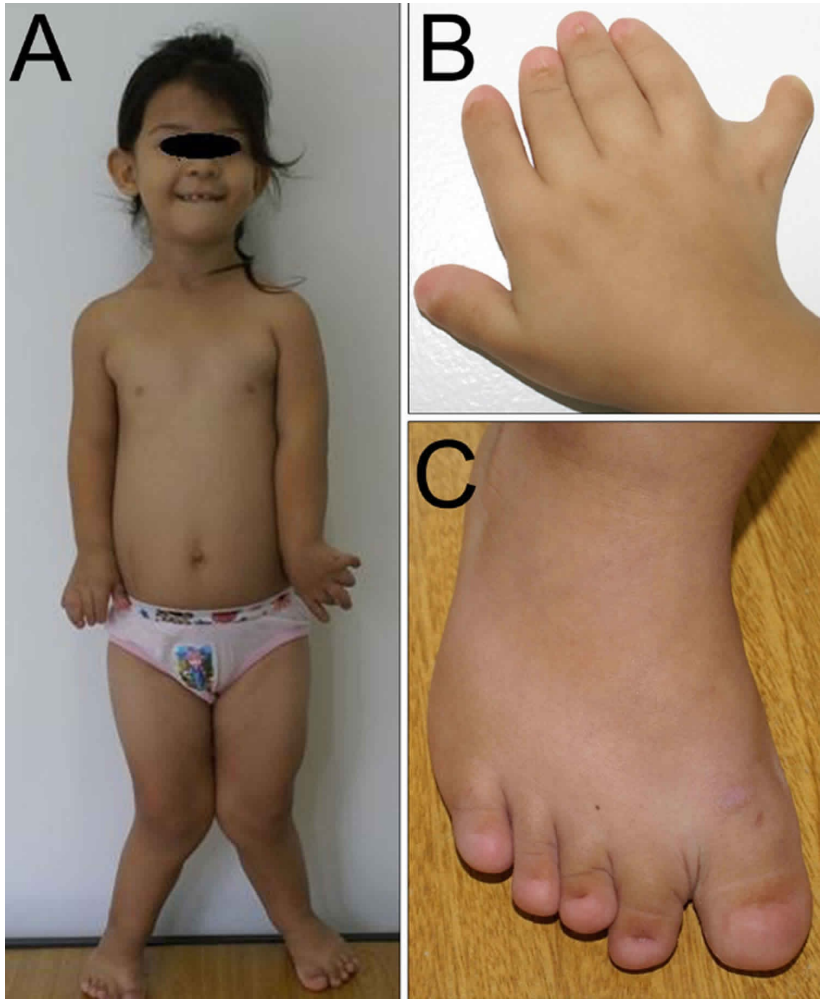
A.Missense
B.Nonsense
C.Frameshift

Case 1

- 4 year old girl with bilateral postaxial polydactyly; Conical shaped tooth; Genu valgum; Long philtrum; Low hanging columella; Nail dysplasia; Short stature; Smooth philtrum; Thin lower lip vermilion.
- Genetic test showed:

Homozygous likely pathogenic variant:

EVC: NM_153717.2:c.2T>A



- What is the diagnosis?
- What does it mean by homozygous variant?
- How this disorder is inherited?
- Describe the molecular change?

Case 2

- 7 year old boy known to have chronic diarrhoea and vomiting since birth.
- Genetic test showed:

Homozygous pathogenic variant in:

SLC26A3:NM_000111.2: c.559G>T ; p.(Gly187*)

- What is the diagnosis?
- What does it mean by homozygous variant?
- How this disorder is inherited?
- Describe the molecular change?
- What is the type of mutation based on mutation name?

References

- Genetic Variation, Comparative Genomics, and the Diagnosis of Disease. Evan E. Eichler. N Engl J Med. 2019 July 04; 381(1): 64–7
- HGVS Recommendations for the Description of Sequence Variants: 2016 Update. Johan T. den Dunnen et al. HUMAN MUTATION, Vol. 37, No. 6, 564–569, 2016
- Tandem repeats mediating genetic plasticity in health and disease. Anthony J. Hannan. Nat Gen 2018

THANK YOU