

## Unit 1 Introduction to Clinical Bioinformatics

### # Cheat Sheet 1 SOP of AOV (Standard Operating procedure for Analysis of Variants)

#### Summary

**Cosmic Track** (gene name, specific base changes, forward or reverse strand, cDNA numbering, variant position, nearby variant, exon number)

**dbSNP** transcript an variant call in **HGVS** format e.g. NM\_000435.2:c.743G>C and SNP ID, Chromosome coordinates and position

**Minor allele, frequency of allele, count of alleles**

**Clinical significance**

**SIFT**

**Mutation taster**

**Polyphen 2**

#### Conservation

Requires a screenshot of **protein domains**.

Nucleotide considerations

**Orthologues**

**BAM** Alignment

Calculation of a **GVGD** output

**Grantham distance** (GD- a measure of physiochemical differences between amino acids and Grantham variation GV – a measure of species conservation)

**Screenshot of a GVG D output, Polyphen – 2 screenshot Hum/Var, SIFT output**

Comparing **amino acid** screenshots

**Splicing**

#### Databases

**gnomAD** screenshot

**dbSNP** screenshot

**Ensembl** screenshots

Specific disease database screenshot

**HGMD** database screenshot

**OMIM** screenshot

**UCSC** screenshot

**GEN ATLAS**

**UNIPROT** screenshot

Written summary of each screenshot

#### Functional

Use Uniprot to identify the protein and domain regions that could be affected by the **variant**

When a missense variant **evaluate** the region where the variant is located and determine the level of local or regional constraint

Screenshot of uniprot for **topology, family** and **domains** and amino acid modification

Write a summary of the **VAF (variant allele frequency)**

Use **decipher** for a screenshot of the gene, protein under view

#### Classification

Evaluate the **RED** evidence of **PATHOGENIC**

Evaluate the **GREEN** evidence of **BENIGN**

Final Classification

1. Benign
2. Likely Benign
3. Uncertain Significance
4. Likely Pathogenic
5. Pathogenic

Use **ACMG** reference criteria

#### References

Make a note of all relevant publications for this and related **variants**