ΑΝΘΡΩΠΙΝΟ ΓΟΔΙΩΜΑ

22.000 ΓΟΝΙΔΙΑ (ΠΕΡΙΠΟΥ)

ΑΛΛΗΛΟΥΧΙΑ 4 ΒΑΣΕΩΝ ( 3ΔΙΣ. ΑΛΛΗΛΛΥΧΙΑ ΒΑΣΕΩΝ)

23 ΖΕΥΓΗ ΧΡΩΜΟΣΩΜΑΤΩΝ

ΜΕΤΑΛΛΑΞΕΙΣ

SNP (SINGLE NUCLEOTIDE POLYMORPHISM) (ΑΛΛΑΓΗ ΜΙΑ ΒΑΣΗΣ (CODON) SE MIA ΑΛΛΗ

SMALL INDELS (INSERTIONS / DELETIONS)

ACTGAGGTATC

ACTG[G]GGTATC ΜΕΤΑΛΛΑΞΗ/ΠΟΛΥΜΟΡΦΙΣΜΟΣ

TGACTCCATAG

ACTGA[-]GTATC (DELETION)

ACTGAGGTA[ACT]TC (INSERTION)

CNV (COPY NUMBER VARIATIONS)

(1 EXONS – 1 CHROMOSOME)

(EXON 2,3 DEL / EXON 18-20 DUP)

(T21, TRISOMY 21, DOWN SYNDROME)

ΓΟΝΙΔΙΟ (GENE)

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Introns (-)

Exons (/)

Human Genomes: hg36 / hg37 / hg38 (T2T)

3 codons -----🡪 aminoacid

ΕΝΤΟΠΙΣΜΟΣ ΑΛΛΑΓΩΝ ΣΤΟ DNA (3 TΡΟΠΟΥΣ)

1. GENOMIC COORDINATES (genomic) g.7:117.123.333 C/T (C > T) (HG37)
2. CFTR (codon) c.1524 C/T ….c.1524 C > T (HG37)
3. CFTR (protein) p.508 PHE/TYR …… OR …… p.508 PHE/PHE

CFTR p.508 DEL PHE ….. // …. CFTR c.1524-1526 del CTT

ΚΑΤΗΓΟΡΙΕΣ ΜΕΤΑΛΛΑΞΕΩΝ

Nonsynonymous (aminoacid change, exonic mutations)

Synonymous (no aminoacid change intronic mutations)

Nonsynonymous: a) Missense b) Nosense

FILTRATION OF GENOMIC INFORMATION

HBB (B-GLOBIN) ΜΙΚΡΟ ΓΟΝΙΔΙΟ (1 EXON)

CFTR (ΚΥΣΤΙΚΗ ΙΝΩΣΗ, CYSTIC FIBROSIS) (27 EXONS)

DMD (180 EXONS)

PROTOCOL OF GENOMIC ANALYSIS

(FAMILY HISTORY)

DNA ISOLATION (BLOOD, SALIVA, BUCCAL SWABS)

1. NEXT GENERATION SEQUENCING
2. ALLIGNMENT WITH HUMAN GENOME (HG36,37,38)
3. VARIANT CALLING (WHOLE EXOME SEQUENCING 30.000-50.000 MUTATIONS // WHOLE GENOME SEQUENCING 6-8.000.000 MUTATIONS)

FROM STEPS 1-2-3 -🡪>> RAW DATA

FASTQ (Q=QUALITY, 20-30-40)

20 1:1.00

30 1:1.000

40:1:10.000

BAM (ALIGNMENT)

VCF

VARIANT ANNOTATION: DATABASES

1. CLINVAR (PATHOGENIC // LIKELY PATHOGENIC // BEGIGN // LIKELY BENIGH // VUS (VARIANT OF UNCKNOWN SIGNIFICANCE)

(REANALYSIS)

B. GNOMAD (population percentage)

i.e 1% -- 10% -- 80% -- 0,000001% --- 0%

1. OMIM (genes clinical characteristics – phenotype)

BRCA1 Cancer

Cftr cyctic fibrosis

Mybpc3 hypertrophic cardiomyopathy

Gjb2 deafness

GENE PANELS (HPO-human phenotype ontology // publications // diagnostic laboratories (blueprint)

**In Silico Predictors**

Transcript-specific predictors SIFT and Polyphen are listed with Variant Effect Predictor annotations.

* CADD: 27.9
* PrimateAI: 0.322

WES VS WGS

ΓΟΝΙΔΙΟ (GENE) – WHOLE EXOME SEQUENCING

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Introns (-), Exons (/)

ΓΟΝΙΔΙΟ (GENE) – WHOLE GENOME SEQUENCING

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Introns (-), Exons (/)