Catch-23

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A NOVEL BY

Challenge: filtering structural variants is limited by population databases

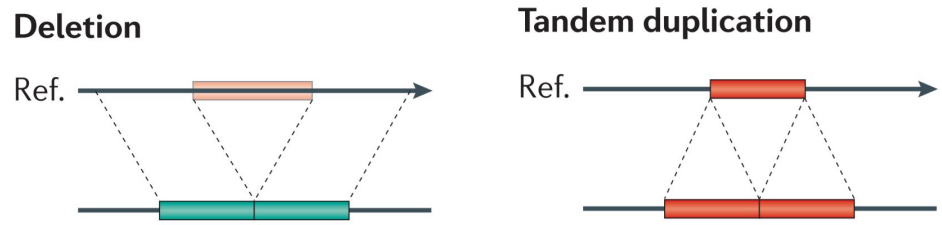
Parliament2 build passing

DNAnexus

16,822

PASS only

6,110



5,102

5,021

gnomAD

genome aggregation database

3,795

Less than 1,000,000 bp

3,243

exonic

188

We explored immune variants which were previously identified

IMMPORT
BIOINFORMATICS FOR THE FUTURE OF IMMUNOLOGY

1,811 immune genes

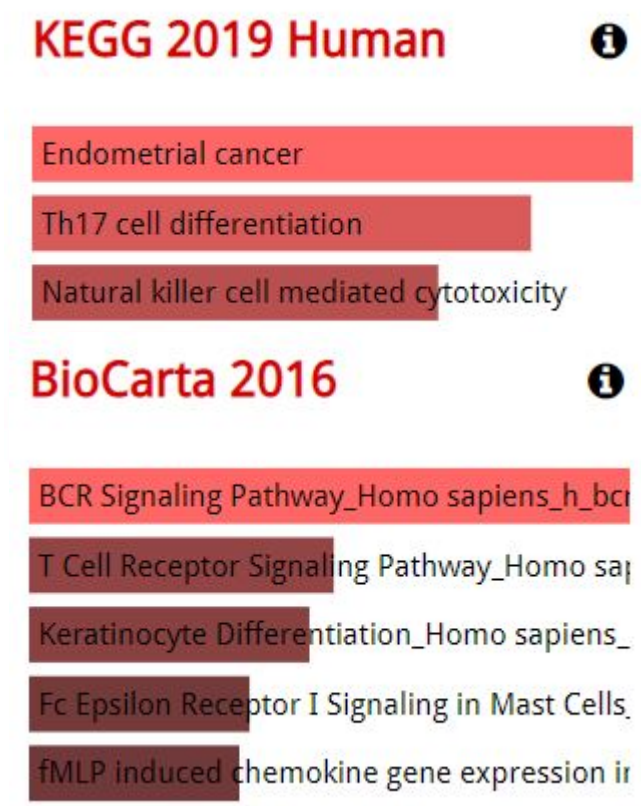
WGS DeepVariant

134,936 variants

Ensembl Variant Effect Predictor
MAF < 1%

693 genes

Enrichr



High impact from VEP
High CADD, Condel, LoFtool

PDGFRL
- Sequence similarity to ligand binding domain of platelet-derived growth factor receptor
- Tumor suppressor?

IFIH1
- Instructions for producing MDA5
- Important role in innate immunity

We identified an intriguing SNV + SV in PDE4DIP by combining approaches

dbscSNV = 0.886
absent from gnomAD

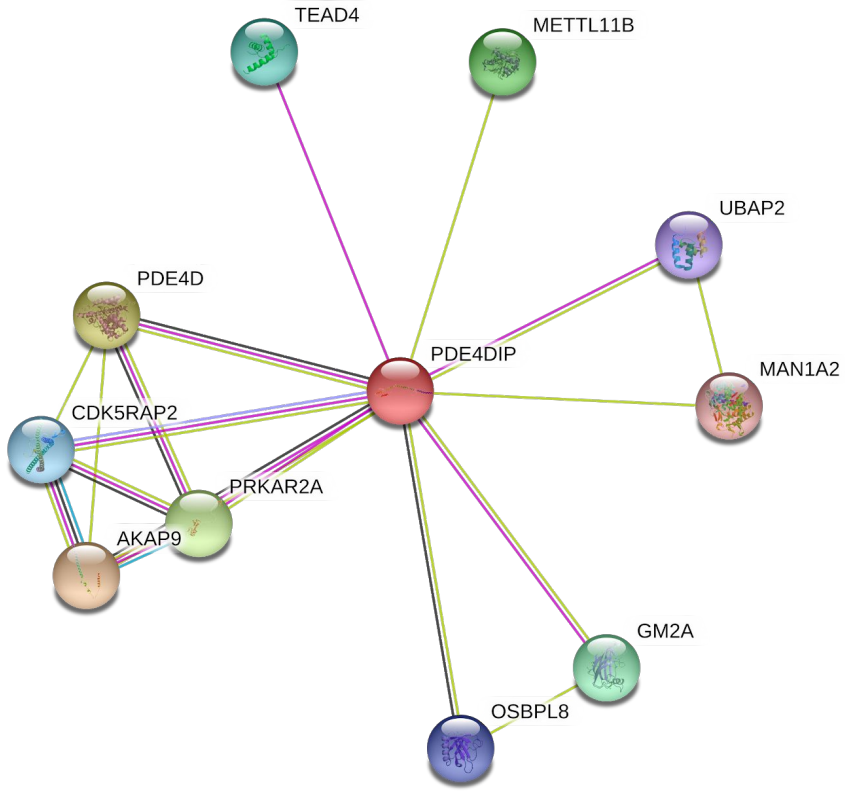
AG|AC exon 13

splice acceptor site

-4 exon het deletion
-Exons 18-21
-Absent from gnomAD SVs
-Predicted by StrVCTURE to be deleterious (0.92)

PDE4DIP (myomegalin) is important for cell movement

- Anchor protein on the Golgi/centrosome
- Important for microtubule assembly and cell movement
- Defects may cause myeloproliferative disorder (MBD) associated with eosinophilia
  - Eosinophils are important for fighting multicellular parasites
  - Associated with allergy and asthma



Transcriptomic and parental data will be used to confirm our findings

- Combine with transcriptomic data
  - How do these variants affect gene expression?
  - How are they manifested at the phenotype level?
    For example, missing receptors on immune cells, different proportions of cells in circulation?
  - Better understand the link between genotype and phenotype
- Genotypes from parents
  - Phasing to confirm compound heterozygote
  - De Novo structural variants and single nucleotide variants