Analyse mit Exomiser:

## yml Datei erstellen mit Pfad zur ped, vcf, proband sample name und phänotypen

## Exomiser Analysis Template.

# These are all the possible options for running exomiser. Use this as a template for

# your own set-up.

---

analysis:

**ped: /PATH/TO/PED**

**proband: PROAND\_SAMPLE\_NAME**

**vcf: /PATH/TO/VCF**

# AUTOSOMAL\_DOMINANT, AUTOSOMAL\_RECESSIVE, X\_RECESSIVE or UNDEFINED

inheritanceModes: {

AUTOSOMAL\_DOMINANT: 0.1,

AUTOSOMAL\_RECESSIVE\_HOM\_ALT: 3.0,

AUTOSOMAL\_RECESSIVE\_COMP\_HET: 5.0,

X\_DOMINANT: 0.1,

X\_RECESSIVE\_HOM\_ALT: 3.0,

X\_RECESSIVE\_COMP\_HET: 5.0,

}

#FULL, SPARSE or PASS\_ONLY

analysisMode: PASS\_ONLY

#hpoIds: ['HP:0100280']

hpoIds: []

#Possible frequencySources:

#Thousand Genomes project http://www.1000genomes.org/

# THOUSAND\_GENOMES,

#ESP project http://evs.gs.washington.edu/EVS/

# ESP\_AFRICAN\_AMERICAN, ESP\_EUROPEAN\_AMERICAN, ESP\_ALL,

#ExAC project http://exac.broadinstitute.org/about

# EXAC\_AFRICAN\_INC\_AFRICAN\_AMERICAN, EXAC\_AMERICAN,

# EXAC\_SOUTH\_ASIAN, EXAC\_EAST\_ASIAN,

# EXAC\_FINNISH, EXAC\_NON\_FINNISH\_EUROPEAN,

# EXAC\_OTHER

frequencySources: [

THOUSAND\_GENOMES,

TOPMED,

UK10K,

ESP\_AFRICAN\_AMERICAN, ESP\_EUROPEAN\_AMERICAN, ESP\_ALL,

EXAC\_AFRICAN\_INC\_AFRICAN\_AMERICAN, EXAC\_AMERICAN,

EXAC\_SOUTH\_ASIAN, EXAC\_EAST\_ASIAN,

EXAC\_FINNISH, EXAC\_NON\_FINNISH\_EUROPEAN,

EXAC\_OTHER,

GNOMAD\_E\_AFR,

GNOMAD\_E\_AMR,

# GNOMAD\_E\_ASJ,

GNOMAD\_E\_EAS,

GNOMAD\_E\_FIN,

GNOMAD\_E\_NFE,

GNOMAD\_E\_OTH,

GNOMAD\_E\_SAS,

GNOMAD\_G\_AFR,

GNOMAD\_G\_AMR,

# GNOMAD\_G\_ASJ,

GNOMAD\_G\_EAS,

GNOMAD\_G\_FIN,

GNOMAD\_G\_NFE,

GNOMAD\_G\_OTH,

GNOMAD\_G\_SAS

]

#Possible pathogenicitySources: POLYPHEN, MUTATION\_TASTER, SIFT, CADD, REMM

#\*WARNING\* if you enable CADD, ensure that you have downloaded and installed the CADD tabix files

#and updated their location in the application.properties. Exomiser will not run without this.

pathogenicitySources: [POLYPHEN, MUTATION\_TASTER, SIFT]

#this is the standard exomiser order.

#all steps are optional

steps: [

#intervalFilter: {interval: 'chr10:123256200-123256300'},

#genePanelFilter: {geneSymbols: []},

#failedVariantFilter: {},

qualityFilter: {minQuality: 20.0},

variantEffectFilter: {remove: [UPSTREAM\_GENE\_VARIANT,

INTERGENIC\_VARIANT,

NON\_CODING\_TRANSCRIPT\_INTRON\_VARIANT,

SYNONYMOUS\_VARIANT,

DOWNSTREAM\_GENE\_VARIANT]},

#knownVariantFilter: {}, #removes variants represented in the database

frequencyFilter: {maxFrequency: 5.0},

pathogenicityFilter: {keepNonPathogenic: true},

#inheritanceFilter and omimPrioritiser should always run AFTER all other filters have completed

#they will analyse genes according to the specified modeOfInheritance above- UNDEFINED will not be analysed.

inheritanceFilter: {},

#omimPrioritiser isn't mandatory.

omimPrioritiser: {},

#priorityScoreFilter: {minPriorityScore: 0.4},

#Other prioritisers: Only combine omimPrioritiser with one of these.

#Don't include any if you only want to filter the variants.

hiPhivePrioritiser: {},

# or run hiPhive in benchmarking mode:

#hiPhivePrioritiser: {runParams: 'mouse'},

#phivePrioritiser: {}

#phenixPrioritiser: {}

#exomeWalkerPrioritiser: {seedGeneIds: [11111, 22222, 33333]}

]

outputOptions:

outputPassVariantsOnly: false

#numGenes options: 0 = all or specify a limit e.g. 500 for the first 500 results

numGenes: 0

#outputPrefix options: specify the path/filename without an extension and this will be added

# according to the outputFormats option. If unspecified this will default to the following:

# {exomiserDir}/results/input-vcf-name-exomiser-results.html

# alternatively, specify a fully qualifed path only. e.g. /users/jules/exomes/analysis

outputPrefix: analysis/results

#out-format options: HTML, TSV-GENE, TSV-VARIANT, VCF (default: HTML)

outputFormats: [TSV-GENE, TSV-VARIANT, VCF, HTML]

## Starten des Durchlaufs

Auf dem cluster mit:

module load IKMB Java/1.8.0 && sbatch --exclude=rzcl236 -p ikmb\_a --qos ikmb\_a -J exomiser --mem=16G -t 2:0:0 --wrap="java -Xms8g -Xmx16g -jar /ifs/data/nfs\_share/ikmb\_repository/software/exomiser/10.0.0/exomiser-cli-10.0.0.jar --analysis analysis/config\_exomiser.yml"

## Ausführen von run\_pipieline.py

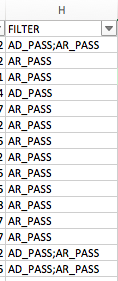
Parameter:

exomiser\_path = '/Users/broder/projects/IBD-DACH\_FT\_3/exomiser/analysis'

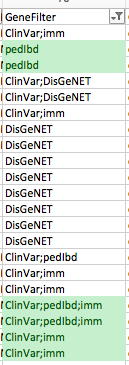
annovar\_path = '/Users/broder/projects/IBD-DACH\_FT\_3/variants.merged.normalized.vcf.gz.annovar.hg19\_multianno.txt'

output\_path = '/Users/broder/projects/IBD-DACH\_FT\_3/result.tsv'

- Merged die Varianten von den verschiedenen Exomiser Inheritance Dateien zusammen



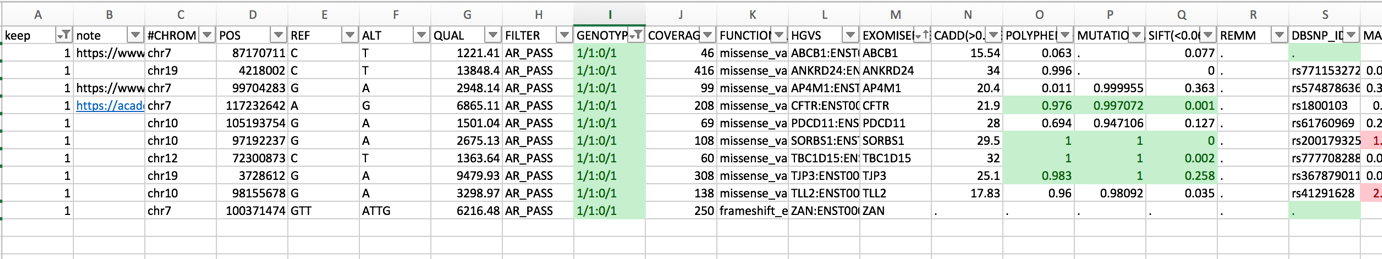
- Wendet die verschiedenen Genlisten auf die Varianten an



- Fügt die AnnoVar Annotation für jede Variante hinten an die Exomiser Outputdatei

## Kopieren der Ergebnisse in das Result Template

## Filtern



## Extrahieren der gefilterten Varianten zu einem vcf

Sub toVcf()

Dim sh As Worksheet

Dim rw As Range

Dim keep As Integer

outputFile = FreeFile

Open "/Users/broder/tmp/vcf\_output.vcf" For Output As #outputFile

Print #outputFile, "#CHROM" & vbTab & "POS" & vbTab & "ID" & vbTab & "REF" & vbTab & "ALT" & vbTab & "QUAL" & vbTab & "FILTER" & vbTab & "INFO"

Set sh = ActiveSheet

start = 3

For Each rw In sh.Rows

If sh.Cells(rw.Row, 1).Value = "1" Then

chromTmp = sh.Cells(rw.Row, start).Value

chrom = Replace(chromTmp, "chr", "")

pos = sh.Cells(rw.Row, start + 1).Value

Id = sh.Cells(rw.Row, start + 16).Value

ref = sh.Cells(rw.Row, start + 2).Value

alt = sh.Cells(rw.Row, start + 3).Value

qual = sh.Cells(rw.Row, start + 4).Value

filterVal = sh.Cells(rw.Row, start + 5).Value

info = "."

Print #outputFile, chrom & vbTab & pos & vbTab & Id & vbTab & ref & vbTab & alt & vbTab & qual & vbTab & filterVal & vbTab & info

ElseIf sh.Cells(rw.Row, start).Value = "" Then

Exit For

End If

Next rw

Close #outputFile

End Sub

-> Einstellen in VarWatch