



Filtre par fréquence
Thresholds dans les gènes AD
< 0,5 % dans les db externes et < 5 % dans la db inhouse

Thresholds pour les autres

Exceptions pour "sauver" des variations

Si classification interne ≥ 3
ou si sur Clinvar, davantage de soumissions pathogènes que
bénins avec une créance d'au moins deux étoiles,
la variation ne sera pas filtrée.

Filtre les variations hors des régions d'épissage ou UTR définies
Ici, celles situées avant les 20 bases précédant un début d'exon
et après les 6 bases suivant une fin d'exon

... sauf exceptions

```
459 },
460 "GNOMAD_EXOMES": {
461 "G": 5000,
462 "AFR": 5000,
463 "AMR": 5000,
464 "EAS": 5000,
465 "FIN": 5000,
466 "NFE": 5000,
467 "OTH": 5000,
468 "SAS": 5000
469 }
470 },
471 "thresholds": {
472 "AD": {
473 "external": 0.005,
474 "internal": 0.05
475 },
476 "default": {
477 "external": 0.01,
478 "internal": 0.05
479 }
480 }
481 },
482 "exceptions": [
483 {
484 "name": "classification",
485 "config": {
486 "classes": ["3", "4", "5"]
487 }
488 },
489 {
490 "name": "external",
491 "config": {
492 "clinvar": {
493 "num_stars": [">=", 2],
494 "combinations": [{"pathogenic", ">"}, {"benign"}]
495 }
496 }
497 }
498 ]
499 },
500 {
501 "name": "region",
502 "config": {
503 "splice_region": [-20, 6],
504 "utr_region": [0, 0]
505 },
506 "exceptions": [
507 {
508 "name": "classification",
509 "config": {
510 "classes": ["3", "4", "5"]
511 }
512 },
513 {
514 "name": "external",
515 "config": {
516 "clinvar": {
517 "num_stars": [">=", 2],
518 "combinations": [{"pathogenic", ">"}, {"benign"}]
519 }
520 }
521 }
522 ],
523 {
524 "name": "consequence",
525 "config": {
526 "genepanel_only": true,
527 "consequences": [
528 "transcript_ablation",
```

Filtre selon les conséquences estimées par VEP



... sauf exceptions

```
521     },
522     {
523       "name": "consequence",
524       "config": {
525         "genepanel_only": true,
526         "consequences": [
527           "transcript_ablation",
528           "splice_donor_variant",
529           "splice_acceptor_variant",
530           "stop_gained",
531           "frameshift_variant",
532           "start_lost",
533           "initiator_codon_variant",
534           "stop_lost",
535           "inframe_insertion",
536           "inframe_deletion",
537           "missense_variant",
538           "protein_altering_variant",
539           "transcript_amplification",
540           "incomplete_terminal_codon_variant",
541           "synonymous_variant",
542           "stop_retained_variant",
543           "coding_sequence_variant"
544         ]
545       }
546     },
547   ],
548 },
549 {
550   "name": "consequence",
551   "config": {
552     "consequences": [
553       "synonymous_variant",
554       "stop_retained_variant",
555       "start_retained_variant"
556     ]
557   },
558   "exceptions": [
559     {
560       "name": "consequence",
561       "config": {
562         "consequences": [
563           "transcript_ablation",
564           "splice_donor_variant",
565           "splice_acceptor_variant",
566           "stop_gained",
567           "frameshift_variant",
568           "start_lost",
569           "initiator_codon_variant",
570           "stop_lost",
571           "inframe_insertion",
572           "inframe_deletion",
573           "missense_variant",
574           "protein_altering_variant",
575           "transcript_amplification",
576           "splice_region_variant",
577           "incomplete_terminal_codon_variant",
578           "coding_sequence_variant",
579           "mature_miRNA_variant",
580           "5_prime_UTR_variant",
581           "3_prime_UTR_variant",
582           "intron_variant",
583           "NMD_transcript_variant"
584         ]
585       }
586     },
587   ],
588   "name": "classification",
589   "config": {
590     "classes": ["3", "4", "5"]
591   }
592 }
```

Filtre les variations C>T, T>C, delCC, delTT, delCT et delTC dans le tractus polypyrimidine, la région précisée ici entre 20 et 3 bases précédant un début d'exon

Filtre les variations avec une balance allélique < 25 %

```
584 }
585 }
586 },
587 {
588   "name": "classification",
589   "config": {
590     "classes": ["3", "4", "5"]
591   }
592 },
593 {
594   "name": "external",
595   "config": {
596     "clinvar": {
597       "num_stars": [">=", 2],
598       "combinations": [{"pathogenic", ">", "benign"}]
599     }
600   }
601 },
602 ],
603 },
604 {
605   "name": "ppy",
606   "config": {
607     "ppy_tract_region": [-20, -3]
608   },
609   "exceptions": [
610     {
611       "name": "classification",
612       "config": {
613         "classes": ["3", "4", "5"]
614       }
615     },
616     {
617       "name": "external",
618       "config": {
619         "clinvar": {
620           "num_stars": [">=", 2],
621           "combinations": [{"pathogenic", ">", "benign"}]
622         }
623       }
624     }
625   ]
626 },
627 {
628   "name": "quality",
629   "config": {
630     "allele_ratio": 0.25
631   },
632   "exceptions": [
633     {
634       "name": "classification",
635       "config": {
636         "classes": ["3", "4", "5"]
637       }
638     },
639     {
640       "name": "external",
641       "config": {
642         "clinvar": {
643           "num_stars": [">=", 2],
644           "combinations": [{"pathogenic", ">", "benign"}]
645         }
646       }
647     }
648   ]
649 },
650 {
651   "name": "segregation",
652   "config": {
```

Filtre par ségrégation

Garde les variations dont le génotype d'un parent est manquant

Garde les variations estimées de novo avec des GQ > 20

Garde les variations pouvant être issues d'une mosaïque parentale

Garde les variations pouvant causer une hétérozygotie composite

Garde les variations pouvant causer une maladie récessive

```
631 },
632 "exceptions": [
633   {
634     "name": "classification",
635     "config": {
636       "classes": ["3", "4", "5"]
637     }
638   },
639   {
640     "name": "external",
641     "config": {
642       "clinvar": {
643         "num_stars": [">=", 2],
644         "combinations": [["pathogenic", ">", "benign"]]
645       }
646     }
647   }
648 ],
649 },
650 {
651   "name": "segregation",
652   "config": {
653     "no_coverage_parents": { "enable": true },
654     "denovo": {
655       "enable": true,
656       "gq_threshold": {
657         "proband": 20,
658         "mother": 20,
659         "father": 20
660       }
661     },
662     "parental_mosaicism": { "enable": true },
663     "compound_heterozygous": { "enable": true },
664     "recessive_homozygous": { "enable": true }
665   },
666   "exceptions": [
667     {
668       "name": "external",
669       "config": {
670         "clinvar": {
671           "num_stars": [">=", 2],
672           "combinations": [["pathogenic", ">", "benign"]]
673         }
674       }
675     }
676   ]
677 },
678 ],
679 },
680 },
681 ],
682 }
```

ADD FILTERED VARIANTS

INCLUDED VARIANTS (3)

INH	GENE	HGVSc	CSQ	HI. COUNT	EXTERNAL	CLASS
AD	CACNA1C	c.3049-10C>T	intron	296	Clinvar	
AD	CHD7	c.4645-9T>C	intron	32	Clinvar	
AD/AR	ITGA2B	c.671-13C>T	intron	74	Clinvar	

Voilà les variations filtrées aux différentes étapes

ALL (654) FREQUENCY (473) REGION (22) CONSEQUENCE (40) PPY (9) QUALITY (8) SEGREGATION (102) ALL GENE

102 VARIANTS FROM CURRENT FILTER SETTINGS

INH	GENE	HGVSc	CSQ	! F S O Q R	QUAL	DP	RATIO	HI. FREQ	HI. COUNT	EXTERNAL	CLASS
AR	ABCG5	c.293C>G	missense		127	32	0.53	0.003226	447	HGMD Clinvar	
AR	ACAD5B	c.1128+25_1...	splice_region...		154	23	0.52	0.007600	97		
AR	ADAMT...	c.1340C>T	missense, spl...		129	24	0.54	0.000566	74		
AR	ADAMT...	c.438G>C	missense		129	35	0.49	0.002188	288	Clinvar	
AD	AKAP9	c.1158A>T	missense		128	51	0.67	0.000736	36	Clinvar	
AD	AQP5	c.767G>A	missense		125	44	0.52	0.001653	233	Clinvar	
XR	AR	c.228_239dup	inframe_inse...	O Q	126	6	1.00	0.040800	524		
AD	ARHGA...	c.2036C>T	missense		121	43	0.42	0.001460	169	Clinvar	
AD	ARID1A	c.609C>A	missense		129	43	0.53	0.000328	7		
AR	ATM	c.295A>G	missense	R	129	36	0.56	0.000912	69	HGMD Clinvar	
AD	ATN1	c.1503_1508del	inframe_dele...	R	134	26	0.38	0.020200	259	HGMD	
AD	ATXN2	c.560_561ins...	inframe_inse...	I	101	38	0.45	0.000928	47		
AR,AD	SLCSA2	c.1961A>G	missense	R	129	25	0.60	0.008445	1383	HGMD Clinvar	
AR	CABP2	c.133G>A	missense		129	35	0.49	0.000887	14		
AD	CACNA1H	c.1310G>A	missense		128	53	0.49	0.000389	91		
AR	CACNA2...	c.2987T>C	missense		125	35	0.40	0.007298	916	Clinvar	
AR	CAPN1	c.2119-15C>G	intron		129	35	0.54	0.005600	563		
AR	CBS	c.1105C>T	missense	R	128	38	0.45	0.005500	747	HGMD Clinvar	
AD	CD96	c.1650-13A>G	intron		129	56	0.48	1.000e-4	7		
AD	CEL	c.2119A>C	missense	I R	75	33	0.45	0.002539	112	HGMD	

INDICATIONS COMMENT

+ 3/654 FILTER TRIODEFAULT FULL QUICK VISUAL

UNCLASSIFIED VARIANTS (16)

INH	GENE	HGVSc	CSQ
AR	FCGR3A	c.512T>A	missense
XD	AMER1	c.1873A>G	missense
XR	GRIA3	c.1181G>A	missense
AD/AR	TTN	c.34474C>A	missense, in...
AR	FMN2	c.3138A>T	synonymous
AR	FMN2	c.3495T>G	synonymous
AD	BRAF	c.2128-16_21...	splice_region...
AD/AR	MSH2	c.942+2del	splice_donor
AR	ARSB	c.312+3A>C	splice_region...
AR	ARSB	c.312+2T>C	splice_donor
AR	SERPINB8	c.197T>C	missense
AD	BRAF	c.2128-5dup	splice_region...
AD	CACNA1C	c.3049-10C>T	intron
AD	CHD7	c.4645-9T>C	intron
AD/AR	F11	c.403G>T	stop_gained
AD/AR	HTT	c.96_110dup	inframe_inse...
AD/AR	ITGA2B	c.671-13C>T	intron
AR	STRC	c.3307-26_33...	intron

Choix du filtre à appliquer

CLASSIFIED VARIANTS (1)

INH	GENE	HGVSc	CSQ	! F S O Q R	CLASS
AD/AR	TTN	c.104251G>C	missense		1

NOT RELEVANT VARIANTS (4)

INH	GENE	HGVSc	CSQ	! F S O Q R	CLASS
AD	DNMT3A	c.2732G>A	missense		
AR	ARSB	c.312_312+1i...	frameshift, s...		
AR	PRKRA	c.785-2_785...	splice_acceptor		
AR	PRKRA	c.785-5_785...	splice_region...		

WARNING 1

Annotation for NM_000569.7 does not match corresponding transcript: ENST000003

CLASSIFICATION

EVALUATION

REPORT

ACMG

SUGGESTED

SHOW REQ

ACMG SUGGESTED

BA1 High frequency

REGION

REGION-COMMENTS