Whole Genome Sequencing Report

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1 Interprétation

LAL-T surexprimant l'oncogène ***TLX1*** sans altération détectable en FISH.

Réarrangement

Inversion du chromosome 10q expliquant probablement la surexpression éctopique de ***TLX1*** (chr10:91,805,243_delins[chr10:101,959,193inv] 20%, chr10:101,959,195_delins[chr10:91,805,247inv] 20%).

Délétions

— 9p chr9:21,646,668-22,027,139 impliquant ***CDKN2A***.
— 13q chr13:49,297,330-50,023,448 impliquant ***DLEU2***.
— Probable délétion hétérozygote du 16q vue en CNV.

Mutations tronquantes

— ***NOTCH1*** (NP_060087.3:p.Gln1584Ter 26%),
— ***LEF1*** (NP_057353.1:p.Arg137AlafsTer4 40%),
— ***PIK3C2A*** (NP_002636.2:p.Glu1103Ter, voie PI3-kinases),
— ***TSPYL2*** (NP_071400.1:p.Tyr461Ter 80%, inhibiteur du cycle cellulaire)
— ***FOXP2*** (chr7:115,545,653-115,545,656inv 46%),
— ***SNX14*** (NP_065201.1:p.Arg763Ter 30%, métabolisme du phosphatidylinositol).

Faux-sens:

— ***FBXW7*** (NP_060785.2:p.Arg385His 50%),
— ***PRKD2*** (NP_057541.2:p.Ile582Thr 43%, voie TCR),
— ***NUTM1*** (NP_786883.2:p.Ser145Phe 38%, voie TERT),
— ***XKR7*** (NP_001011718.1:p.Ala468Thr 38%, rôle dans l'apoptose)

L'ensemble des mutations somatiques de structure ont été annotées ainsi que l'ensemble des mutations somatiques codantes.

2 Sample identity

RIVOALEN

3 Alignement

Diagnostic sample

Id	RIVOALEN
Time Point	diag
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/08/27 15h02
Number Of Reads	20.2 M
Yield Gb	60.61
Mean Coverage	19.44
N50	5 k
Median Length	2218
Mean Length	3005
Median Identity	99.25
Mean Identity	106.5
Run(s)	cdd24: 44% 8f340: 9% f119e: 47%

MRD sample

Id	RIVOALEN
Time Point	mrd
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/08/02 05h14
Number Of Reads	5.6 M
Yield Gb	38.98
Mean Coverage	12.5
N50	8.5 k
Median Length	6882
Mean Length	6986
Median Identity	99.32
Mean Identity	95.94
Run(s)	8eec0: 100%

Values computed by cramino v0.14.5

3.1 Normalized read count by chromosome

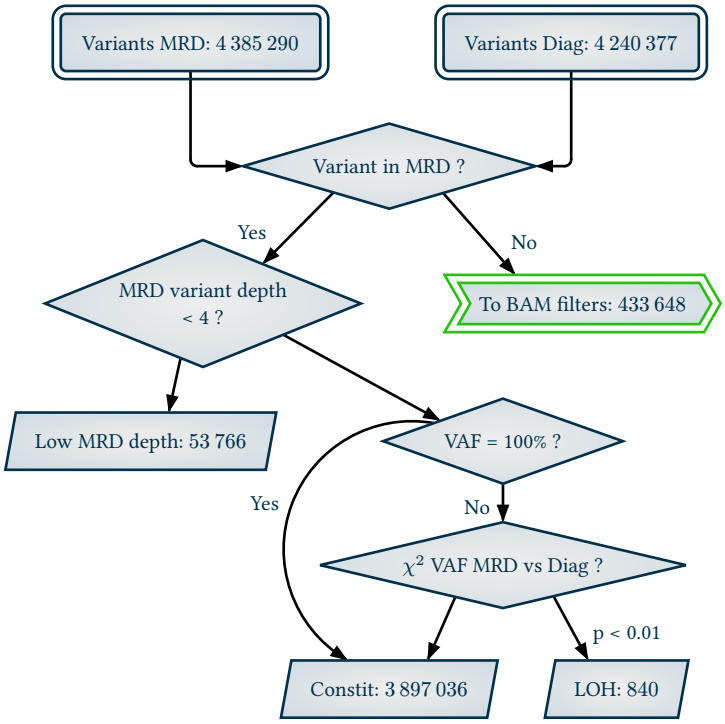
	chr1	chr2	chr3	chr4	chr5	chr6	chr7	chr8	chr9	chr10	chr11	chr12	chr13
diag	0.98	1.03	1	1	1.01	1.01	1.03	1	0.87	1.04	1.01	1.02	0.93
mrd	0.99	1.03	1.02	1	1.02	1.02	1.02	1.02	0.86	1.03	1.01	1.03	0.95

	chr14	chr15	chr16	chr17	chr18	chr19	chr20	chr21	chr22	chrX	chrY	chrM
diag	0.99	0.95	0.71	1.02	0.99	0.97	1.01	1.03	0.97	0.51	0.36	201.73
mrd	0.99	0.96	0.9	1.03	0.98	0.98	1	1.01	0.96	0.51	0.34	50.88

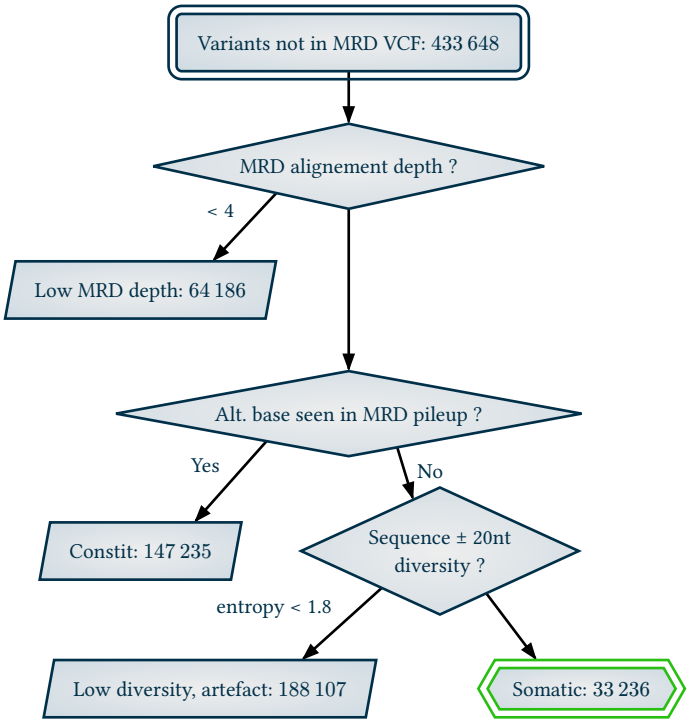
4 Variants

4.1 Variants calling

VCF filters

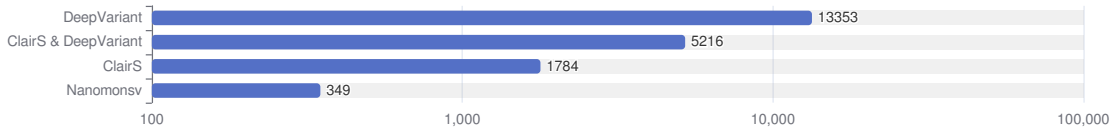


BAM filters

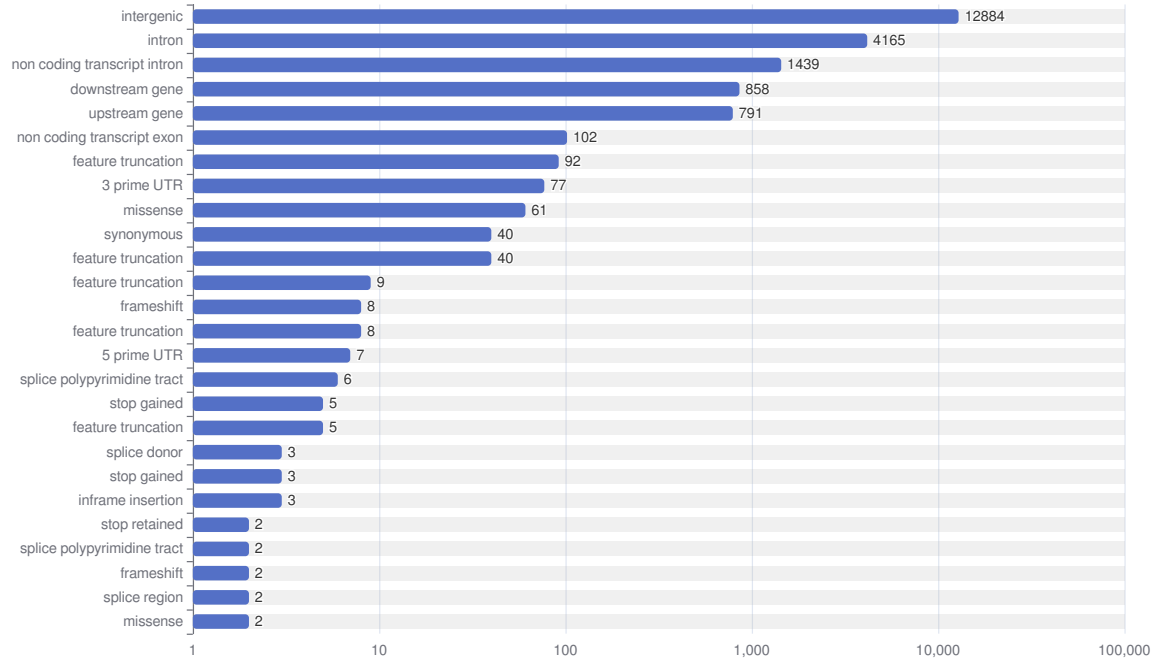


4.2 Somatic variants

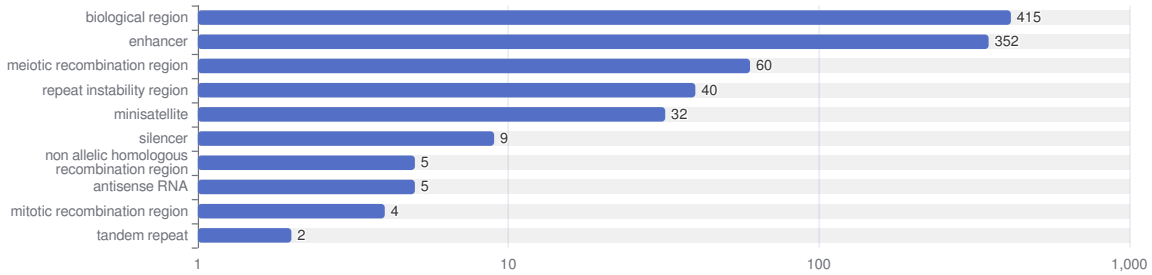
Callers



Consequences (VEP)



NCBI features



4.3 Selected Variants

Pathogenics

chr4:155,651,387 C›T
missense variant ***FBXW7***
NM_018315.5:c.1154G>A
NP_060785.2:p.Arg385His
VAF: 51.93% Cosmic: 245 DeepVariant: Qual: 34.9, GT: 0/1, GQ: 35, DP: 14, AD: [7, 7], VAF: 0.5, PL: [34, 0, 65] ClairS: Qual: 14.09, GT: 0/1, GQ: 14, DP: 13, AF: 0.5385, AD: [0, 7], NAF: 0, NDP: 11, NAD: [0, 0], AU: 0, CU: 6, GU: 0, TU: 7, NAU: 0, NCU: 11, NGU: 0, NTU: 0, H, FAU: 0, FCU: 4, FGU: 0, FTU: 3, RAU: 0, RCU: 2, RGU: 0, RTU: 4

chr9:21,646,668 c›<DEL>
intergenic variant
VAF: 72.73% Nanomonsv: TR: 11, VR: 8, SVTYPE: DEL, SVLEN: −380471, END: 22027139, SVINSLEN: 9, SVINSSEQ: CGTGGGACT

chr9:148,734,041 G›A
stop gained ***NOTCH1***
NM_017617.5:c.4750C>T
NP_060087.3:p.Gln1584Ter
VAF: 26.32% Cosmic: 3 DeepVariant: Qual: 7.5, GT: 0/1, GQ: 8, DP: 19, AD: [14, 5], VAF: 0.263158, PL: [6, 0, 32]

chr10:101,959,193 A›A]chr10:91805243]
VAF: 19.57% Nanomonsv: TR: 46, VR: 9, SVTYPE: BND, MATEID: r_65_0

chr10:101,959,195 G›[chr10:91805247[G
VAF: 19.57% Nanomonsv: TR: 46, VR: 9, SVTYPE: BND, MATEID: r_66_0

Likely Pathogenics

chr4:111,465,897 T›TCAAGCCCCTGC
frameshift variant ***LEF1***
NM_016269.5:c.408_409insGCAGGGGCTTG
NP_057353.1:p.Arg137AlafsTer4
VAF: 40% DeepVariant: Qual: 23.8, GT: 0/1, GQ: 24, DP: 20, AD: [10, 8], VAF: 0.4, PL: [23, 0, 39]

chr6:86,730,986 G›A
stop gained ***SNX14***
NM_020468.6:c.2287C>T
NP_065201.1:p.Arg763Ter
VAF: 30% GnomAD: 0.0000065 DeepVariant: Qual: 15.4, GT: 0/1, GQ: 15, DP: 10, AD: [7, 3], VAF: 0.3, PL: [15, 0, 37]

chr7:115,545,653 t›t]chr7:115545656]
feature truncation, intron variant, non coding transcript variant ***FOXP2***
VAF: 23.08% Nanomonsv: TR: 13, VR: 3, SVTYPE: BND, MATEID: r_351_0

chr7:115,545,656 a›a]chr7:115545653]
feature truncation, intron variant, non coding transcript variant ***FOXP2***
VAF: 23.08% Nanomonsv: TR: 13, VR: 3, SVTYPE: BND, MATEID: r_351_1

chr9:148,734,043 T›C
missense variant ***NOTCH1***
NM_017617.5:c.4748A>G
NP_060087.3:p.Glu1583Gly
VAF: 26.32% DeepVariant: Qual: 7.3, GT: 0/1, GQ: 7, DP: 19, AD: [13, 5], VAF: 0.263158, PL: [6, 0, 32]

chr11:17,212,287 C›A
stop gained ***PIK3C2A***
NM_002645.4:c.3307G>T
NP_002636.2:p.Glu1103Ter
VAF: 42.22% Cosmic: 1 DeepVariant: Qual: 20.9, GT: 0/1, GQ: 21, DP: 10, AD: [6, 4], VAF: 0.4, PL: [20, 0, 45] ClairS: Qual: 11.731, GT: 0/1, GQ: 11, DP: 9, AF: 0.4444, AD: [0, 4], NAF: 0, NDP: 12, NAD: [0, 0], AU: 4, CU: 5, GU: 0, TU: 0, NAU: 0, NCU: 12, NGU: 0, NTU: 0, FAU: 3, FCU: 2, FGU: 0, FTU: 0, RAU: 1, RCU: 3, RGU: 0, RTU: 0

chr13:49,297,330 A›<DEL>
intron variant, non coding transcript variant ***DLEU2***
VAF: 34.62% Nanomonsv: TR: 26, VR: 9, SVTYPE: DEL, SVLEN: −726118, END: 50023448

chr15:32,148,854 C›T
missense variant ***NUTM1***
NM_175741.3:c.434C>T
NP_786883.2:p.Ser145Phe
VAF: 37.5% DeepVariant: Qual: 6.4, GT: 0/1, GQ: 6, DP: 8, AD: [5, 3], VAF: 0.375, PL: [5, 0, 32]

chr19:49,516,230 A>G
missense variant ***PRKD2***
NM_016457.5:c.1745T>C
NP_057541.2:p.Ile582Thr

VAF: 42.73% Cosmic: 1

DeepVariant:

Qual: 28.2,

GT: 0/1, GQ: 28, DP: 11, AD: [6, 5], VAF: 0.454545, PL: [28, 0, 52]

ClairS:

Qual: 7.384,

GT: 0/1, GQ: 7, DP: 10, AF: 0.4, AD: [0, 4], NAF: 0, NDP: 8, NAD: [0, 0], AU: 6, CU: 0, GU: 4, TU: 0, NAU: 8, NCU: 0, NGU: 0, NTU: 0, H, FAU: 3, FCU: 0, FGU: 2, FTU: 0, RAU: 3, RCU: 0, RGU: 2, RTU: 0

chr19:49,516,231 T>G
missense variant ***PRKD2***
NM_016457.5:c.1744A>C
NP_057541.2:p.Ile582Leu

VAF: 41.67%

DeepVariant:

Qual: 27.6,

GT: 0/1, GQ: 28, DP: 12, AD: [6, 6], VAF: 0.5, PL: [27, 0, 47]

ClairS:

Qual: 4.802,

GT: 0/1, GQ: 4, DP: 9, AF: 0.3333, AD: [0, 3], NAF: 0, NDP: 8, NAD: [0, 0], AU: 0, CU: 0, GU: 3, TU: 6, NAU: 0, NCU: 0, NGU: 0, NTU: 8, H, FAU: 0, FCU: 0, FGU: 1, FTU: 3, RAU: 0, RCU: 0, RGU: 2, RTU: 3

chr20:33,721,751 G›A
missense variant ***XKR7***
NM_001011718.2:c.1402G>A
NP_001011718.1:p.Ala468Thr
VAF: 39.05% Cosmic: 3 GnomAD: 0.0000195 DeepVariant: Qual: 23.1, GT: 0/1, GQ: 23, DP: 21, AD: [13, 8], VAF: 0.380952, PL: [23, 0, 51] ClairS: Qual: 16.297, GT: 0/1, GQ: 16, DP: 20, AF: 0.4, AD: [0, 8], NAF: 0, NDP: 13, NAD: [0, 0], AU: 8, CU: 0, GU: 12, TU: 0, NAU: 0, NCU: 0, NGU: 13, NTU: 0, H, FAU: 6, FCU: 0, FGU: 5, FTU: 0, RAU: 2, RCU: 0, RGU: 7, RTU: 0

chrX:52,372,010 A›AGAGGT
frameshift variant, stop gained ***TSPYL2***
NM_022117.4:c.1382_1383insGAGGT
NP_071400.1:p.Tyr461Ter
VAF: 80% DeepVariant: Qual: 22.9, GT: 1/1, GQ: 12, DP: 10, AD: [1, 8], VAF: 0.8, PL: [22, 11, 0]

Variants of uncertain significance

chr1:127,591,141 g›gGATACAACTCGAGTGGAAAGGAATGG...

intergenic variant

VAF: 20.59%

Nanomonsv:

TR: 34, VR: 7, SVTYPE: INS, END: 127591151, SVINSLEN: 230, SVINSSEQ:

```
GATACAACTCGAGTGGAAAGGAATGGAATGGAAAGGAATGGAATGGAAAGGAAAGGAATA
GAATGCAATGGAATGCAATGGTATGGAATGGAGTTAACCCGAGTGGAATGGAATGGAATG
GAATGGAATGAAATTGAATGCATTGCAATGCAATGGAATGGAGTGGAAAGGAATAAACAC
CTGTGGAAAGGAATGCAATGGAATGGAGCGGACTGGAATAAACACCAGTG
```

chr1:128,311,472 a›aCTCTTCACTGATCACCCAGGTGATGT...

intergenic variant

VAF: 41.67%

Nanomonsv:

TR: 24, VR: 10, SVTYPE: INS, END: 128311472, SVINSLEN: 69, SVINSSEQ:

```
CTCTTCACTGATCACCCAGGTGATGTAACTCTGGTCTAAGCTCTGCCTAAAGTGGCATTG
TGACAGATC
```

chr1:128,312,855 c›cCAGGTGATGTAACTCTTGTCTAGGCT...

intergenic variant

VAF: 46.15%

Nanomonsv:

TR: 26, VR: 12, SVTYPE: INS, END: 128312856, SVINSLEN: 71, SVINSSEQ:

```
CAGGTGATGTAACTCTTGTCTAGGCTCCACCTACTGGGGGTATTATGACGTATCTCTGCA
GTGATCACCCA
```

chr1:223,766,278 t›[chr1:223766390[g
feature truncation, intron variant ***CNIH3***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, MATEID: r_36_1

chr1:223,766,390 g›[chr1:223766278[g
feature truncation, intron variant ***CNIH3***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, MATEID: r_36_0

chr2:16,728,198 g›g]chr2:16728220]
VAF: 23.08% Nanomonsv: TR: 13, VR: 3, SVTYPE: BND, MATEID: r_186_1

chr2:16,728,220 t›t]chr2:16728198]
VAF: 23.08% Nanomonsv: TR: 13, VR: 3, SVTYPE: BND, MATEID: r_186_0

chr2:114,076,138 g›gACTCAGAGGACACAGTACCCTAAATA...

intergenic variant

VAF: 57.14%

Nanomonsv:

TR: 35, VR: 20, SVTYPE: INS, END: 114076138, SVINSLEN: 256, SVINSSEQ:

```
ACTCAGAGGACACAGTACCCTAAATAAATGAATAGATACCCTGAGCTCATGACTCAGAGG
ACACAGTACCCTAAATAAATGAATAGATACCCTGAGCTCATGACTCAGAGGACGCAGTAC
CCTAAATAAATGAATAGATACACTGAGCTCATGACTCAGAGGACACAGTACCCTAAATAA
ATGAATAGACACACTGAGCTCATGACTCAGAGGACACAGTACCCTAAATAAATGAATAGA
TACCCTGAGCTCATAA
```

chr3:51,267,933 C›T

stop gained ***DOCK3***

NM_004947.5:c.2023C>T

NP_004938.1:p.Arg675Ter

VAF: 61.11% Cosmic: 1 GnomAD: 0

ClairS:

Qual: 17.271,

GT: 0/1, GQ: 17, DP: 18, AF: 0.6111, AD: [0, 11], NAF: 0, NDP: 8, NAD: [0, 0], AU: 0, CU: 7, GU: 0, TU: 11, NAU: 0, NCU: 8, NGU: 0, NTU: 0, H, FAU: 0, FCU: 4, FGU: 0, FTU: 6, RAU: 0, RCU: 3, RGU: 0, RTU: 5

chr4:3,858,985 g›gCACTGGGGCTCAGTCTTGAGGAATAC...

intergenic variant

VAF: 40.91%

Nanomonsv:

TR: 22, VR: 9, SVTYPE: INS, END: 3858985, SVINSLEN: 66, SVINSSEQ:

```
CACTGGGGCTCAGTCTTGAGGAATACATTTACCTGGTGCCTGCTGTATACTGGCCACAGG
CTAAAC
```

chr5:14,698,067 A›G
missense variant ***ANKH***
NM_054027.6:c.331T>C
NP_473368.1:p.Tyr111His

VAF: 68.75%

DeepVariant:

Qual: 24.9,

GT: 0/1, GQ: 25, DP: 16, AD: [5, 11], VAF: 0.6875, PL: [24, 0, 46]

ClairS:

Qual: 18.177,

GT: 0/1, GQ: 18, DP: 16, AF: 0.6875, AD: [0, 11], NAF: 0, NDP: 14, NAD: [0, 0], AU: 5, CU: 0, GU: 11, TU: 0, NAU: 14, NCU: 0, NGU: 0, NTU: 0, H, FAU: 1, FCU: 0, FGU: 3, FTU: 0, RAU: 4, RCU: 0, RGU: 8, RTU: 0

chr5:29,374,810 t›[chr5:29375027[C

VAF: 27.27%

Nanomonsv:

TR: 11, VR: 3, SVTYPE: BND, MATEID: r_288_1

chr5:29,375,027 C›[chr5:29374810[C

VAF: 27.27%

Nanomonsv:

TR: 11, VR: 3, SVTYPE: BND, MATEID: r_288_0

chr5:138,218,187 G›A
missense variant ***KLHL3***
NM_017415.3:c.470C>T
NP_059111.2:p.Ala157Val

VAF: 57.14%

DeepVariant:

Qual: 24.2,

GT: 0/1, GQ: 24, DP: 7, AD: [3, 4], VAF: 0.571429, PL: [24, 0, 39]

ClairS:

Qual: 14.824,

GT: 0/1, GQ: 14, DP: 7, AF: 0.5714, AD: [0, 4], NAF: 0, NDP: 16, NAD: [0, 0], AU: 4, CU: 0, GU: 3, TU: 0, NAU: 0, NCU: 0, NGU: 16, NTU: 0, FAU: 3, FCU: 0, FGU: 1, FTU: 0, RAU: 1, RCU: 0, RGU: 2, RTU: 0

chr5:143,814,076 C›A
missense variant ***NR3C1***
NM_000176.3:c.2036G>T
NP_000167.1:p.Gly679Val

VAF: 36.94%

DeepVariant:

Qual: 22.6,

GT: 0/1, GQ: 23, DP: 20, AD: [13, 7], VAF: 0.35, PL: [22, 0, 47]

ClairS:

Qual: 17.03,

GT: 0/1, GQ: 17, DP: 18, AF: 0.3889, AD: [0, 7], NAF: 0, NDP: 12, NAD: [0, 0], AU: 7, CU: 11, GU: 0, TU: 0, NAU: 0, NCU: 12, NGU: 0, NTU: 0, FAU: 2, FCU: 6, FGU: 0, FTU: 0, RAU: 5, RCU: 5, RGU: 0, RTU: 0

chr6:12,511,961 g›gCT]chr6:12511977]
VAF: 21.43% Nanomonsv: TR: 14, VR: 3, SVTYPE: BND, SVINSLEN: 2, SVINSSEQ: CT , MATEID: r_313_1

chr6:12,511,977 t›tAG]chr6:12511961]
VAF: 21.43% Nanomonsv: TR: 14, VR: 3, SVTYPE: BND, SVINSLEN: 2, SVINSSEQ: AG , MATEID: r_313_0

chr6:83,584,985 G›A
missense variant ***TPBG***
NM_006670.5:c.578G>A
NP_006661.1:p.Arg193Gln
VAF: 46.67% DeepVariant: Qual: 31.2, GT: 0/1, GQ: 31, DP: 15, AD: [8, 7], VAF: 0.466667, PL: [31, 0, 56] ClairS: Qual: 14.338, GT: 0/1, GQ: 14, DP: 15, AF: 0.4667, AD: [0, 7], NAF: 0, NDP: 7, NAD: [0, 0], AU: 7, CU: 0, GU: 8, TU: 0, NAU: 0, NCU: 0, NGU: 7, NTU: 0, H, FAU: 2, FCU: 0, FGU: 3, FTU: 0, RAU: 5, RCU: 0, RGU: 5, RTU: 0

chr6:99,846,077 C›C]chr6:99846106]

VAF: 20%

Nanomonsv:

TR: 15, VR: 3, SVTYPE: BND, MATEID: r_331_1

chr6:99,846,106 T›T]chr6:99846077]

VAF: 20%

Nanomonsv:

TR: 15, VR: 3, SVTYPE: BND, MATEID: r_331_0

chr6:165,105,613 t›tTTTTTTTTTTTTTTTTTTTTTTTTT...

intergenic variant

VAF: 57.14%

Nanomonsv:

TR: 14, VR: 8, SVTYPE: INS, END: 165105619, SVINSLEN: 102, SVINSSEQ:

TTTTTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTCTCGCTCTGTCGCCCAGGCTGGAG
TGCAGTGGCGGGATCTCGGCTCACTGCAAGCTCCGCCTCCCG

chr7:12,468,072 C›CT

frameshift variant, splice region variant ***VWDE***

NM_001135924.3:c.4462dup

NP_001129396.1:p.Ser1488LysfsTer4

VAF: 50%

DeepVariant:

Qual: 4.5,

GT: 1/1, GQ: 3, DP: 6, AD: [2, 3], VAF: 0.5, PL: [1, 5, 0]

chr7:16,920,077 g›gTGGGATGGCGGCCAGGCAGAGACGCT...
downstream gene variant ***AGR2***

VAF: 28.57%

Nanomonsv:

TR: 14, VR: 4, SVTYPE: INS, END: 16920077, SVINSLEN: 81, SVINSSEQ:

```
TGGGATGGCGGCCAGGCAGAGACGCTCCTCACTTCCTAGATGGGATGGCGGCCAGGAAGA
GGCGCTCCTCACTTCCTAGAT
```

chr7:23,949,707 a›aTCTACCATTGTATTACTGGTTTTGTT...
intron variant ***STK31***

VAF: 43.75%

Nanomonsv:

TR: 16, VR: 7, SVTYPE: INS, END: 23949707, SVINSLEN: 82, SVINSSEQ:

```
TCTACCATTGTATTACTGGTTTTGTTTGTTTCTTGTTTCTTTTTCTTTTTTTCCCTTCCT
GTGCATTACTTGAAAAAATTTT
```

chr7:75,602,735 C›T
missense variant ***CLIP2***
NM_003388.5:c.2978C>T
NP_003379.4:p.Thr993Met

VAF: 35.71%

ClairS:

Qual: 13.946,

GT: 0/1, GQ: 13, DP: 14, AF: 0.3571, AD: [0, 5], NAF: 0, NDP: 7, NAD: [0, 0], AU: 0, CU: 9, GU: 0, TU: 5, NAU: 0, NCU: 7, NGU: 0, NTU: 0, H, FAU: 0, FCU: 3, FGU: 0, FTU: 1, RAU: 0, RCU: 6, RGU: 0, RTU: 4

chr8:87,231,277 C>T
missense variant, splice region variant ***ATP6V0D2***
NM_152565.1:c.302C>T
NP_689778.1:p.Thr101Met

VAF: 46.15% Cosmic: 7 GnomAD: 0.0000065

DeepVariant:

Qual: 23,

GT: 0/1, GQ: 23, DP: 13, AD: [7, 6], VAF: 0.461538, PL: [22, 0, 48]

ClairS:

Qual: 13.68,

GT: 0/1, GQ: 13, DP: 13, AF: 0.4615, AD: [0, 6], NAF: 0, NDP: 7, NAD: [0, 0], AU: 0, CU: 7, GU: 0, TU: 6, NAU: 0, NCU: 7, NGU: 0, NTU: 0, H, FAU: 0, FCU: 3, FGU: 0, FTU: 5, RAU: 0, RCU: 4, RGU: 0, RTU: 1

chr9:113,078,614 T>[chr9:113078874[A
feature truncation, intron variant, non coding transcript variant ***LOC105376181***

VAF: 20%

Nanomonsv:

TR: 20, VR: 4, SVTYPE: BND, MATEID: r_385_1

chr9:113,078,874 A>[chr9:113078614[A
downstream gene variant ***LOC105376181***

VAF: 20%

Nanomonsv:

TR: 20, VR: 4, SVTYPE: BND, MATEID: r_385_0

chr10:13,185,828 G›A
missense variant ***MCM10***
NM_018518.5:c.296G>A
NP_060988.3:p.Arg99Lys

VAF: 58.33%

DeepVariant:

Qual: 26.8,

GT: 0/1, GQ: 27, DP: 12, AD: [5, 7], VAF: 0.583333, PL: [26, 0, 48]

ClairS:

Qual: 15.288,

GT: 0/1, GQ: 15, DP: 12, AF: 0.5833, AD: [0, 7], NAF: 0, NDP: 12, NAD: [0, 0], AU: 7, CU: 0, GU: 5, TU: 0, NAU: 0, NCU: 0, NGU: 12, NTU: 0, H, FAU: 4, FCU: 0, FGU: 2, FTU: 0, RAU: 3, RCU: 0, RGU: 3, RTU: 0

chr10:21,823,787 C›[chr10:21823758[C
feature truncation, intron variant ***DNAJC1***

VAF: 23.08%

Nanomonsv:

TR: 13, VR: 3, SVTYPE: BND, MATEID: r_47_0

chr10:66,799,944 a›[chr10:66799955[CATAAATTATA...
feature truncation, intron variant ***CTNNA3***

VAF: 25%

Nanomonsv:

TR: 16, VR: 4, SVTYPE: BND, SVINSLEN: 64, SVINSSEQ:

```
CATAAATTATACGGTTATATATTTATTTAAACATTTGTAATAGTGTCTGGCACATACATA
TATT
```

, MATEID: r_56_0

chr10:66,799,955 t›[chr10:66799944[AATATATGTAT...
feature truncation, intron variant ***CTNNA3***

VAF: 25%

Nanomonsv:

TR: 16, VR: 4, SVTYPE: BND, SVINSLEN: 64, SVINSSEQ:

```
AATATATGTATGTGCCAGACACTATTACAAATGTTTAAATAAATATATAACCGTATAATT
TATG
```

, MATEID: r_56_1

chr10:132,084,393 A›AGGTAGCTGCTCCAGGTAGCAGACTCCAGG
intron variant ***TCERG1L***
NM_174937.4:c.1035-2679_1035-2678insCCTGGAGTCTG...

VAF: 30.77% Cosmic: 8

DeepVariant:

Qual: 27.5,

GT: 0/1, GQ: 27, DP: 13, AD: [9, 4], VAF: 0.307692, PL: [27, 0, 52]

chr15:48,383,092 C›T
missense variant ***TRPM7***
NM_017672.6:c.4859G>A
NP_060142.3:p.Gly1620Glu

VAF: 41.67%

ClairS:

Qual: 12.883,

GT: 0/1, GQ: 12, DP: 12, AF: 0.4167, AD: [0, 5], NAF: 0, NDP: 12, NAD: [0, 0], AU: 0, CU: 7, GU: 0, TU: 5, NAU: 0, NCU: 12, NGU: 0, NTU: 0, H, FAU: 0, FCU: 3, FGU: 0, FTU: 2, RAU: 0, RCU: 4, RGU: 0, RTU: 3

DeepVariant:

Qual: 34.2,

GT: 0/1, GQ: 34, DP: 12, AD: [7, 5], VAF: 0.416667, PL: [34, 0, 61]

chr15:64,586,443 G›[chr15:64586655[C
feature truncation, intron variant ***SMAD6***
VAF: 11.11% Nanomonsv: TR: 27, VR: 3, SVTYPE: BND, MATEID: r_146_1

chr15:64,586,655 C›[chr15:64586443[C
feature truncation, intron variant ***SMAD6***
VAF: 11.11% Nanomonsv: TR: 27, VR: 3, SVTYPE: BND, MATEID: r_146_0

chr17:17,739,829 C›G
missense variant ***RAI1***
NM_030665.4:c.269C>G
NP_109590.3:p.Ala90Gly
VAF: 64.08% DeepVariant: Qual: 31.6, GT: 0/1, GQ: 32, DP: 20, AD: [7, 13], VAF: 0.65, PL: [31, 0, 54] ClairS: Qual: 17.421, GT: 0/1, GQ: 17, DP: 19, AF: 0.6316, AD: [0, 12], NAF: 0, NDP: 4, NAD: [0, 0], AU: 0, CU: 7, GU: 12, TU: 0, NAU: 0, NCU: 4, NGU: 0, NTU: 0, H, FAU: 0, FCU: 2, FGU: 8, FTU: 0, RAU: 0, RCU: 5, RGU: 4, RTU: 0

chr19:10,866,698 t›<DUP>
intron variant ***DNM2***
VAF: 16.67% Nanomonsv: TR: 48, VR: 8, SVTYPE: DUP, SVLEN: 35244, END: 10901942

chr22:33,166,328 t›[chr22:33166347[t
feature truncation, intron variant ***SYN3***
VAF: 15% Nanomonsv: TR: 20, VR: 3, SVTYPE: BND, MATEID: r_233_1

chr22:33,166,347 t›[chr22:33166328[t
feature truncation, intron variant ***SYN3***
VAF: 15% Nanomonsv: TR: 20, VR: 3, SVTYPE: BND, MATEID: r_233_0

chrX:7,397,394 A›G
missense variant ***VCX***
NM_013452.3:c.322A>G
NP_038480.2:p.Ser108Gly
VAF: 37.5% GnomAD: 0.0017 DeepVariant: Qual: 4.3, GT: 0/1, GQ: 4, DP: 8, AD: [5, 3], VAF: 0.375, PL: [2, 0, 25]

chrX:7,397,395 G›C
missense variant ***VCX***
NM_013452.3:c.323G>C
NP_038480.2:p.Ser108Thr
VAF: 37.5% DeepVariant: Qual: 5.7, GT: 0/1, GQ: 6, DP: 8, AD: [5, 3], VAF: 0.375, PL: [4, 0, 31]

chrX:20,160,919 t›t]chrX:20160964]
VAF: 42.86% Nanomonsv: TR: 7, VR: 3, SVTYPE: BND, MATEID: r_650_1

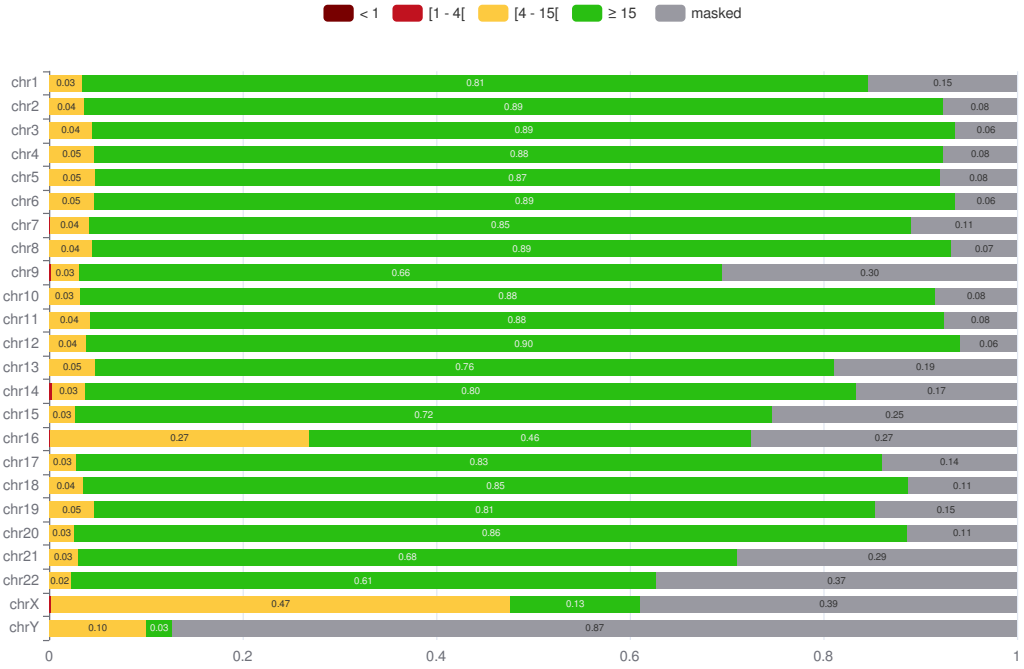
chrX:20,160,964 t›t]chrX:20160919]
VAF: 42.86% Nanomonsv: TR: 7, VR: 3, SVTYPE: BND, MATEID: r_650_0

chrX:43,120,542 G›[chrX:43120572[C
feature truncation, intron variant ***MAOA***
VAF: 30% Nanomonsv: TR: 10, VR: 3, SVTYPE: BND, MATEID: r_652_1

chrX:43,120,572 C›[chrX:43120542[C
feature truncation, intron variant ***MAOA***
VAF: 30% Nanomonsv: TR: 10, VR: 3, SVTYPE: BND, MATEID: r_652_0

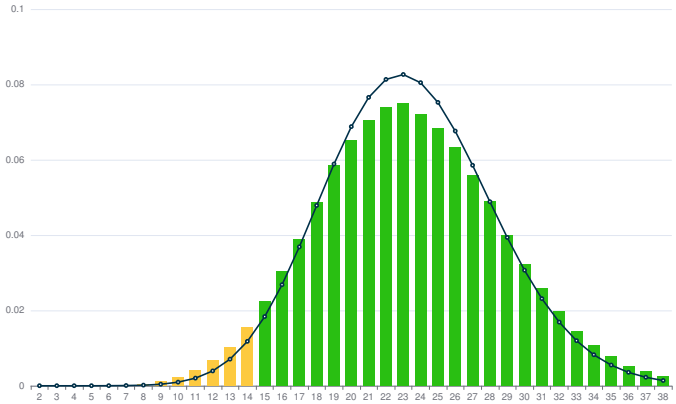
5 Coverage by chromosome

5.1 Proportion at given depth by chromosome

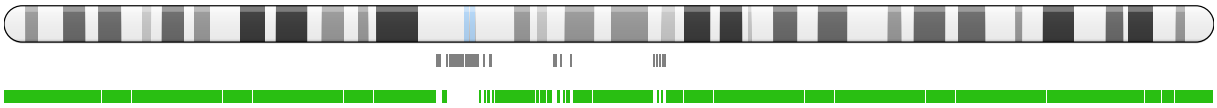


chr1

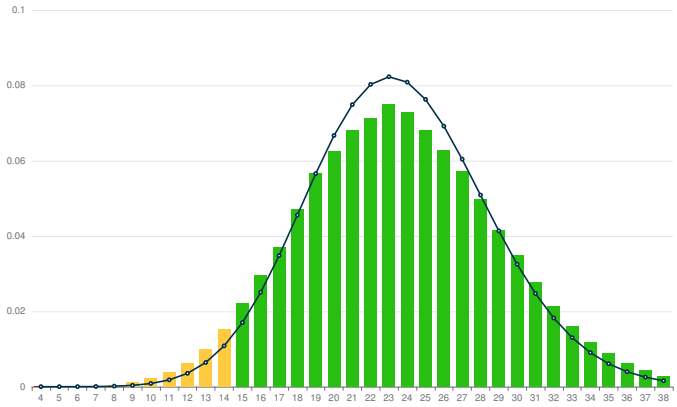
Mean	23.37
Standard dev.	5.35
< 1	0%
[1 - 4[	0%
[4 - 15[	4.1%
≥ 15	95.9%



chr2

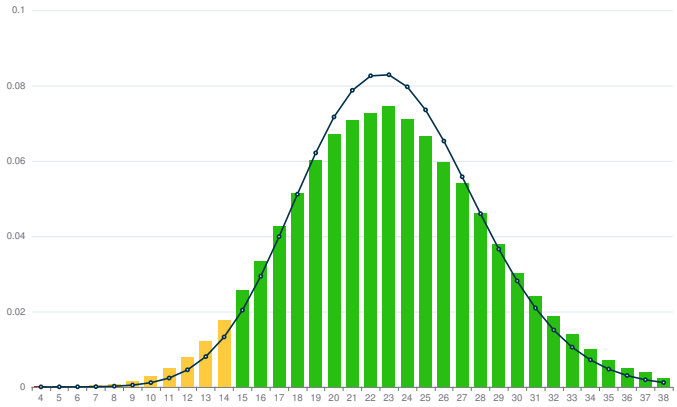


Mean	23.58
Standard dev.	5.42
< 1	0%
[1 - 4[	0%
[4 - 15[	3.9%
≥ 15	96.1%



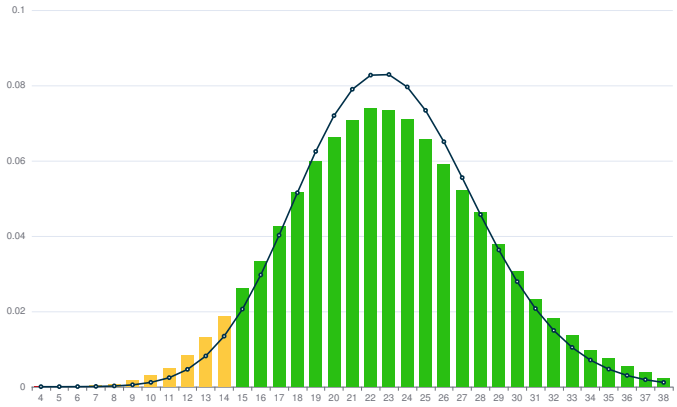
chr3

Mean	23.08
Standard dev.	5.4
< 1	0%
[1 - 4[	0%
[4 - 15[	4.8%
≥ 15	95.2%



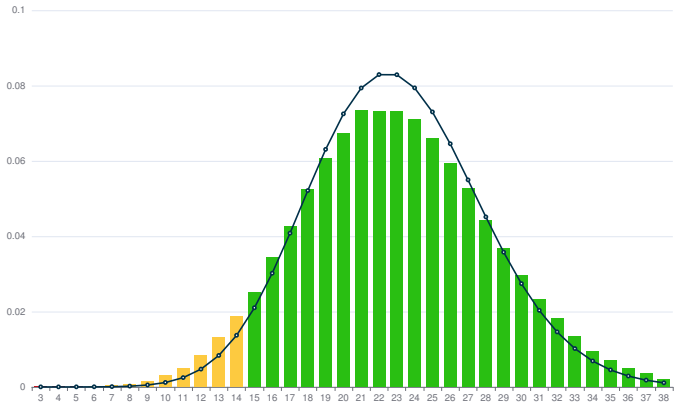
chr4

Mean	23.05
Standard dev.	5.47
< 1	0%
[1 - 4[	0%
[4 - 15[	5.1%
≥ 15	94.9%



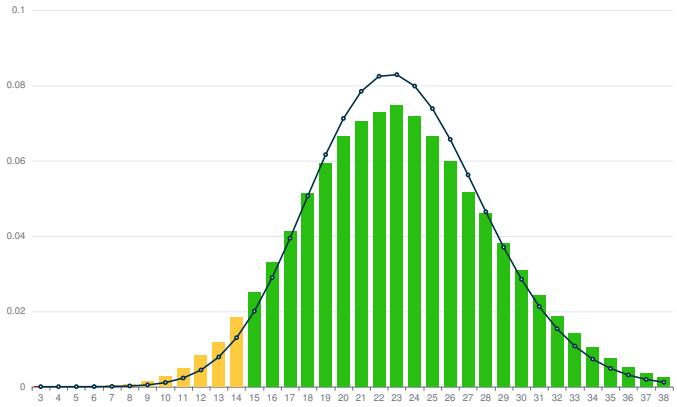
chr5

Mean	22.99
Standard dev.	5.5
< 1	0%
[1 - 4[	0%
[4 - 15[	5.1%
≥ 15	94.9%



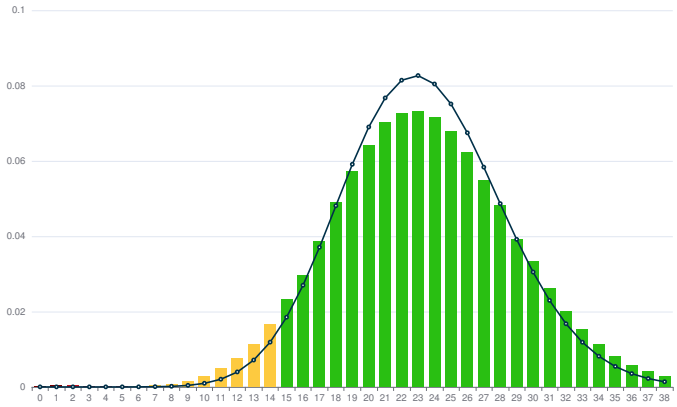
chr6

Mean	23.12
Standard dev.	5.47
< 1	0%
[1 - 4[	0%
[4 - 15[	4.9%
≥ 15	95.1%



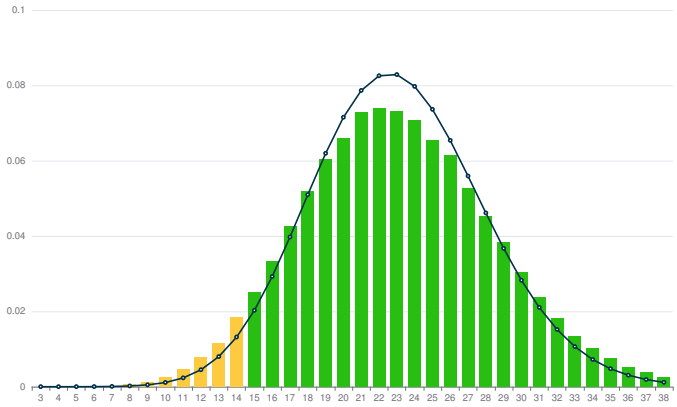
chr7

Mean	23.35
Standard dev.	5.63
< 1	0%
[1 - 4[	0.1%
[4 - 15[	4.6%
≥ 15	95.3%

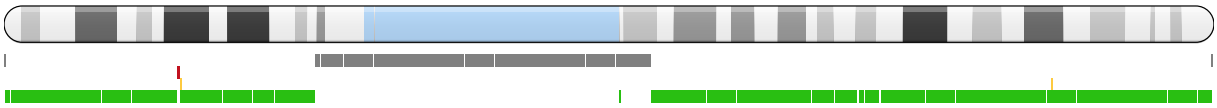


chr8

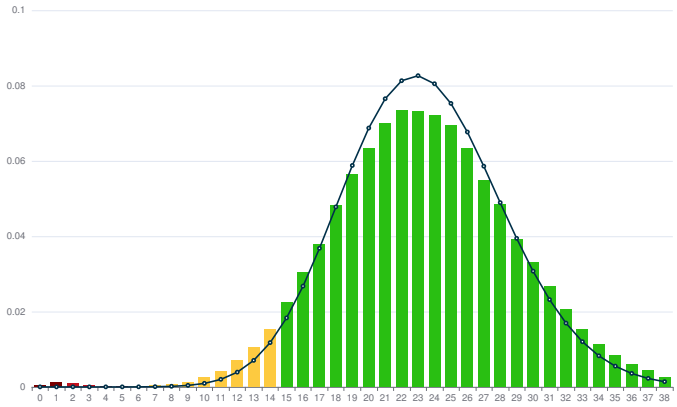
Mean	23.09
Standard dev.	5.39
< 1	0%
[1 - 4[	0%
[4 - 15[	4.8%
≥ 15	95.2%



chr9

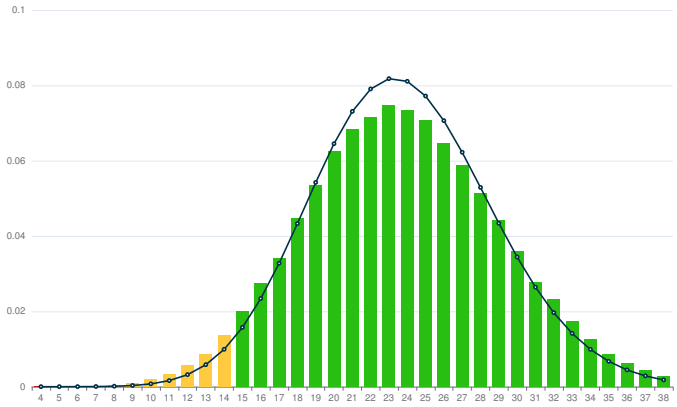


Mean	23.38
Standard dev.	5.62
< 1	0.1%
[1 - 4[	0.3%
[4 - 15[	4.2%
≥ 15	95.5%



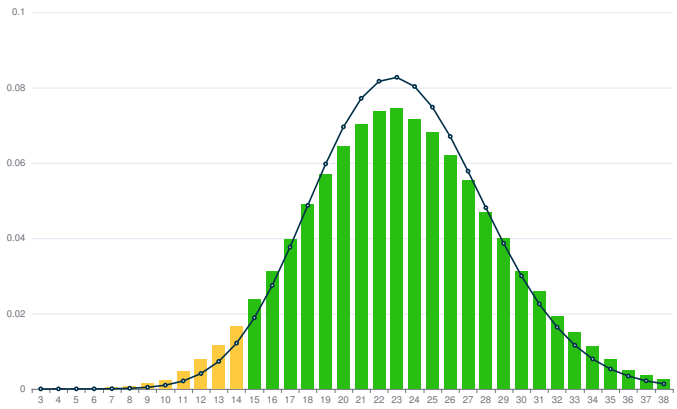
chr10

Mean	23.79
Standard dev.	5.38
< 1	0%
[1 - 4[	0%
[4 - 15[	3.5%
≥ 15	96.5%



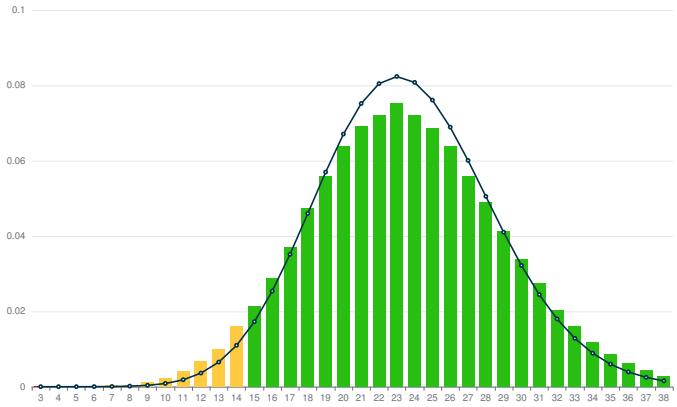
chr11

Mean	23.29
Standard dev.	5.42
< 1	0%
[1 - 4[	0%
[4 - 15[	4.6%
≥ 15	95.4%

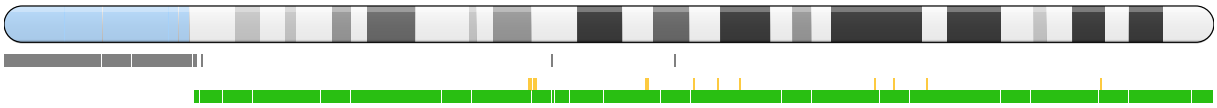


chr12

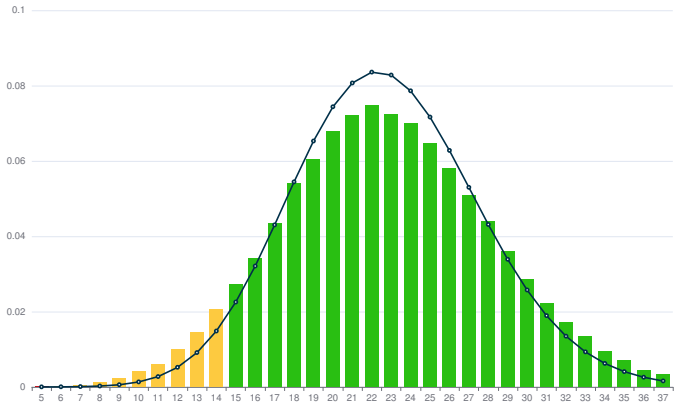
Mean	23.54
Standard dev.	5.43
< 1	0%
[1 - 4[	0%
[4 - 15[	4.1%
≥ 15	95.9%



chr13

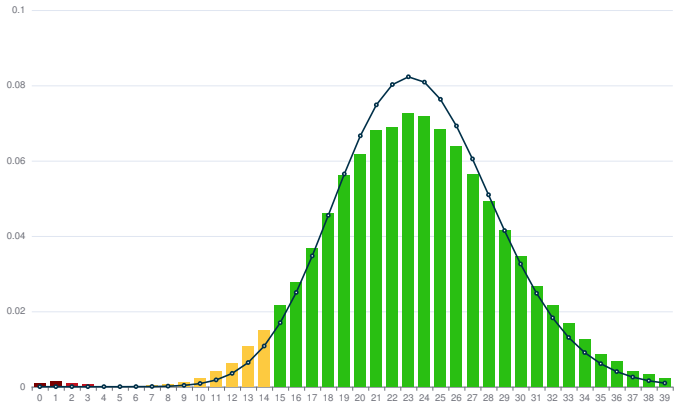


Mean	22.79
Standard dev.	5.46
< 1	0%
[1 - 4[	0%
[4 - 15[	5.9%
≥ 15	94.1%



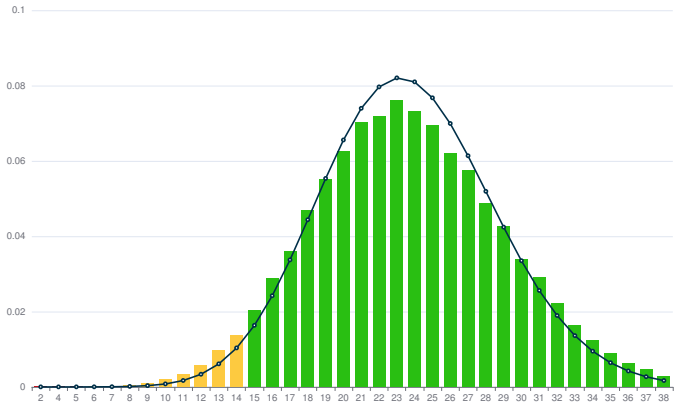
chr14

Mean	23.59
Standard dev.	5.78
< 1	0.1%
[1 - 4[	0.3%
[4 - 15[	4.1%
≥ 15	95.5%

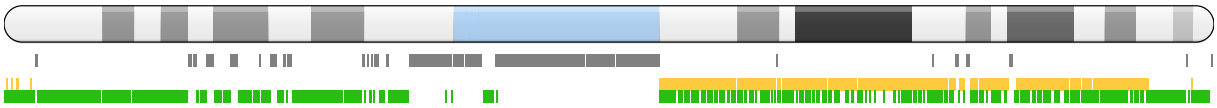


chr15

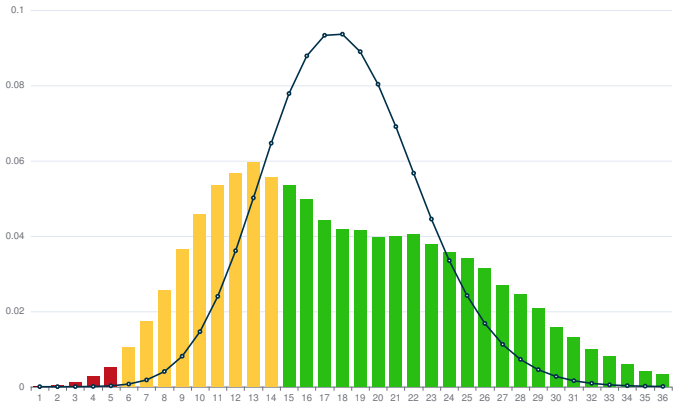
Mean	23.69
Standard dev.	5.43
< 1	0%
[1 - 4[	0%
[4 - 15[	3.6%
≥ 15	96.4%



chr16

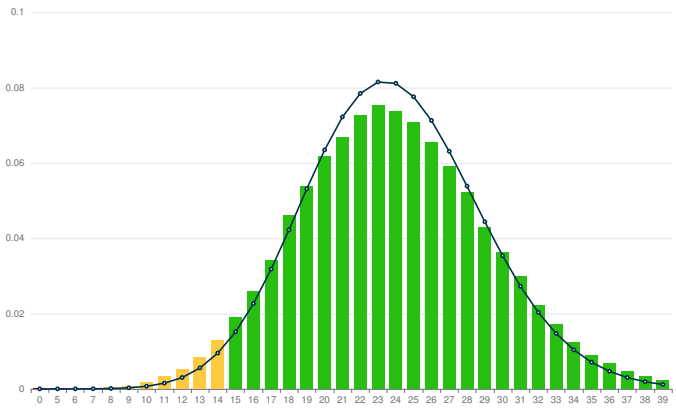


Mean	18.06
Standard dev.	7.13
< 1	0%
[1 - 4[	0.2%
[4 - 15[	36.9%
≥ 15	62.9%

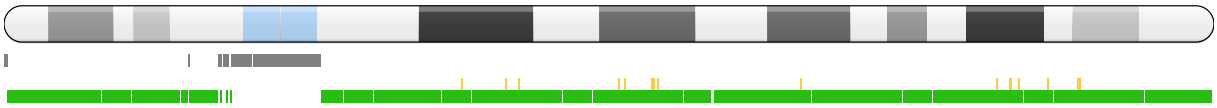


chr17

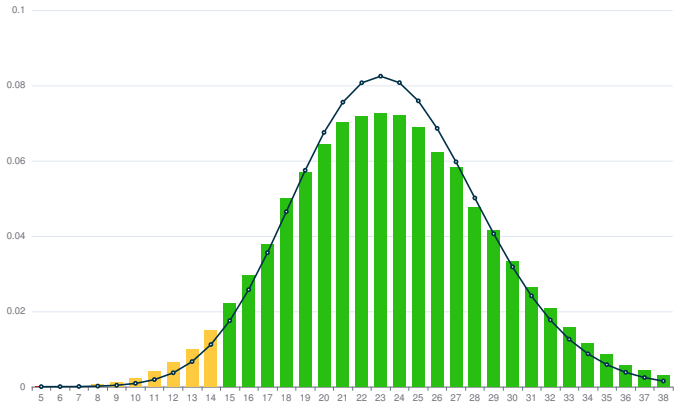
Mean	23.9
Standard dev.	5.44
< 1	0%
[1 - 4[	0%
[4 - 15[	3.2%
≥ 15	96.8%



chr18

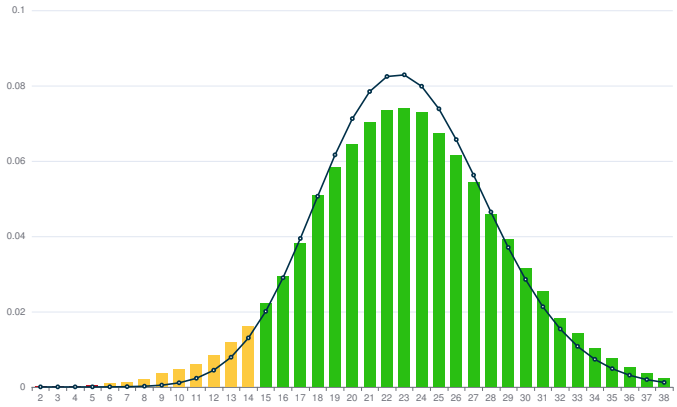


Mean	23.5
Standard dev.	5.41
< 1	0%
[1 - 4[	0%
[4 - 15[	4%
≥ 15	96%

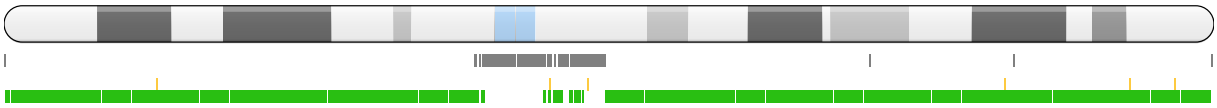


chr19

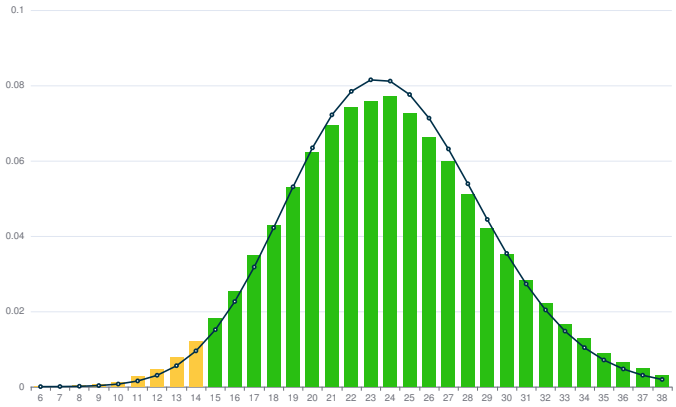
Mean	23.12
Standard dev.	5.55
< 1	0%
[1 - 4[	0%
[4 - 15[	5.5%
≥ 15	94.5%



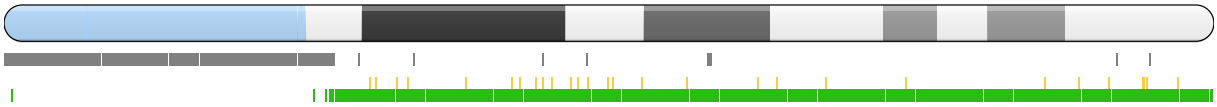
chr20



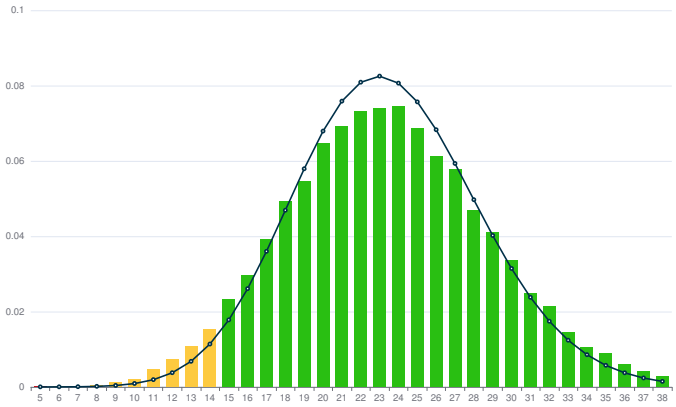
Mean	23.9
Standard dev.	5.31
< 1	0%
[1 - 4[	0%
[4 - 15[	3%
≥ 15	97%



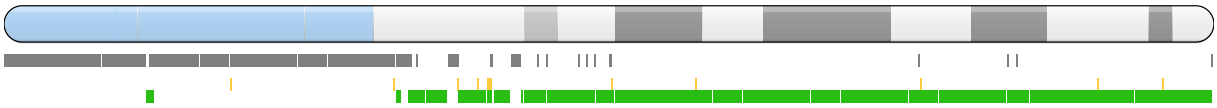
chr21



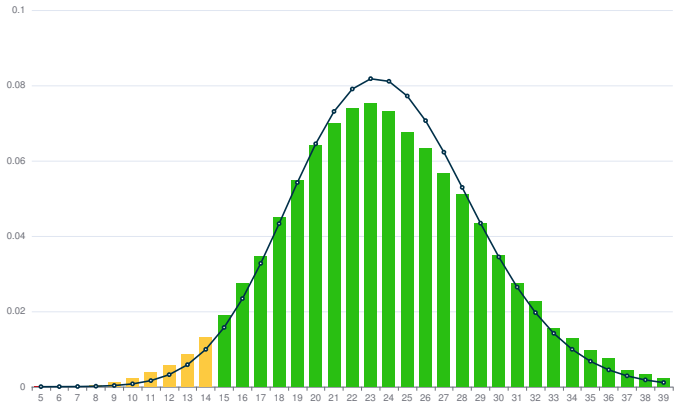
Mean	23.46
Standard dev.	5.46
< 1	0%
[1 - 4[	0%
[4 - 15[	4.2%
≥ 15	95.8%



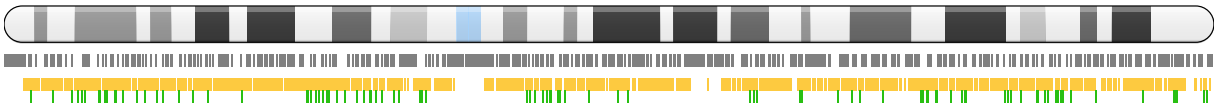
chr22



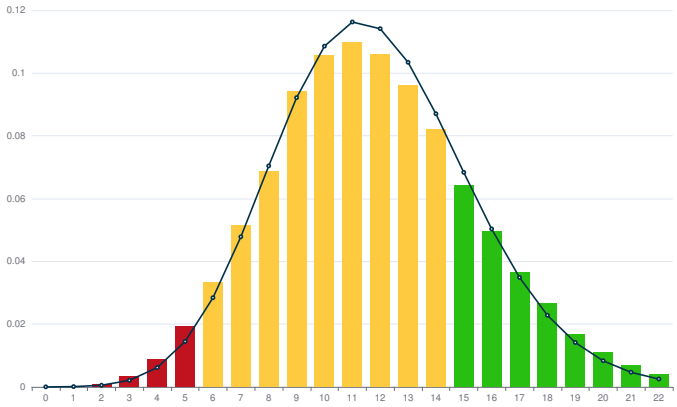
Mean	23.8
Standard dev.	5.48
< 1	0%
[1 - 4[	0%
[4 - 15[	3.5%
≥ 15	96.5%



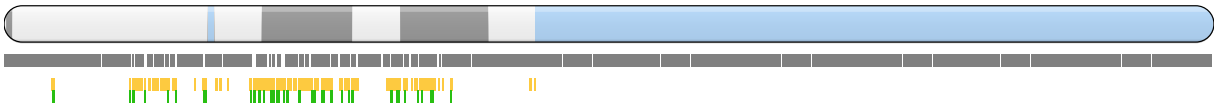
chrX



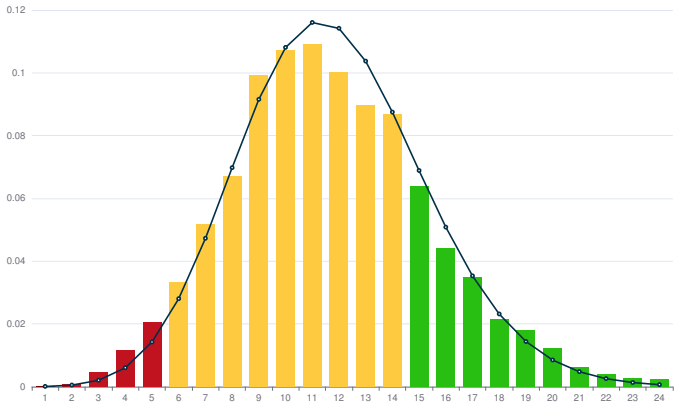
Mean	11.78
Standard dev.	3.71
< 1	0%
[1 - 4[	0.5%
[4 - 15[	77.5%
≥ 15	22%



chrY



Mean	11.81
Standard dev.	4.04
< 1	0%
[1 - 4[	0.6%
[4 - 15[	77.7%
≥ 15	21.7%



6 Method

6.1 Sample preparation and sequencing

1. DNA sampling and collection in EDTA tubes.
2. Buffy coat: pooling of multiple EDTA tubes then centrifugation (1200 rpm 10 minutes).
3. DNA extraction according to Maxwell® Promega RSC Buffy Coat DNA Kit.
4. Nanodrop DNA quantification.
5. DNA shearing: 3µg of DNA mechanically sheared by Covaris g-TUBE (8000 rpm, 1 minute).
6. DNA size qualification aiming a median of 10 kb determined by TapeStation.

Values computed by Pandora development version

7. Libary was constructed following the Oxford Nanopore Technologies Ligation Sequencing Kit V14 (SQK-LSK114) protocol with 1.5 µg as input DNA.
8. Qubit quantification
9. After evaluation of flowcell (rev 10) for pore availability (> 6000 available pores). Two distinct barcoded libraries were pooled for each flowcell.
10. sequencing run was initiated and controlled using MinKNOW software (sequencing 80 hours, data output format: Raw pod5 files).

6.2 Bioinformatic analysis

1. Orchestration and global analysis realized by in-house software (source code is accessible at Github).
2. Basecalling and alignment: dorado v0.8.2 with parameters “sup,5mC_5hmC –trim all” with alignment on hs1 genome (T2T chm13v2.0).
3. Variant calling was realized with ClairS v0.4.0, DeepVariant v1.6.1, DeepSomatic v1.7.0, Nanomonsv v0.7.2.
4. Variants filtering and merging done with in-house software.
5. Annotation: ensembl-VEP 112 with gene features defined by RefSeq Liftoff v5.1. SNP from gnomAD_4-2022_10 and Cosmic v99.
6. Interpretation and report generation performed on a local web service also published in open source.