Whole Genome Sequencing Report

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1 Interprétation

LAL-T présentant une surexpression mono-allélique et ectopique de l'oncogène ***TAL1***.

Absence d'altération somatique aux alentours du locus de *TAL1*.

Insertions

— Présence d'une insertion intronique au sein de ***MYB*** (chr6:136,381,931) de 334nt correspondant au 2ème exon de ***GRHL1*** avec formation d'un transcrit chimérique vu en RNA-seq.
— Duplication en tandem dans le gène ***PDLIM2*** (PDZ And LIM Domain 2) gène réputé suppresseur de tumeur dans le LNH-T.

Délétions

— 9p (chr9:21,990,115-22,024,026) impliquant ***CDKN2A***.
— ***AEBP2*** (membre du complexe PRC2) allant jusqu'au pseudo-gène voisin en 3' (chr12:19,317,878-19,544,792) avec formation d'un transcrit de fusion chimérique en RNA-seq.

Mutations tronquantes

— ***PHF6*** (NP_115711.2:p.Thr12TyrfsTer10, 35%).
— ***NOTCH1*** (PEST NP_060087.3:p.Ile2456GlyfsTer23, 61%, ainsi qu'une mutation HD NP_060087.3:p.Leu1678Pro 24%).

Faux-sens

— ***BCL11B*** (NP_075049.1:p.Ser766Thr, 27%).

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

2 Sample identity

CAMARA

3 Alignement

Diagnostic sample

Id	CAMARA
Time Point	diag
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2023/12/11 12h31
Number Of Reads	12.5 M
Yield Gb	62.83
Mean Coverage	20.16
N50	9 k
Median Length	3453
Mean Length	5016
Median Identity	99.36
Mean Identity	113.6
Run(s)	4dd9b: 100%

MRD sample

Id	CAMARA
Time Point	mrd
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2023/12/11 15h03
Number Of Reads	6.4 M
Yield Gb	39.42
Mean Coverage	12.65
N50	10.6 k
Median Length	4260
Mean Length	6153
Median Identity	99.36
Mean Identity	99.96
Run(s)	d817b: 100%

Values computed by cramino v0.14.5

3.1 Normalized read count by chromosome

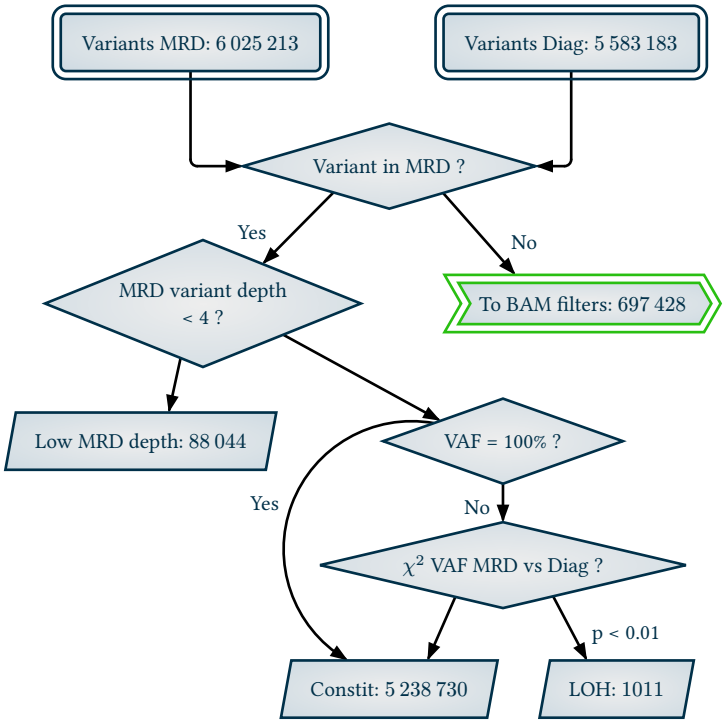
	chr1	chr2	chr3	chr4	chr5	chr6	chr7	chr8	chr9	chr10	chr11	chr12	chr13
diag	0.98	1.01	0.99	0.96	0.99	1	1	1	0.86	1.03	1	1.01	0.95
mrd	0.99	1.01	0.99	0.94	0.98	1.01	1.01	0.99	0.86	1.04	1	1.02	0.94

	chr14	chr15	chr16	chr17	chr18	chr19	chr20	chr21	chr22	chrX	chrY	chrM
diag	1.01	0.99	0.94	1.05	0.97	1.02	1.01	1.05	1.02	0.97	0.03	112.3
mrd	1.02	1	0.95	1.11	0.98	1.08	1.02	1.05	1.05	0.92	0.03	22.27

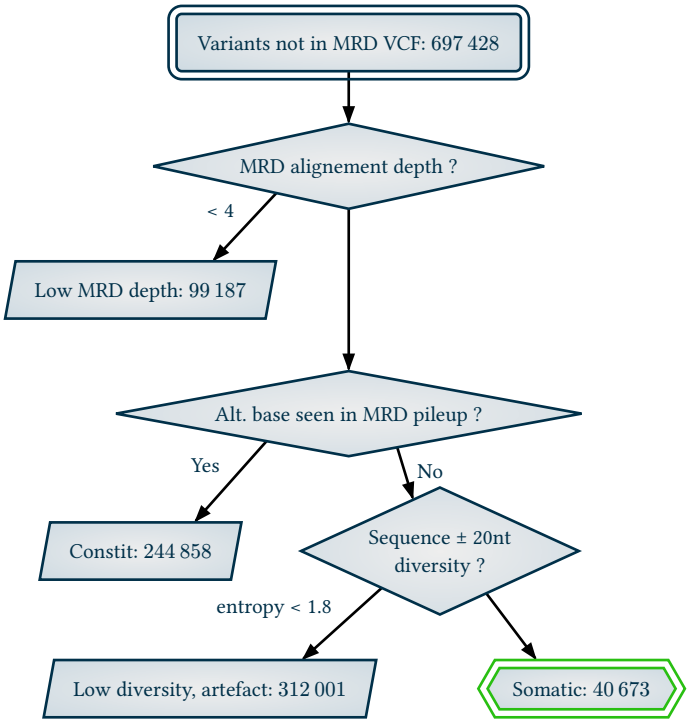
4 Variants

4.1 Variants calling

VCF filters

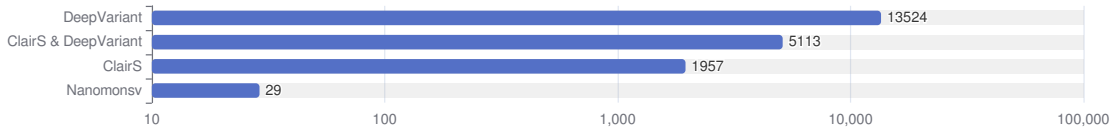


BAM filters

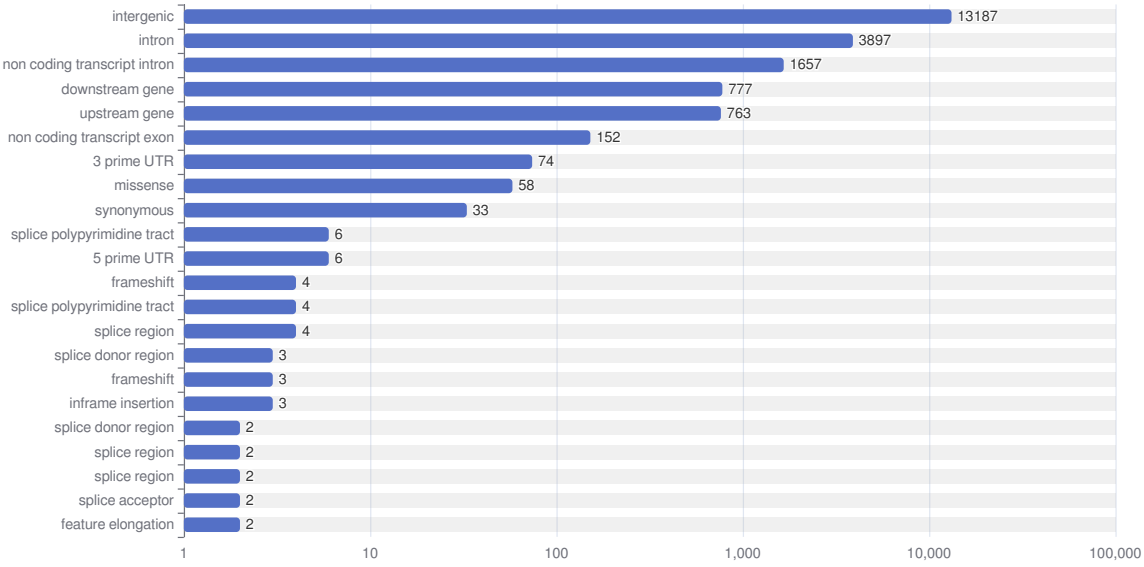


4.2 Somatic variants

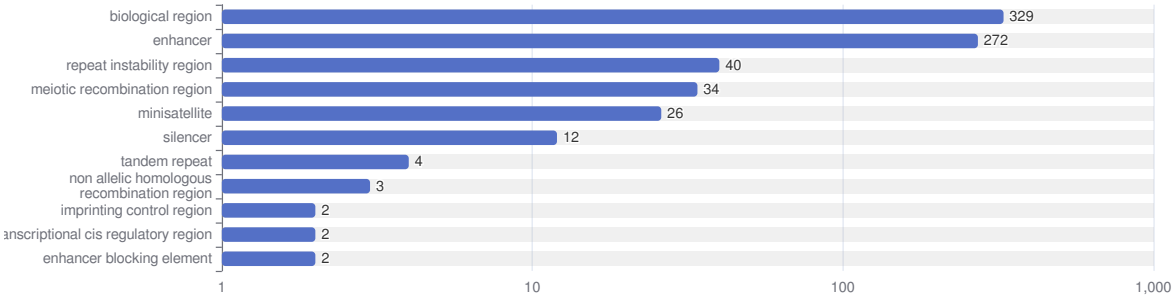
Callers



Consequences (VEP)



NCBI features



4.3 Selected Variants

Pathogenics

chr9:21,990,115 A›<DEL>
upstream gene variant ***CDKN2A***
VAF: 29.41% Nanomonsv: TR: 17, VR: 5, SVTYPE: DEL, SVLEN: −33911, END: 22024026, SVINSLEN: 2, SVINSSEQ: TT

chr9:148,725,472 T›TCCTCC
frameshift variant ***NOTCH1***
NM_017617.5:c.7365_7366insGGAGG
NP_060087.3:p.Ile2456GlyfsTer23
VAF: 61.11% DeepVariant: Qual: 35.1, GT: 0/1, GQ: 35, DP: 18, AD: [6, 11], VAF: 0.611111, PL: [35, 0, 54]

chr9:148,732,416 A›G
missense variant ***NOTCH1***
NM_017617.5:c.5033T>C
NP_060087.3:p.Leu1678Pro

VAF: 24.4% Cosmic: 101

ClairS:

Qual: 14.272,

GT: 0/1, GQ: 14, DP: 20, AF: 0.25, AD: [0, 5], NAF: 0, NDP: 5, NAD: [0, 0], AU: 15, CU: 0, GU: 5, TU: 0, NAU: 5, NCU: 0, NGU: 0, NTU: 0, H, FAU: 7, FCU: 0, FGU: 2, FTU: 0, RAU: 8, RCU: 0, RGU: 3, RTU: 0

DeepVariant:

Qual: 3,

GT: 0/1, GQ: 3, DP: 21, AD: [16, 5], VAF: 0.238095, PL: [0, 0, 36]

chrX:132,702,800 C›CT
frameshift variant ***PHF6***
NM_032335.3:c.33dup
NP_115711.2:p.Thr12TyrfsTer10

VAF: 35.29%

DeepVariant:

Qual: 24.4,

GT: 0/1, GQ: 24, DP: 17, AD: [11, 6], VAF: 0.352941, PL: [24, 0, 50]

Likely Pathogenics

chr6:136,381,931 A›ACATTAAAAGGTTTTAAAAATTTGTTT...
intron variant ***MYB***

VAF: 30.43%

Nanomonsv:

TR: 23, VR: 7, SVTYPE: INS, END: 136382077, SVINSLEN: 334, SVINSSEQ:

```
CATTAAAAGGTTTTAAAAATTTGTTTAGTGTATTTTATCAGTAAAGTGTTTTTTTTCTCT
CAGTCCCAGACCCCACAGCGGCGGTCCTACACTAGTGAGGATGAGGCCTGGAAATCCTTC
CTGGAAAACCCTCTCACTGCAGCGACCAAAGCGATGATGAGCATCAATGGAGACGAAGAC
AGCGCCGCTGCGCTGGGCCTGCTCTATGACTACTACAAGGTGGGTTTGCCTGCCTTTAAA
ACCCTTAACAGCAGTCTCCGAAACCTCAGGAAGCCAAGTCCCCTGAAGCATATGTAGCCC
TGAATGACGTGGCCTTTGTTTTGTCTTTTGCATC
```

chr6:136,382,001 A›ACCCCACAGCGGCGGTCCTACACTAGT...
intron variant ***MYB***
NM_005375.4:c.763-81_763-80insCCCCACAGCGGCGGTCC...

VAF: 35.29%

DeepVariant:

Qual: 14.2,

GT: 0/1, GQ: 14, DP: 17, AD: [10, 6], VAF: 0.352941, PL: [14, 0, 39]

chr8:22,862,977 C›CGCATGCCTCCCTCCCTCTCTGGACCC...
intron variant ***PDLIM2***

VAF: 69.23%

Nanomonsv:

TR: 26, VR: 18, SVTYPE: INS, END: 22863020, SVINSLEN: 106, SVINSSEQ:

```
GCATGCCTCCCTCCCTCTCTGGACCCTGGCAGTCTCTGCGCCCTGGCTCCGAGGGAAGGG
GCAGGGGGCCCGCTGGTCGGCGAGGGCTGGGAGCCCCCGACACCTT
```

chr12:19,317,878 G›<DEL>
intron variant ***AEBP2***

VAF: 34.48%

Nanomonsv:

TR: 29, VR: 10, SVTYPE: DEL, SVLEN: −226914, END: 19544792, SVINSLEN: 38, SVINSSEQ:

TCCGGGATGGCTTTGAATGTGTGTAGAGAGAGTGGGTG

chr14:93,405,883 C›G
missense variant ***BCL11B***
NM_022898.3:c.2297G>C
NP_075049.1:p.Ser766Thr

VAF: 26.67%

ClairS:

Qual: 15.36,

GT: 0/1, GQ: 15, DP: 15, AF: 0.2667, AD: [0, 4], NAF: 0, NDP: 13, NAD: [0, 0], AU: 0, CU: 11, GU: 4, TU: 0, NAU: 0, NCU: 13, NGU: 0, NTU: 0, H, FAU: 0, FCU: 4, FGU: 3, FTU: 0, RAU: 0, RCU: 7, RGU: 1, RTU: 0

DeepVariant:

Qual: 16.1,

GT: 0/1, GQ: 16, DP: 15, AD: [11, 4], VAF: 0.266667, PL: [15, 0, 44]

Variants of uncertain significance

chr1:170,470,452 G›A
missense variant ***FMO3***
NM_006894.6:c.895G>A
NP_008825.4:p.Val299Ile

VAF: 81.38% GnomAD: 0.0000065

DeepVariant:

Qual: 33.1,

GT: 0/1, GQ: 33, DP: 22, AD: [4, 18], VAF: 0.818182, PL: [33, 0, 42]

ClairS:

Qual: 21.248,

GT: 0/1, GQ: 21, DP: 21, AF: 0.8095, AD: [0, 17], NAF: 0, NDP: 13, NAD: [0, 0], AU: 17, CU: 0, GU: 4, TU: 0, NAU: 0, NCU: 0, NGU: 13, NTU: 0, H, FAU: 7, FCU: 0, FGU: 1, FTU: 0, RAU: 10, RCU: 0, RGU: 3, RTU: 0

chr1:209,894,386 G›GTGGAATAGTGTGATGGGGAATAGTGT...
intron variant ***HHAT***

VAF: 33.33%

Nanomonsv:

TR: 21, VR: 7, SVTYPE: INS, END: 209894478, SVINSLEN: 97, SVINSSEQ:

```
TGGAATAGTGTGATGGGGAATAGTGTTACAGTGGAATAGTGTGACGGGAACAGTGTGATG
GGAATAGTGTGACAGTGGAATAGTGTGACAGTGGAAC
```

chr4:8,163,315 C›<DEL>
intron variant ***SH3TC1***

VAF: 30.43%

Nanomonsv:

TR: 23, VR: 7, SVTYPE: DEL, SVLEN: −49, END: 8163364

chr5:57,739,547 A>T
missense variant ***SETD9***
NM_153706.4:c.226A>T
NP_714917.2:p.Thr76Ser

VAF: 55.54%

DeepVariant:

Qual: 37.3,

GT: 0/1, GQ: 37, DP: 23, AD: [10, 13], VAF: 0.565217, PL: [37, 0, 70]

ClairS:

Qual: 16.542,

GT: 0/1, GQ: 16, DP: 22, AF: 0.5455, AD: [0, 12], NAF: 0, NDP: 4, NAD: [0, 0], AU: 10, CU: 0, GU: 0, TU: 12, NAU: 4, NCU: 0, NGU: 0, NTU: 0, H, FAU: 5, FCU: 0, FGU: 0, FTU: 4, RAU: 5, RCU: 0, RGU: 0, RTU: 8

chr10:105,697,325 T>TTTTTTTTTTTTTTTTTTTTTTTTTTT...
intron variant ***SORCS3***

VAF: 12.5%

Nanomonsv:

TR: 24, VR: 3, SVTYPE: INS, END: 105697325, SVINSLEN: 619, SVINSSEQ:

```
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTCTCGCTCTGTCGCC
CAGGCTGGACTGCAGTGGCGCGATCTCGGCTCACTGCAAGCTCCGCCTCCCGGGTTCACG
CCATTCTCCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCACCCGCTACCACGCCCG
GCTAATTTTTTGTATTTTTAGTAGAGACGGGGTTTCACCGTGTTAGCCAGGATGGTCTCG
ATCTCCTGACCTCGTGATCCGCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAGGCGTG
AGCCACCGCGCCCGGCCCGGACTGTTGCTTTTAAGAAATGGTCTGCTCTTTATAATCTCT
TCACTAAGCTCCTTGCTCTCTGTGTGTGTGTGCGCATGTGTGTGTGTGCGTGTGTGTGCA
TGCATGCGTGCGCATGCACATGCATTTTGTACAAAAACATACCACTTTTTATTCCATTTT
CAGCTGAGTGACAATATGGTACATTCTGTTTTGGGGATTCCTTGGCCCATGGAGAGGTCT
TGAGGAATTCATGAACACCCAGATATGAAGTGGAAATTTTTATGTGAATACATTATATAT
TTCTTTGGAGAGAGTATCT
```

chr11:113,409,794 C>G
missense variant ***ANKK1***
NM_178510.2:c.1324C>G
NP_848605.1:p.Arg442Gly

VAF: 44%

ClairS:

Qual: 17.543,

GT: 0/1, GQ: 17, DP: 25, AF: 0.44, AD: [0, 11], NAF: 0, NDP: 6, NAD: [0, 0], AU: 0, CU: 14, GU: 11, TU: 0, NAU: 0, NCU: 6, NGU: 0, NTU: 0, H, FAU: 0, FCU: 10, FGU: 6, FTU: 0, RAU: 0, RCU: 4, RGU: 5, RTU: 0

DeepVariant:

Qual: 38.9,

GT: 0/1, GQ: 39, DP: 25, AD: [14, 11], VAF: 0.44, PL: [38, 0, 72]

chr15:18,987,076 G>A
missense variant ***OR4M2B***
NM_001395296.1:c.851G>A
NP_001382225.1:p.Arg284His

VAF: 22.73% Cosmic: 10 GnomAD: 0.0079115

ClairS:

Qual: 11.797,

GT: 0/1, GQ: 11, DP: 22, AF: 0.2273, AD: [0, 5], NAF: 0, NDP: 11, NAD: [0, 0], AU: 5, CU: 0, GU: 17, TU: 0, NAU: 0, NCU: 0, NGU: 11, NTU: 0, H, FAU: 3, FCU: 0, FGU: 8, FTU: 0, RAU: 2, RCU: 0, RGU: 9, RTU: 0

DeepVariant:

Qual: 30.8,

GT: 0/1, GQ: 31, DP: 22, AD: [17, 5], VAF: 0.227273, PL: [30, 0, 63]

chr16:22,136,495 A><DEL>
intergenic variant ***MOSMO***

VAF: 7.32%

Nanomonsv:

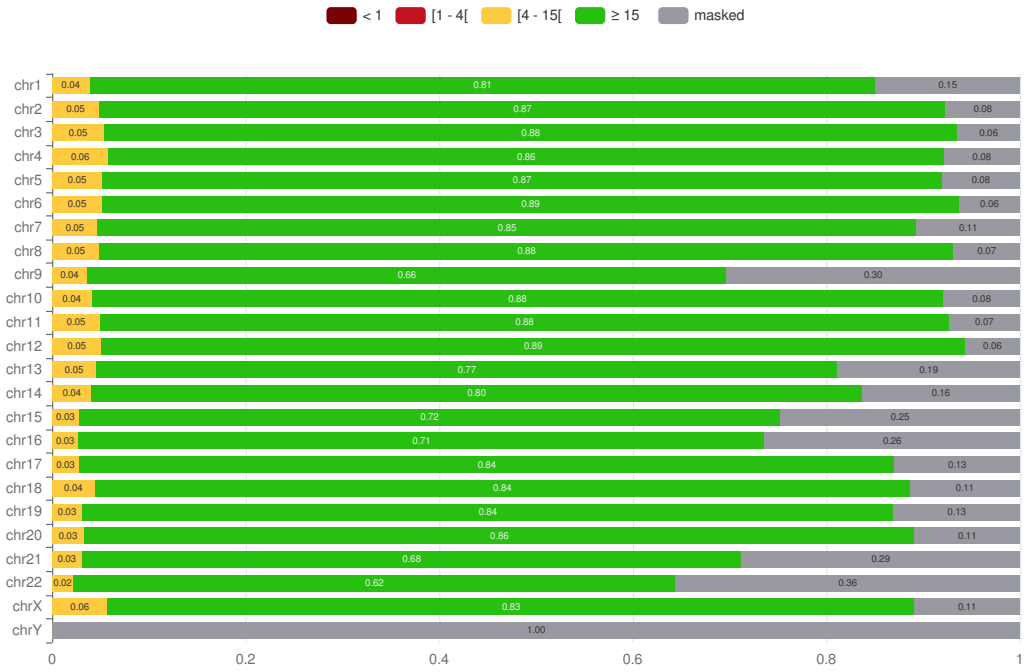
TR: 41, VR: 3, SVTYPE: DEL, SVLEN: −4996, END: 22141491

chr16:22,141,703 T›<DEL>
feature truncation, frameshift variant ***MOSMO***
VAF: 7.14% Nanomonsv: TR: 42, VR: 3, SVTYPE: DEL, SVLEN: −67080, END: 22208783

chr16:30,611,829 G›C
missense variant ***NPIPB4***
NM_001310148.2:c.808C>G
NP_001297077.1:p.Leu270Val
VAF: 66.67% DeepVariant: Qual: 5.9, GT: 0/1, GQ: 5, DP: 6, AD: [2, 4], VAF: 0.666667, PL: [4, 0, 13]

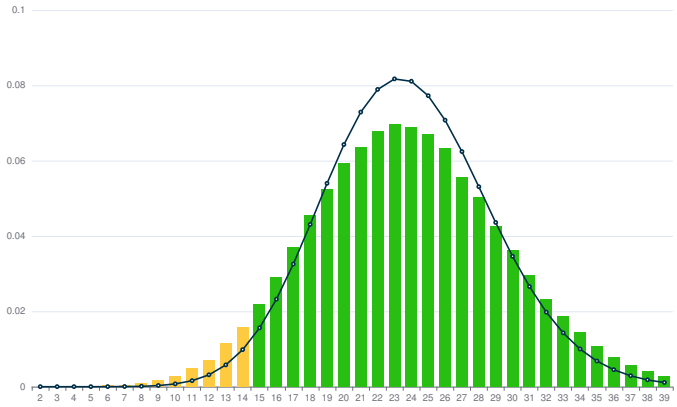
5 Coverage by chromosome

5.1 Proportion at given depth by chromosome

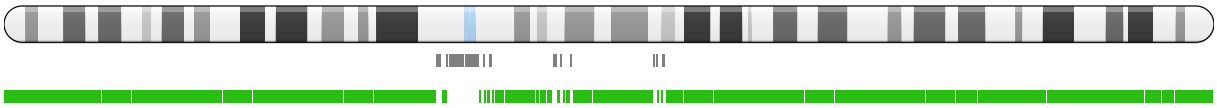


chr1

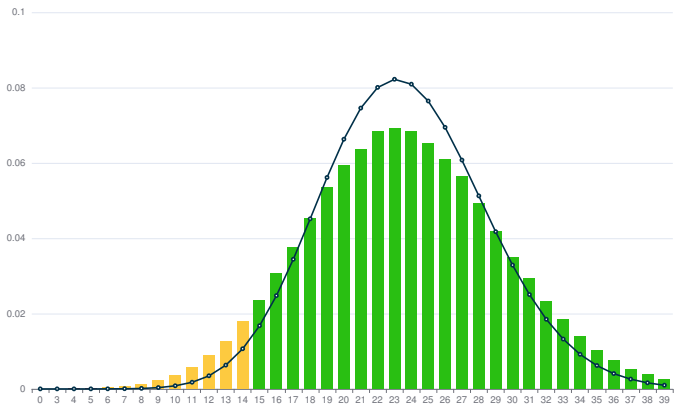
Mean	23.82
Standard dev.	5.8
< 1	0%
[1 - 4[	0%
[4 - 15[	4.6%
≥ 15	95.4%



chr2

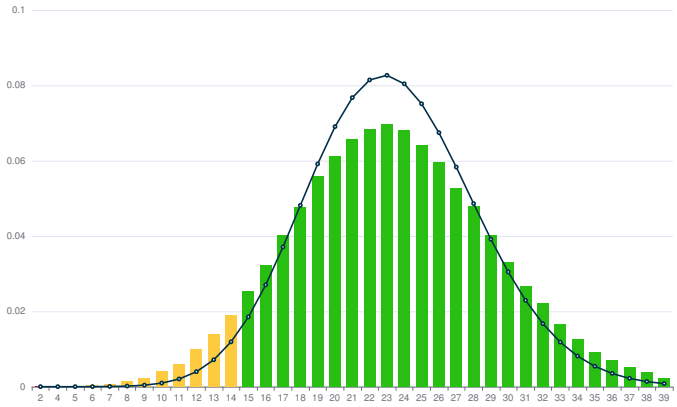


Mean	23.62
Standard dev.	5.81
< 1	0%
[1 - 4[	0%
[4 - 15[	5.3%
≥ 15	94.7%



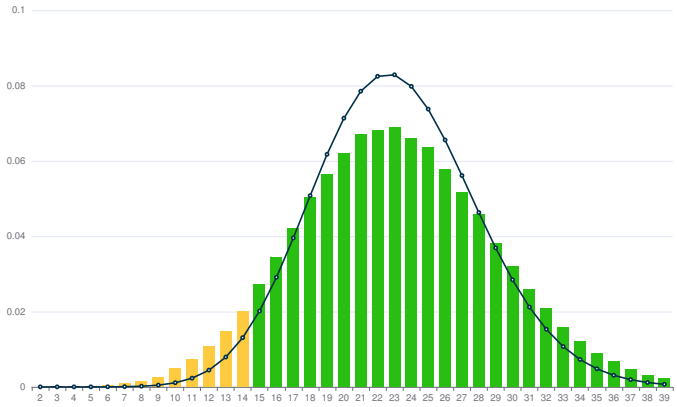
chr3

Mean	23.35
Standard dev.	5.81
< 1	0%
[1 - 4[	0%
[4 - 15[	5.8%
≥ 15	94.2%

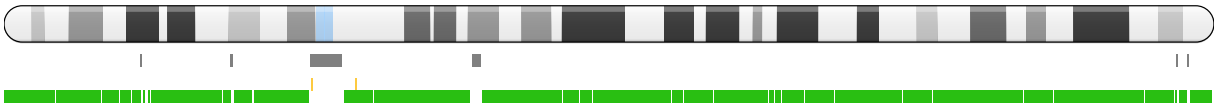


chr4

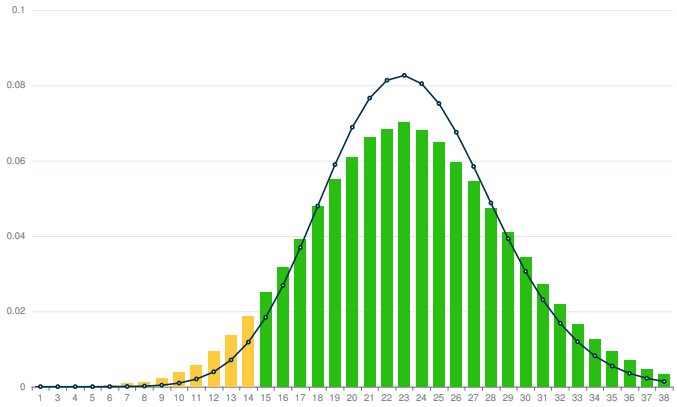
Mean	23.11
Standard dev.	5.84
< 1	0%
[1 - 4[	0%
[4 - 15[	6.4%
≥ 15	93.6%



chr5

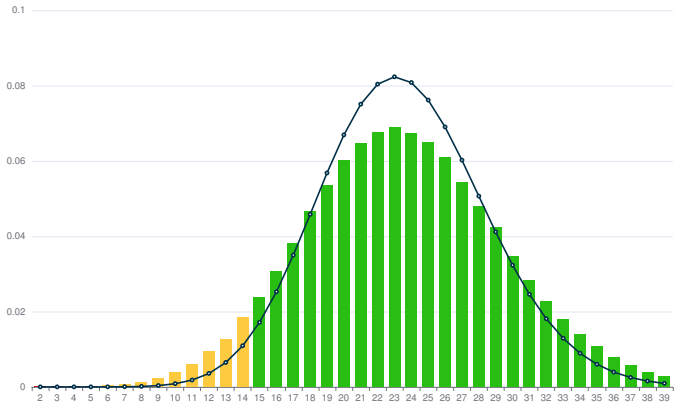


Mean	23.36
Standard dev.	5.74
< 1	0%
[1 - 4[	0%
[4 - 15[	5.6%
≥ 15	94.4%

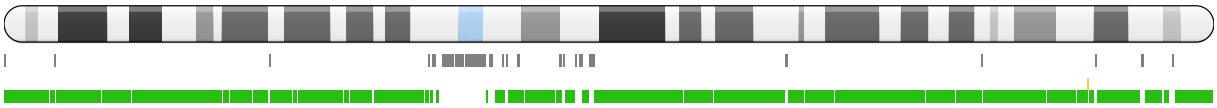


chr6

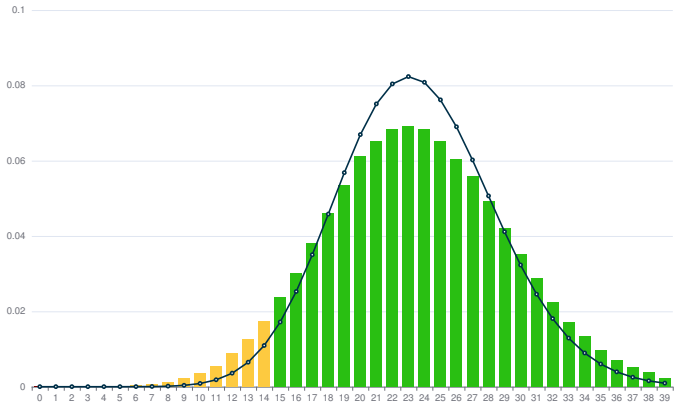
Mean	23.56
Standard dev.	5.85
< 1	0%
[1 - 4[	0%
[4 - 15[	5.5%
≥ 15	94.5%



chr7

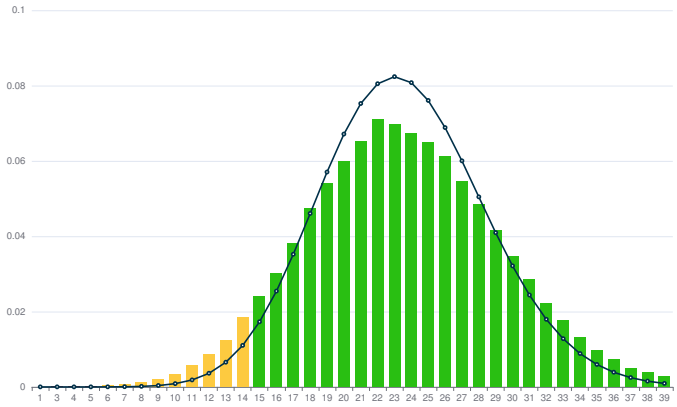


Mean	23.56
Standard dev.	5.85
< 1	0%
[1 - 4[	0%
[4 - 15[	5.2%
≥ 15	94.7%

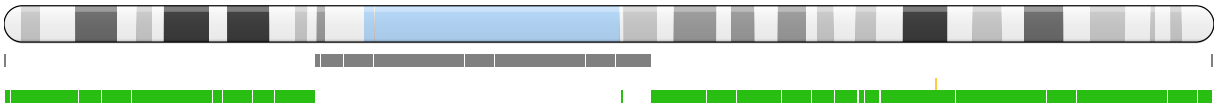


chr8

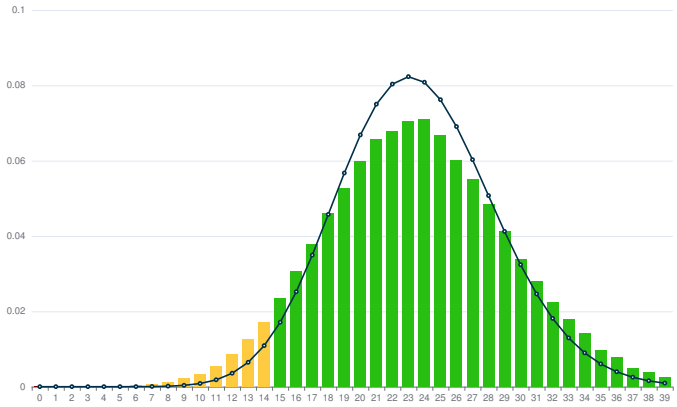
Mean	23.54
Standard dev.	5.78
< 1	0%
[1 - 4[	0%
[4 - 15[	5.3%
≥ 15	94.7%



chr9

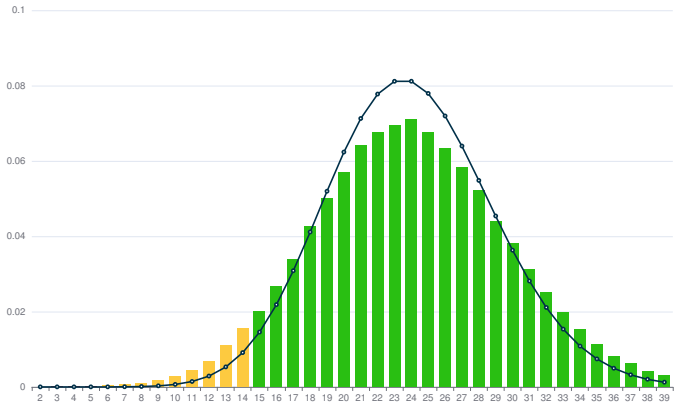


Mean	23.57
Standard dev.	5.79
< 1	0%
[1 - 4[	0%
[4 - 15[	5.2%
≥ 15	94.8%



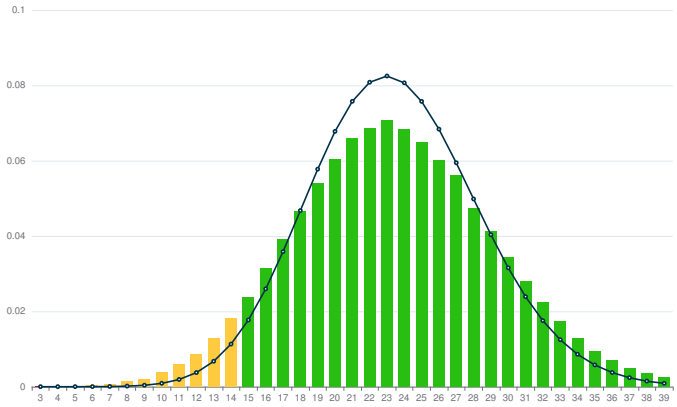
chr10

Mean	24
Standard dev.	5.76
< 1	0%
[1 - 4[	0%
[4 - 15[	4.5%
≥ 15	95.5%

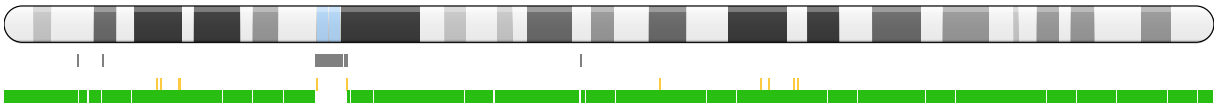


chr11

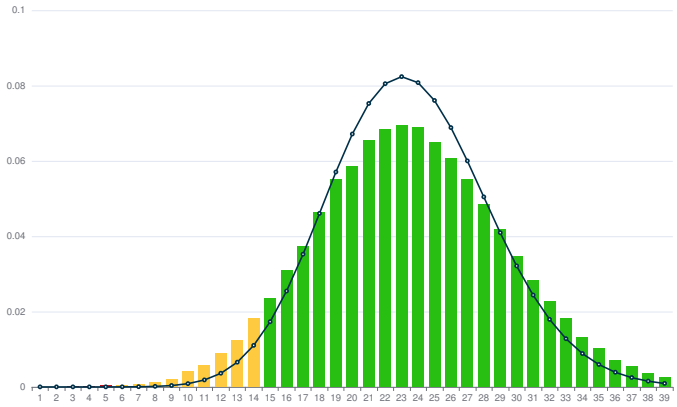
Mean	23.47
Standard dev.	5.75
< 1	0%
[1 - 4[	0%
[4 - 15[	5.4%
≥ 15	94.6%



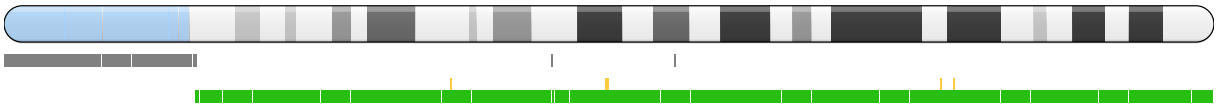
chr12



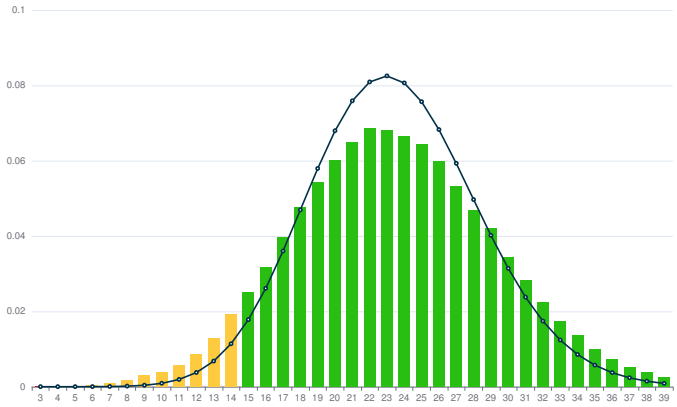
Mean	23.54
Standard dev.	5.81
< 1	0%
[1 - 4[	0%
[4 - 15[	5.4%
≥ 15	94.6%



chr13

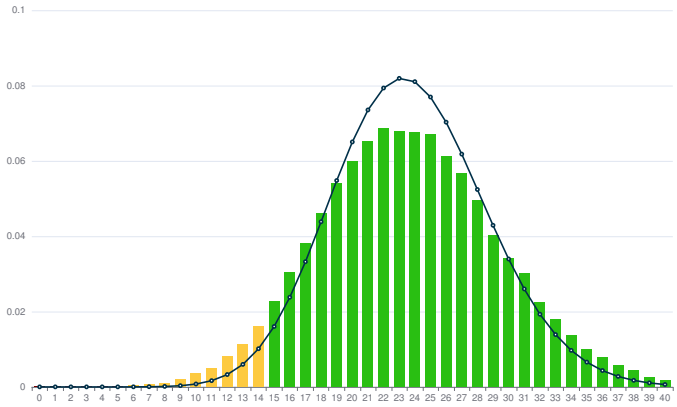


Mean	23.46
Standard dev.	5.86
< 1	0%
[1 - 4[	0%
[4 - 15[	5.6%
≥ 15	94.4%



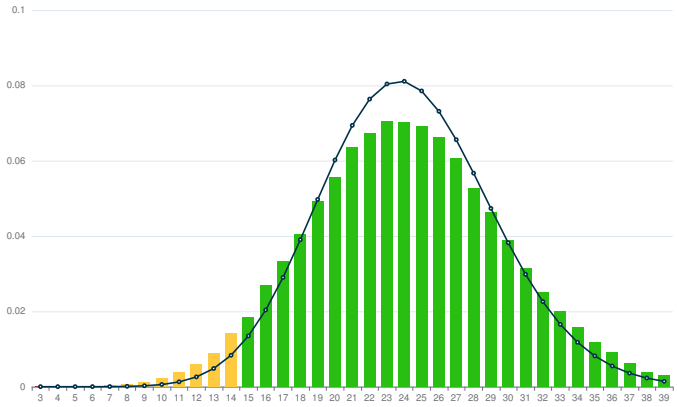
chr14

Mean	23.74
Standard dev.	6.09
< 1	0%
[1 - 4[	0%
[4 - 15[	4.8%
≥ 15	95.1%



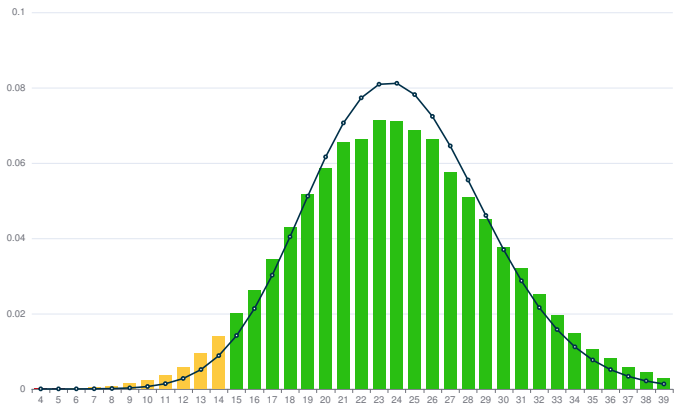
chr15

Mean	24.21
Standard dev.	5.69
< 1	0%
[1 - 4[	0%
[4 - 15[	3.7%
≥ 15	96.3%

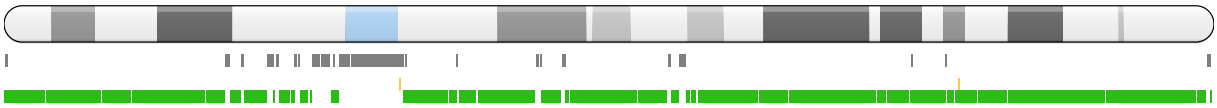


chr16

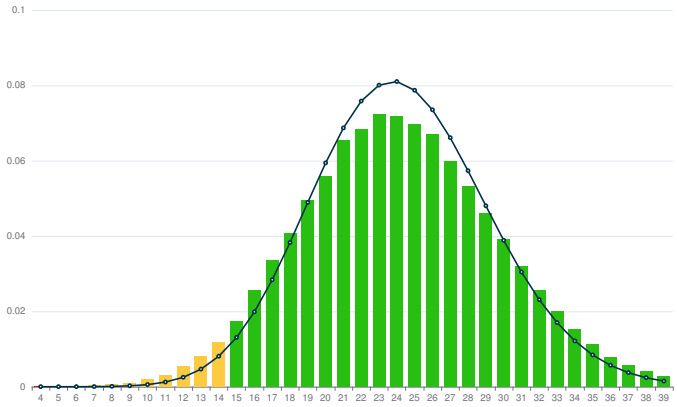
Mean	24.07
Standard dev.	5.7
< 1	0%
[1 - 4[	0%
[4 - 15[	3.7%
≥ 15	96.3%



chr17

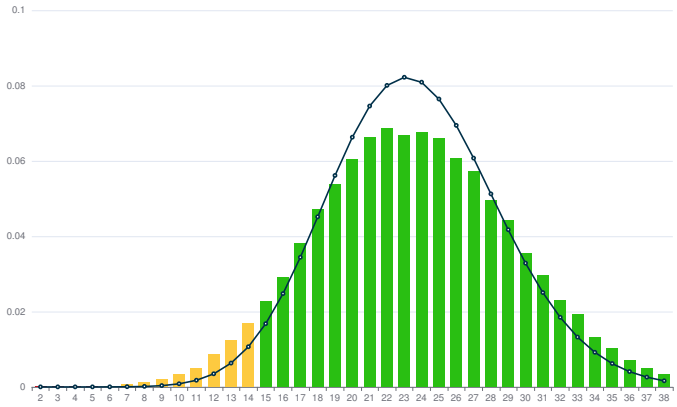


Mean	24.28
Standard dev.	5.87
< 1	0%
[1 - 4[	0%
[4 - 15[	3.2%
≥ 15	96.8%



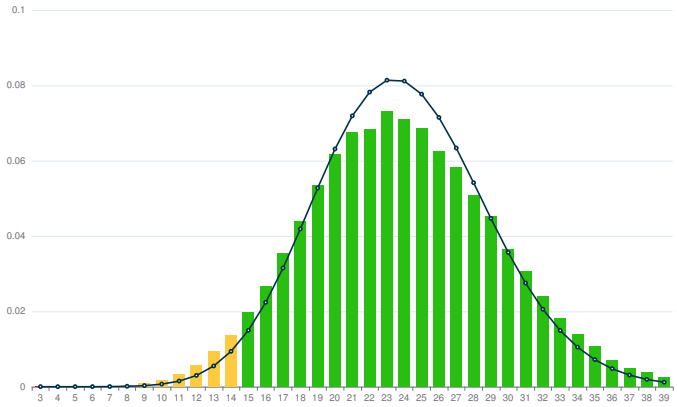
chr18

Mean	23.62
Standard dev.	5.71
< 1	0%
[1 - 4[	0%
[4 - 15[	5%
≥ 15	95%

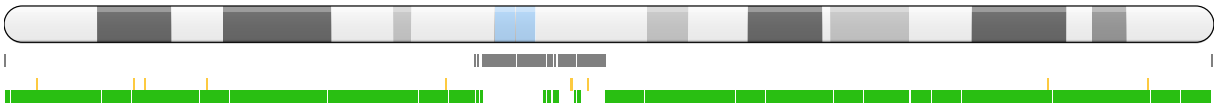


chr19

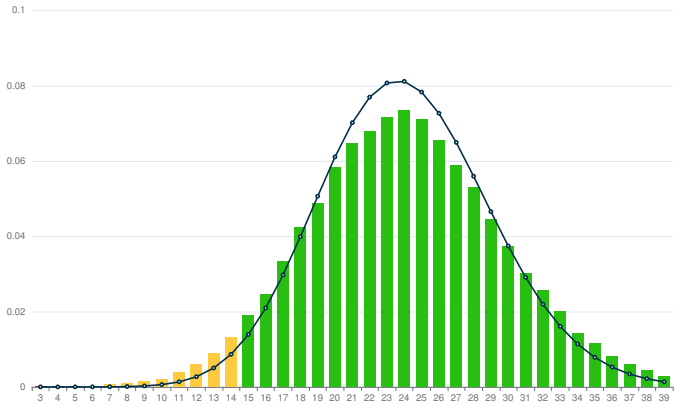
Mean	23.93
Standard dev.	5.53
< 1	0%
[1 - 4[	0%
[4 - 15[	3.6%
≥ 15	96.4%



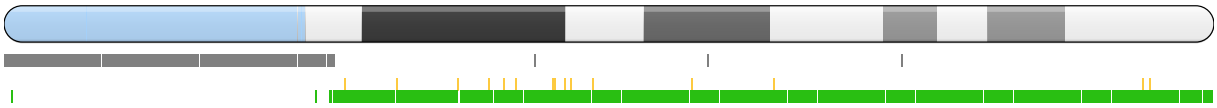
chr20



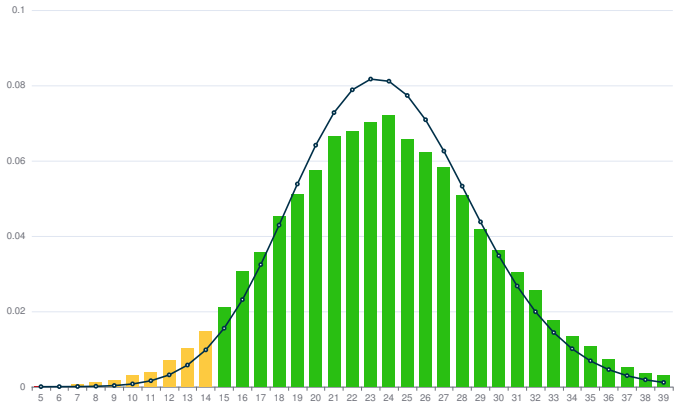
Mean	24.13
Standard dev.	5.65
< 1	0%
[1 - 4[	0%
[4 - 15[	3.7%
≥ 15	96.3%



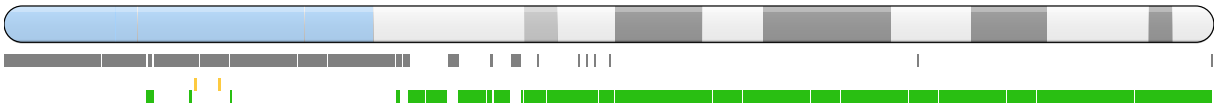
chr21



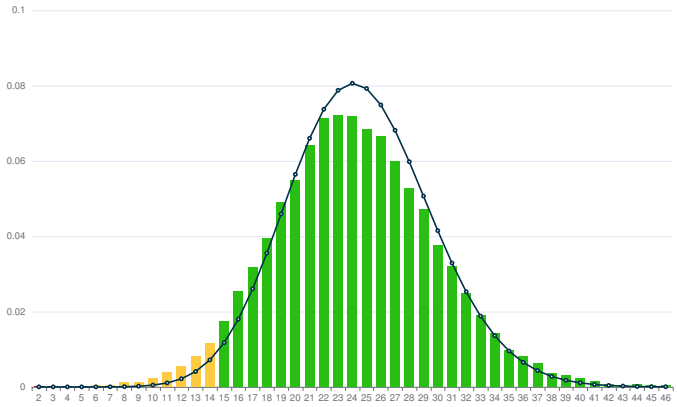
Mean	23.83
Standard dev.	5.73
< 1	0%
[1 - 4[	0%
[4 - 15[	4.3%
≥ 15	95.7%



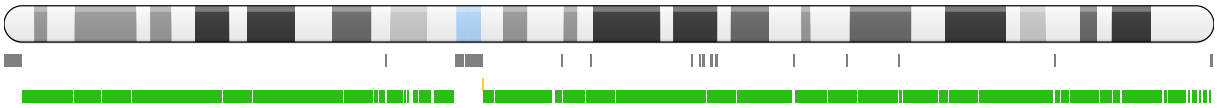
chr22



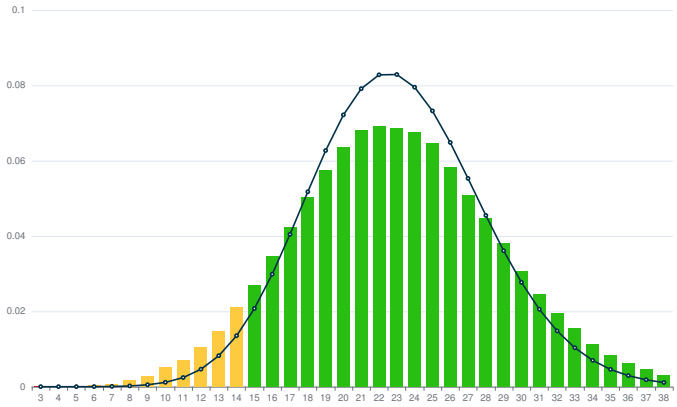
Mean	24.57
Standard dev.	6.84
< 1	0%
[1 - 4[	0%
[4 - 15[	3.4%
≥ 15	96.6%



chrX

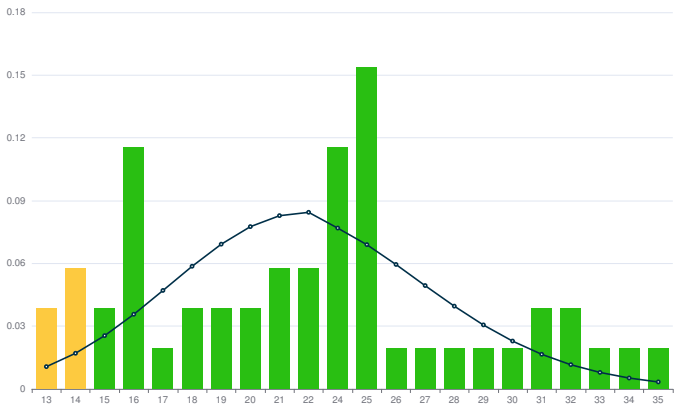


Mean	23.02
Standard dev.	5.81
< 1	0%
[1 - 4[	0%
[4 - 15[	6.5%
≥ 15	93.5%



chrY

Mean	22.42
Standard dev.	5.98
< 1	0%
[1 - 4[	0%
[4 - 15[	9.6%
≥ 15	90.4%



Values computed by Pandora development version

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.
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.