Whole Genome Sequencing Report

Table of Contents

1 Interprétation

LAL-T présentant une surexpression de ***TLX1***.

Réarrangements

— Détection d'une inversion du chr10 en *de novo* (chr10:101959873_delins[chr10:91810279inv]) pouvant expliquer la surexpression de ***TLX1***.
— Translocation t(11;14) ***LMO2::TRDJ2***.

Délétions larges

— 9p de 1.5 et 0.8 mb (chr9:21,114,072-22,647,809 et chr9:21,456,537-22,302,985) impliquant ***CDKN2A*** (délétion homozygote).
— 6q de 39 mb (chr6:77,403,969-116,633,781, heterozygote).
— 14q 1 mb (chr14:93,166,921-94,282,138) impliquant notamment ***BCL11B***.
— de 207 kb (chr2:213,629,607-213,836,391) impliquant notamment ***IKZF2***.

Mutations tronquantes

— ***NOTCH1*** (NP_060087.3:p.Glu2506ArgfsTer2 30%).
— ***PTEN*** (chr10:88,748,618-88,812,354_del ~20%).
— ***PHF6*** (NP_115711.2:p.Arg116Ter 79%).
— délétion des deux premiers exons de ***XBP1*** (chr22:29,260,470-29,273,269).
— délétion du dernier exon de ***PMAIP1*** (voie de l'apoptose).
— délétion des trois premiers exons de ***LEF1*** (chr4:111,443,866-111,469,588).
— délétion de 81 kb dans ***MCM9*** (chr6:119,998,943-120,080,085).
— délétion de 159 kb impliquant les premiers exons de ***KDM6A*** (chrX:44,279,685-44,439,058 homozygote).

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

2 Sample identity

CHAMPION

3 Alignement

Diagnostic sample

Id	CHAMPION
Time Point	diag
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/08/27 06h58
Number Of Reads	17.8 M
Yield Gb	99.71
Mean Coverage	31.99
N50	8 k
Median Length	5497
Mean Length	5588
Median Identity	99.4
Mean Identity	117.38
Run(s)	aaa1e: 67% 9b3eb: 33%

MRD sample

Id	CHAMPION
Time Point	mrd
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/08/17 13h33
Number Of Reads	14 M
Yield Gb	64.6
Mean Coverage	20.72
N50	7.7 k
Median Length	3926
Mean Length	4626
Median Identity	99.34
Mean Identity	114.66
Run(s)	d3af9: 100%

Values computed by cramino v0.14.5

3.1 Normalized read count by chromosome

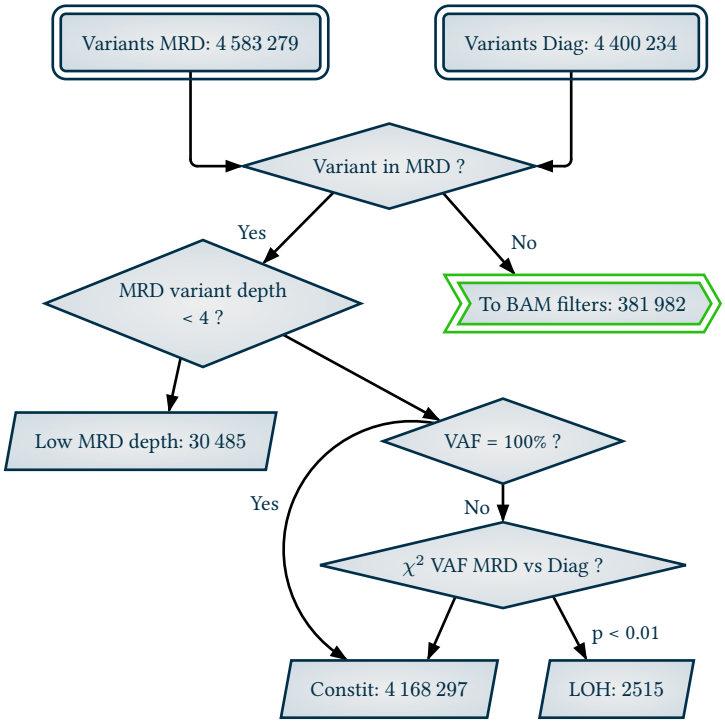
	chr1	chr2	chr3	chr4	chr5	chr6	chr7	chr8	chr9	chr10	chr11	chr12	chr13
diag	0.98	1.03	1.01	0.99	1.01	1	1.02	1.42	0.85	1.03	1	1.02	0.96
mrd	0.98	1.02	0.99	0.96	0.99	1.01	1.02	1	0.85	1.03	1	1.02	0.93

	chr14	chr15	chr16	chr17	chr18	chr19	chr20	chr21	chr22	chrX	chrY	chrM
diag	0.98	0.96	0.9	1.01	0.98	0.98	1	1.03	1.04	0.5	0.35	98.22
mrd	0.98	0.95	0.91	1.04	0.97	1.01	1.01	1	1.05	0.49	0.31	38.31

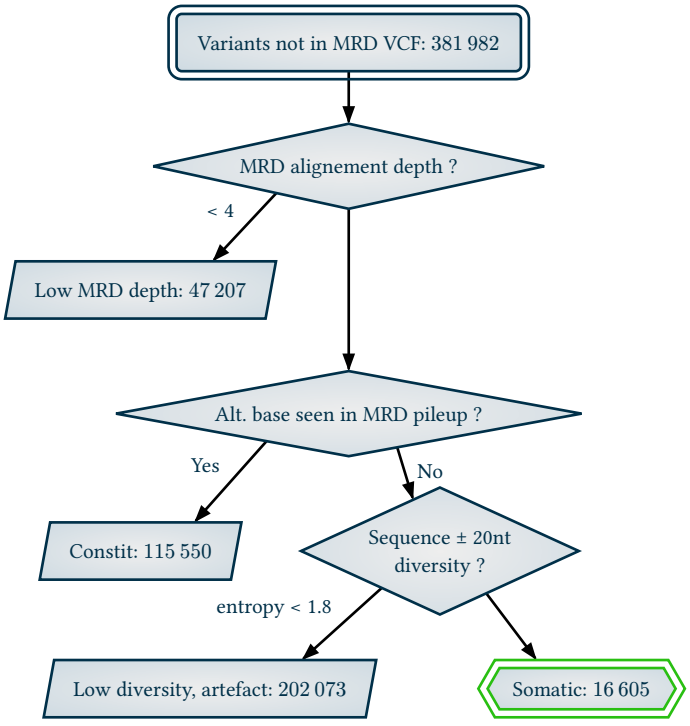
4 Variants

4.1 Variants calling

VCF filters

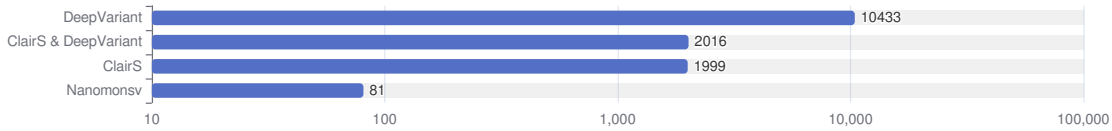


BAM filters

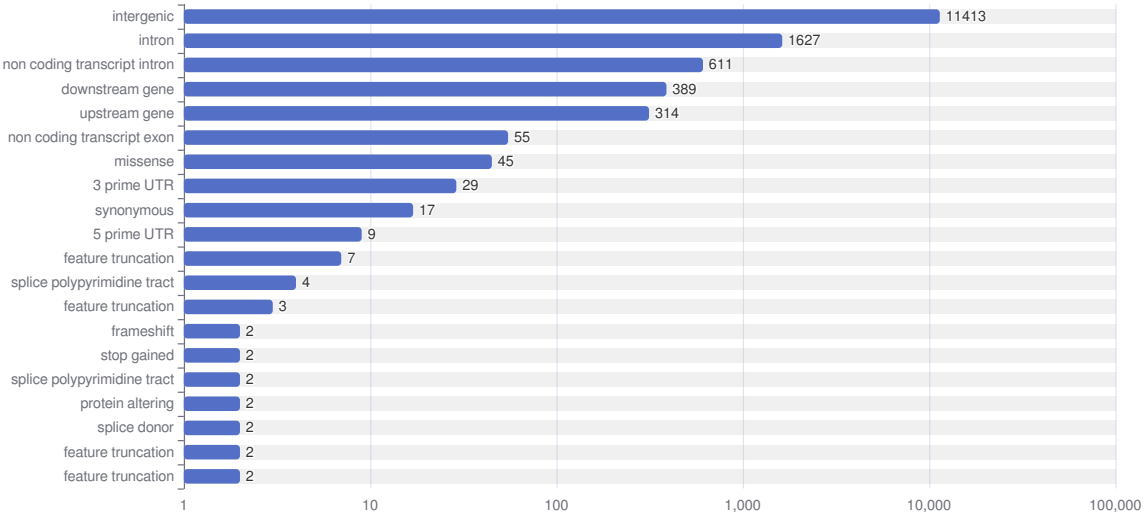


4.2 Somatic variants

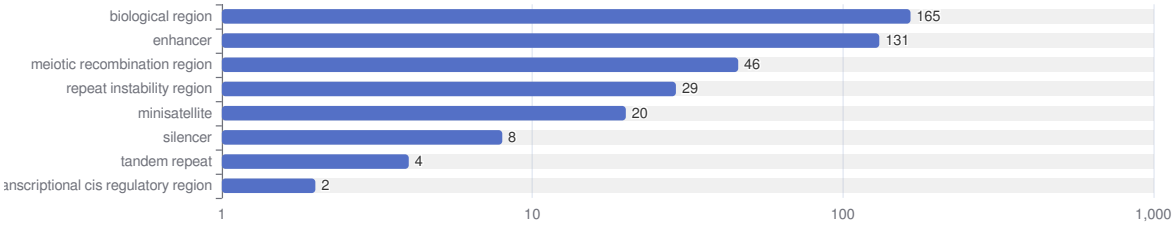
Callers



Consequences (VEP)



NCBI features



4.3 Selected Variants

Pathogenics

chr4:111,443,866 A›<DEL>
intron variant ***LEF1***
VAF: 34.88% Nanomonsv: TR: 43, VR: 15, SVTYPE: DEL, SVLEN: −25722, END: 111469588, SVINSLEN: 1, SVINSSEQ: A

chr9:148,725,322 C›CACCG
frameshift variant ***NOTCH1***
NM_017617.5:c.7515_7516insCGGT
NP_060087.3:p.Glu2506ArgfsTer2
VAF: 30.3% DeepVariant: Qual: 24.3, GT: 0/1, GQ: 24, DP: 33, AD: [23, 10], VAF: 0.30303, PL: [24, 0, 50]

chr9:148,732,403 G›T
missense variant ***NOTCH1***
NM_017617.5:c.5046C>A
NP_060087.3:p.Asn1682Lys
VAF: 32.14% ClairS: Qual: 17.601, GT: 0/1, GQ: 17, DP: 28, AF: 0.3214, AD: [0, 9], NAF: 0, NDP: 14, NAD: [0, 0], AU: 0, CU: 0, GU: 19, TU: 9, NAU: 0, NCU: 0, NGU: 14, NTU: 0, H, FAU: 0, FCU: 0, FGU: 11, FTU: 4, RAU: 0, RCU: 0, RGU: 8, RTU: 5

chr10:88,748,366 C›<DEL>
5 prime UTR variant, feature truncation ***PTEN***

VAF: 12.77%

Nanomonsv:

TR: 47, VR: 6, SVTYPE: DEL, SVLEN: −14655, END: 88763021, SVINSLEN: 8, SVINSSEQ:

TCCGTCCA

chr10:88,748,618 G›GAATCGAAGGGC]chr10:88813830]
feature truncation, intron variant ***PTEN***

VAF: 11.11%

Nanomonsv:

TR: 36, VR: 4, SVTYPE: BND, SVINSLEN: 11, SVINSSEQ:

AATCGAAGGGC

, MATEID: r_20_1

chr10:88,813,830 t›tGCCCTTCGATT]chr10:88748618]
feature truncation, intron variant ***PTEN***

VAF: 11.11%

Nanomonsv:

TR: 36, VR: 4, SVTYPE: BND, SVINSLEN: 11, SVINSSEQ:

GCCCTTCGATT

, MATEID: r_20_0

chr10:101,959,873 G›G]chr10:91813718]

VAF: 23.81%

Nanomonsv:

TR: 63, VR: 15, SVTYPE: BND, MATEID: r_21_0

chr10:101,959,874 G›[chr10:91813721[G
VAF: 14.29% Nanomonsv: TR: 63, VR: 9, SVTYPE: BND, MATEID: r_22_0

chr11:34,032,967 g›[chr14:16654047[T
upstream gene variant ***LMO2***
VAF: 20.97% Nanomonsv: TR: 62, VR: 13, SVTYPE: BND, MATEID: r_25_1

chr11:34,036,922 C›]chr14:16654048]CAGGGGTTTCA...
feature truncation, intron variant, non coding transcript variant ***LOC105376621***
VAF: 20.69% Nanomonsv: TR: 58, VR: 12, SVTYPE: BND, SVINSLEN: 31, SVINSSEQ: CAGGGGTTTCAGCCCTCTGACTTCTAAAGTA , MATEID: r_26_1

chr14:16,654,047 T›[chr11:34032967[T
upstream gene variant ***TRDJ2***
VAF: 20.97% Nanomonsv: TR: 62, VR: 13, SVTYPE: BND, MATEID: r_25_0

chr14:16,654,048 G›GTACTTTAGAAGTCAGAGGGCTGAAAC...
upstream gene variant ***TRDJ2***

VAF: 20.69%

Nanomonsv:

TR: 58, VR: 12, SVTYPE: BND, SVINSLEN: 31, SVINSSEQ:

TACTTTAGAAGTCAGAGGGCTGAAACCCCTG

, MATEID: r_26_0

chrX:132,718,755 C›T
stop gained ***PHF6***
NM_032335.3:c.346C>T
NP_115711.2:p.Arg116Ter

VAF: 79.29% Cosmic: 20

DeepVariant:

Qual: 28.6,

GT: 0/1, GQ: 24, DP: 15, AD: [3, 12], VAF: 0.8, PL: [28, 0, 26]

ClairS:

Qual: 16.964,

GT: 0/1, GQ: 16, DP: 14, AF: 0.7857, AD: [0, 11], NAF: 0, NDP: 5, NAD: [0, 0], AU: 0, CU: 3, GU: 0, TU: 11, NAU: 0, NCU: 5, NGU: 0, NTU: 0, FAU: 0, FCU: 1, FGU: 0, FTU: 8, RAU: 0, RCU: 2, RGU: 0, RTU: 3

Likely Pathogenics

chr1:7,892,796 G›A
missense variant ***RERE***
NM_012102.4:c.3428C>T
NP_036234.3:p.Ser1143Leu

VAF: 17.59%

DeepVariant:

Qual: 3.4,

GT: 0/1, GQ: 3, DP: 30, AD: [25, 5], VAF: 0.166667, PL: [0, 0, 35]

ClairS:

Qual: 12.637,

GT: 0/1, GQ: 12, DP: 27, AF: 0.1852, AD: [0, 5], NAF: 0, NDP: 8, NAD: [0, 0], AU: 5, CU: 0, GU: 22, TU: 0, NAU: 0, NCU: 0, NGU: 8, NTU: 0, H, FAU: 4, FCU: 0, FGU: 9, FTU: 0, RAU: 1, RCU: 0, RGU: 13, RTU: 0

chr2:213,629,607 A›<DEL>
intron variant ***IKZF2***

VAF: 11.36%

Nanomonsv:

TR: 44, VR: 5, SVTYPE: DEL, SVLEN: −206784, END: 213836391, SVINSLEN: 11, SVINSSEQ:

GGTGGGAAGGG

chr6:77,403,969 A›<DEL>
intergenic variant

VAF: 7.27%

Nanomonsv:

TR: 55, VR: 4, SVTYPE: DEL, SVLEN: −39229812, END: 116633781, SVINSLEN: 26, SVINSSEQ:

CACAGGAAGTGGACACTTCCTGTGTC

chr6:119,998,943 A›<DEL>
downstream gene variant ***MCM9***
VAF: 14.55% Nanomonsv: TR: 55, VR: 8, SVTYPE: DEL, SVLEN: −81142, END: 120080085

chr9:21,114,072 t›<DEL>
intergenic variant
VAF: 19.61% Nanomonsv: TR: 51, VR: 10, SVTYPE: DEL, SVLEN: −1533737, END: 22647809, SVINSLEN: 13, SVINSSEQ: CCATTTAATTAAC

chr9:21,456,537 a›<DEL>
downstream gene variant ***IFNA1***
VAF: 33.33% Nanomonsv: TR: 21, VR: 7, SVTYPE: DEL, SVLEN: −846448, END: 22302985, SVINSLEN: 9, SVINSSEQ: AATAGAAGA

chr12:10,301,388 g›<DEL>
intron variant ***KLRC3***
VAF: 15.91% Nanomonsv: TR: 44, VR: 7, SVTYPE: DEL, SVLEN: −227, END: 10301615

chr14:93,166,921 a›<DEL>
intergenic variant
VAF: 28.33% Nanomonsv: TR: 60, VR: 17, SVTYPE: DEL, SVLEN: −1115217, END: 94282138, SVINSLEN: 5, SVINSSEQ: ACATG

chr18:60,104,834 C›<DEL>
intron variant ***PMAIP1***
VAF: 5.48% Nanomonsv: TR: 73, VR: 4, SVTYPE: DEL, SVLEN: −57279, END: 60162113, SVINSLEN: 4, SVINSSEQ: TAAG

chr18:60,104,866 C›<DEL>
intron variant ***PMAIP1***
VAF: 7.69% Nanomonsv: TR: 78, VR: 6, SVTYPE: DEL, SVLEN: −119000, END: 60223866, SVINSLEN: 6, SVINSSEQ: CCGGGG

chr22:29,260,470 C›<DEL>
intron variant ***XBP1***
VAF: 12.5% Nanomonsv: TR: 32, VR: 4, SVTYPE: DEL, SVLEN: −12799, END: 29273269, SVINSLEN: 3, SVINSSEQ: TCC

chrX:44,279,685 G›<DEL>
intergenic variant
VAF: 45.45% Nanomonsv: TR: 22, VR: 10, SVTYPE: DEL, SVLEN: −159373, END: 44439058, SVINSLEN: 8, SVINSSEQ: CCTCTTTA

Variants of uncertain significance

chr1:282,123 G›A
intron variant, non coding transcript variant ***LINC01128***
NR_047519.1:n.721-237G>A
VAF: 59.99% GnomAD: 0.0000065 DeepVariant: Qual: 29, GT: 0/1, GQ: 29, DP: 28, AD: [11, 17], VAF: 0.607143, PL: [28, 0, 59] ClairS: Qual: 18.36, GT: 0/1, GQ: 18, DP: 27, AF: 0.5926, AD: [0, 16], NAF: 0, NDP: 22, NAD: [0, 0], AU: 16, CU: 0, GU: 11, TU: 0, NAU: 0, NCU: 0, NGU: 22, NTU: 0, FAU: 8, FCU: 0, FGU: 4, FTU: 0, RAU: 8, RCU: 0, RGU: 7, RTU: 0

chr1:155,013,137 c›cAAAAAAATAAAAATAAAAATAATAAA...

intron variant ***SYT11***

VAF: 10%

Nanomonsv:

TR: 40, VR: 4, SVTYPE: INS, END: 155013187, SVINSLEN: 90, SVINSSEQ:

AAAAAAATAAAAATAAAAATAATAAAAATAAAATAAAACTGGCTGAGGATACTTTCCATG
GATACGATTAAGAGCTGACAATAGGCCGGG

chr2:66,003,465 a›<DUP>

intron variant, non coding transcript variant ***LINC02934***

VAF: 35.94%

Nanomonsv:

TR: 64, VR: 23, SVTYPE: DUP, SVLEN: 1981, END: 66005446, SVINSLEN: 4, SVINSSEQ:

AGGC

chr3:2,447,907 g›gCCCCATATTATAAGCAAAGAACCTGA...

intron variant ***CNTN4***

VAF: 13.04%

Nanomonsv:

TR: 23, VR: 3, SVTYPE: INS, END: 2447907, SVINSLEN: 267, SVINSSEQ:

CCCCATATTATAAGCAAAGAACCTGAGGCTCAAAGAAGCTAACTTGCCTGTTGTTACATG
GCAAGAGTATGGCCAGAATTCAAGTCTAGGTTGTTTAAGTTCCAAAGTCTATGTGTGTTT
CCTACTCCATTAGTGATCTCCTCTCCTCTAGGATACCTTTCATATTAATTTGATACTCAG
TAAGTATTTCATGATTGAAGTGATTTCTGTGCTTGTTGCATGGATATCCTCGAATCCTGT
AGCATTCTGACAGGGTAAATATAATCC

chr4:39,338,509 t›tGTGACACTGACAGATCCATTATTTTA...
upstream gene variant ***RFC1***

VAF: 10.53%

Nanomonsv:

TR: 38, VR: 4, SVTYPE: INS, END: 39338624, SVINSLEN: 206, SVINSSEQ:

```
GTGACACTGACAGATCCATTATTTTAAAACATAATGGAGATCTTCACTTTTAGCTTCATG
CAGTGTTTTTCTTAGTATCATTAAATTCTGTTCATCCCTTTCAGCATAAAACTTCAACAT
TTTACCCTTATGTTTCTTCAGGTCTTTTTTTTTTTTAATTTTTAATTATTTTTTCCTCTG
TTTCTTTTGTTGAAACAGGGTCTCAC
```

chr4:191,351,430 G›A
missense variant ***ZFP42***
NM_174900.5:c.679G>A
NP_777560.2:p.Val227Ile

VAF: 30.43% Cosmic: 6 GnomAD: 0.000013

ClairS:

Qual: 16.885,

GT: 0/1, GQ: 16, DP: 23, AF: 0.3043, AD: [0, 7], NAF: 0, NDP: 16, NAD: [0, 0], AU: 7, CU: 0, GU: 16, TU: 0, NAU: 0, NCU: 0, NGU: 16, NTU: 0, H, FAU: 1, FCU: 0, FGU: 9, FTU: 0, RAU: 6, RCU: 0, RGU: 7, RTU: 0

chr8:2,871,658 C›<DEL>
intron variant ***CSMD1***

VAF: 10.31%

Nanomonsv:

TR: 97, VR: 10, SVTYPE: DEL, SVLEN: −33923, END: 2905581, SVINSLEN: 2, SVINSSEQ:

```
GA
```

chr10:26,696,899 t›<DEL>
intron variant, non coding transcript variant ***SELENOOLP***

VAF: 51.72%

Nanomonsv:

TR: 29, VR: 15, SVTYPE: DEL, SVLEN: −182, END: 26697081, SVINSLEN: 1, SVINSSEQ:

A

chr11:34,365,072 c›cTTTTTTGTTTGTTTTCTTTTTGAGAT...
intron variant ***ABTB2***

VAF: 22.58%

Nanomonsv:

TR: 31, VR: 7, SVTYPE: INS, END: 34365072, SVINSLEN: 325, SVINSSEQ:

TTTTTTGTTTGTTTTCTTTTTGAGATAAGGTCTCACTTTGTTGCCCAGGCTGGAGTGCAG
TGGTGTAATCTTGGCTCAGTAGCATGATCTTGGCTCACTGCAACCTCTGCATCCCAGGTT
CAAGCAATTCTCCTGCCTCAGCCACCTGAGTATCTGGGATTACAGGCACGTGCCACCACA
CCTGGCTAATTTTTGTATTTTAAGTAGGGACAGGGTTTCGCAATGTTGGCCAGGCTGGTT
TCAAACTCCTGACCTCAGGTGATCCGCCCGCCTCGGCCTCCCAAAGTGCTGGGATTACAG
GCGTGAGCCACCACACTTGGCCTAT

chr18:15,803,744 g›<DEL>
intergenic variant

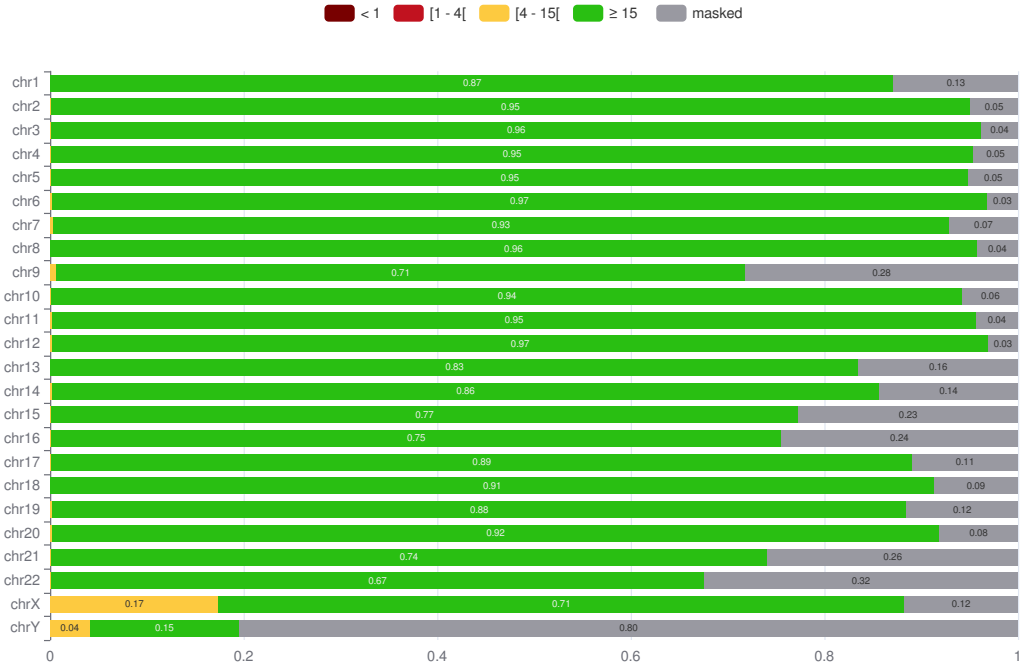
VAF: 48.15%

Nanomonsv:

TR: 27, VR: 13, SVTYPE: DEL, SVLEN: −2721, END: 15806465

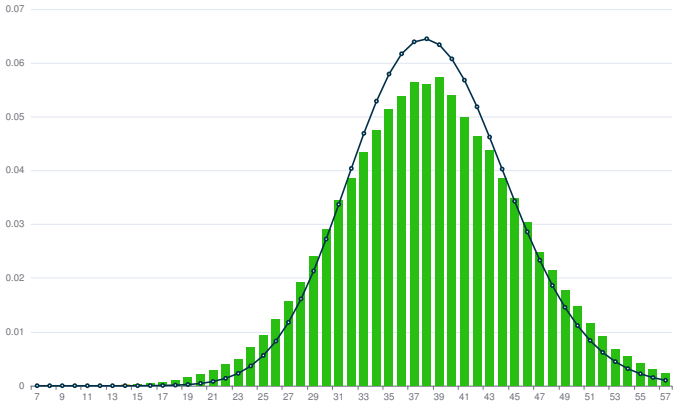
5 Coverage by chromosome

5.1 Proportion at given depth by chromosome

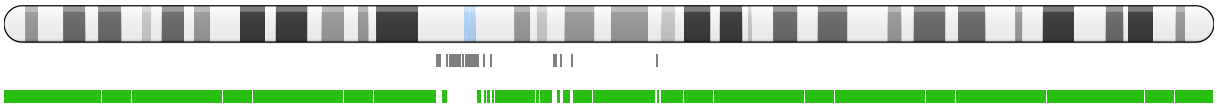


chr1

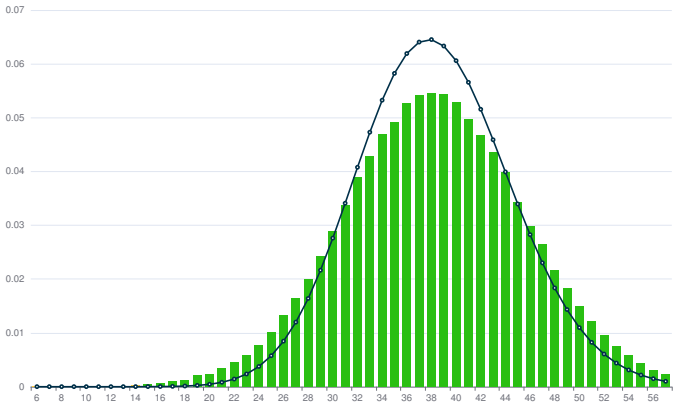
Mean	38.34
Standard dev.	7.31
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



chr2

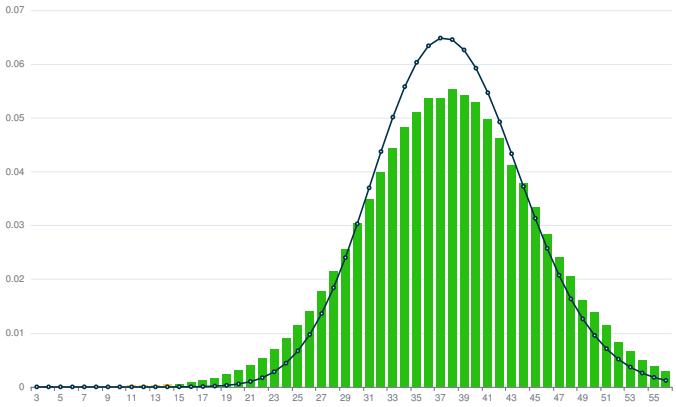


Mean	38.28
Standard dev.	7.43
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



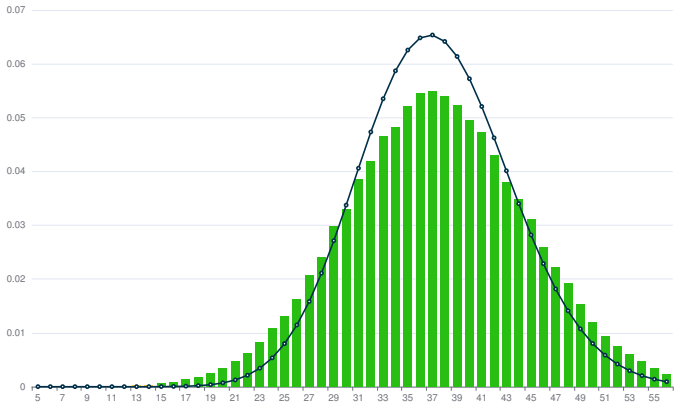
chr3

Mean	37.84
Standard dev.	7.42
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%

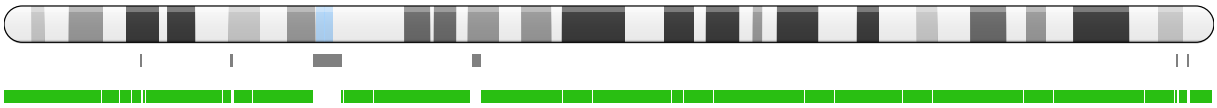


chr4

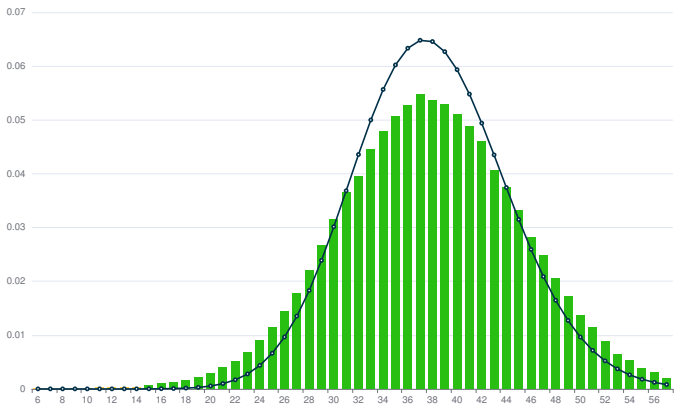
Mean	37.3
Standard dev.	7.57
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



chr5

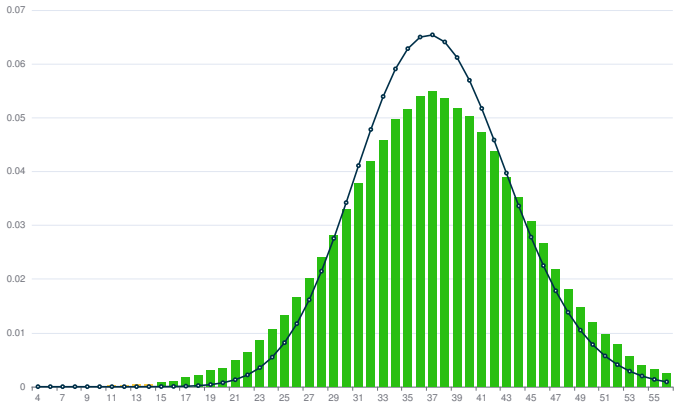


Mean	37.86
Standard dev.	7.67
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



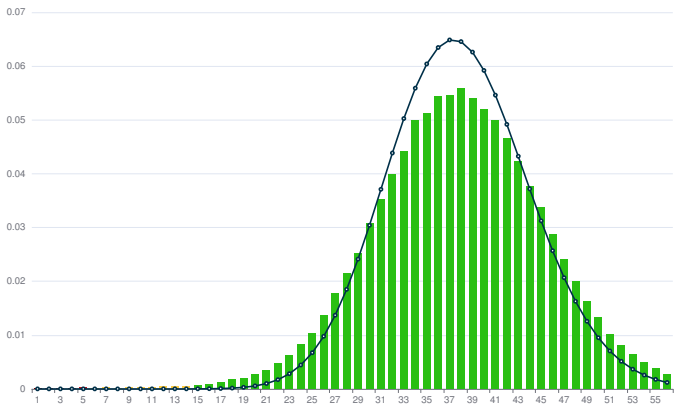
chr6

Mean	37.23
Standard dev.	7.52
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



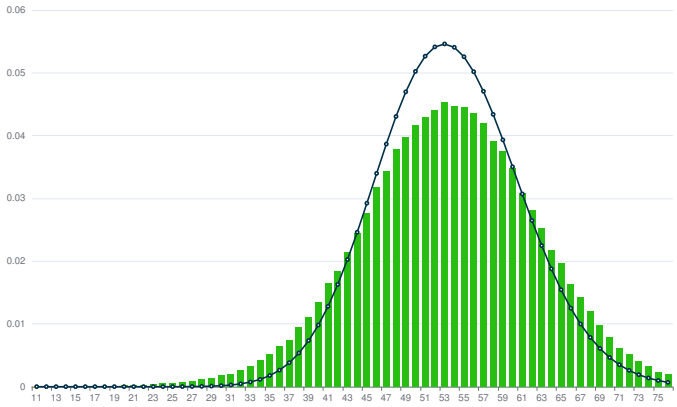
chr7

Mean	37.82
Standard dev.	7.55
< 1	0%
[1 - 4[	0%
[4 - 15[	0.3%
≥ 15	99.7%

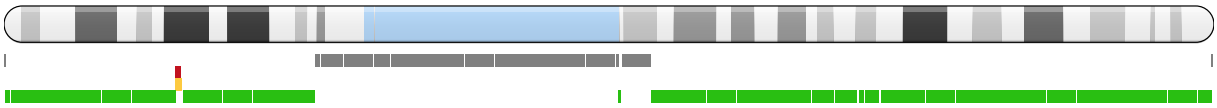


chr8

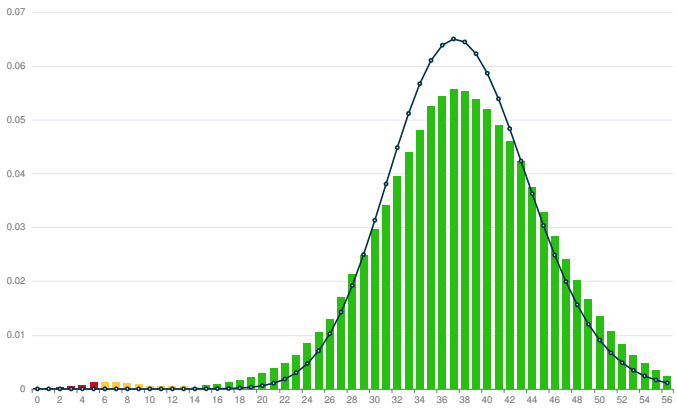
Mean	53.46
Standard dev.	9.05
< 1	0%
[1 - 4[	0%
[4 - 15[	0%
≥ 15	100%



chr9

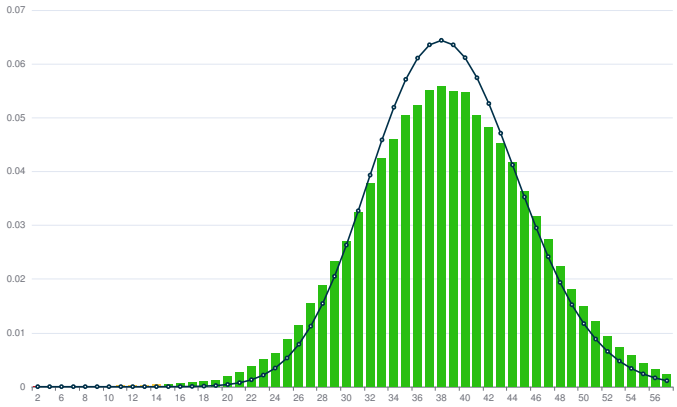


Mean	37.67
Standard dev.	7.89
< 1	0%
[1 - 4[	0.1%
[4 - 15[	0.8%
≥ 15	99.1%



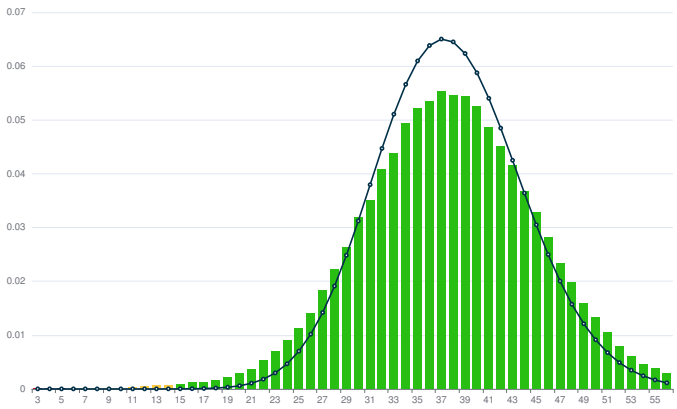
chr10

Mean	38.5
Standard dev.	7.29
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



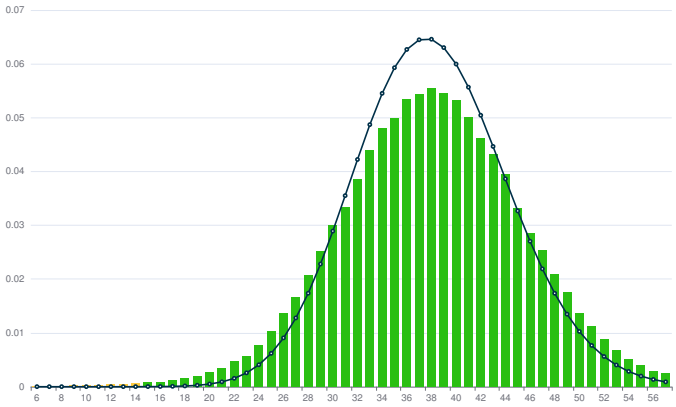
chr11

Mean	37.69
Standard dev.	7.43
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



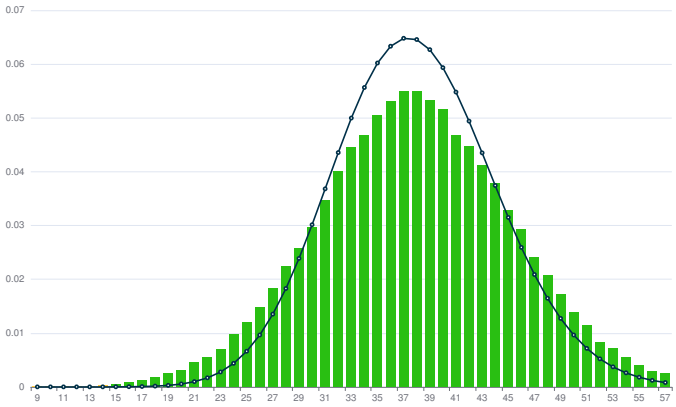
chr12

Mean	38.06
Standard dev.	7.52
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



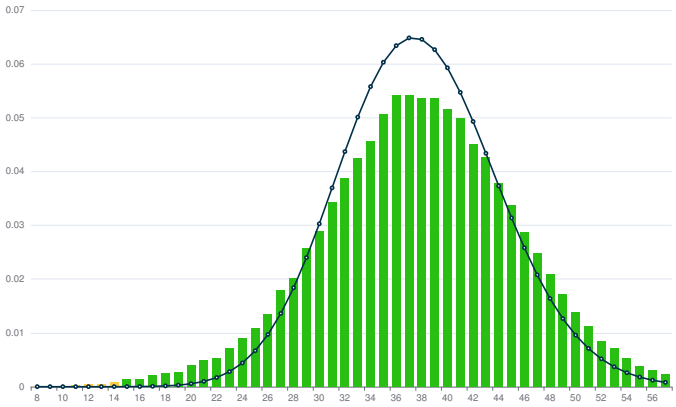
chr13

Mean	37.86
Standard dev.	7.52
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



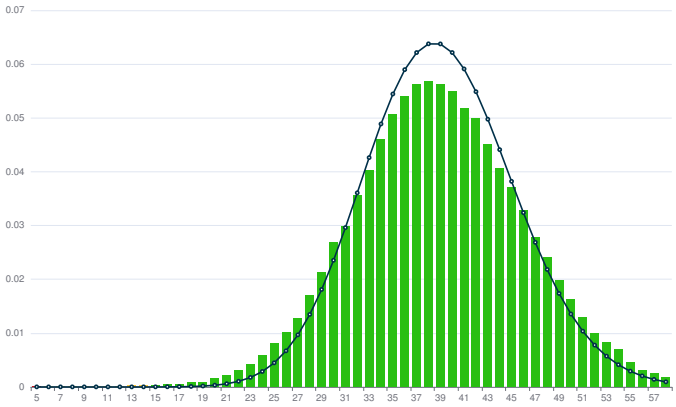
chr14

Mean	37.84
Standard dev.	7.66
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



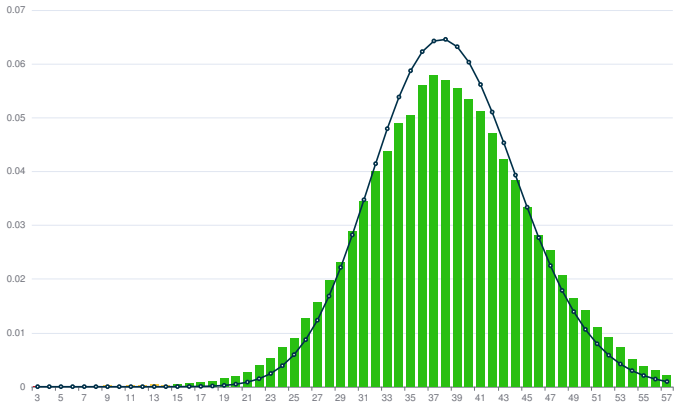
chr15

Mean	38.99
Standard dev.	7.5
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



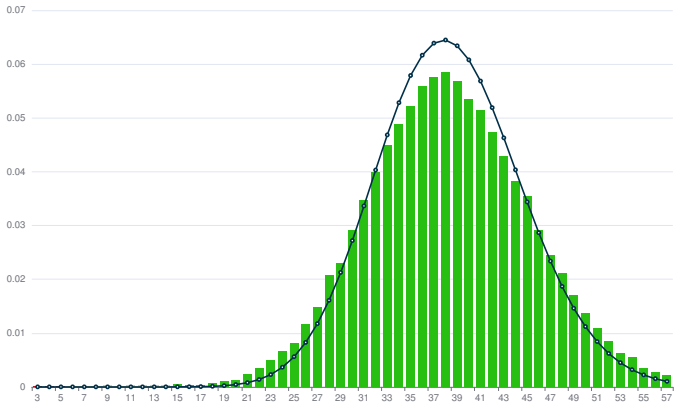
chr16

Mean	38.18
Standard dev.	7.3
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



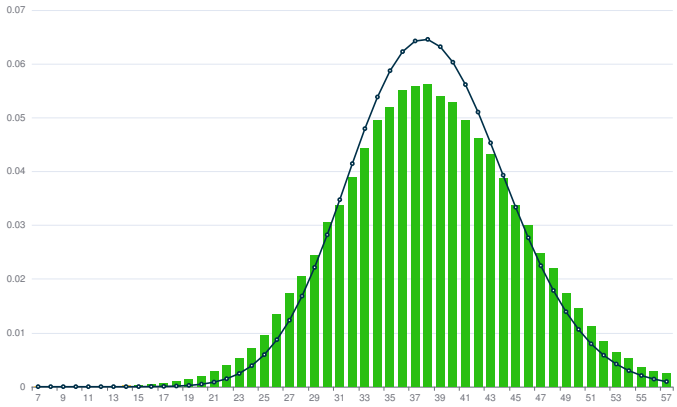
chr17

Mean	38.35
Standard dev.	7.39
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



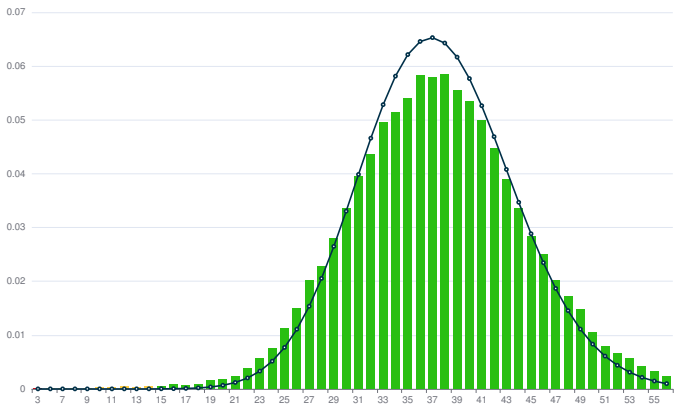
chr18

Mean	38.18
Standard dev.	7.22
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



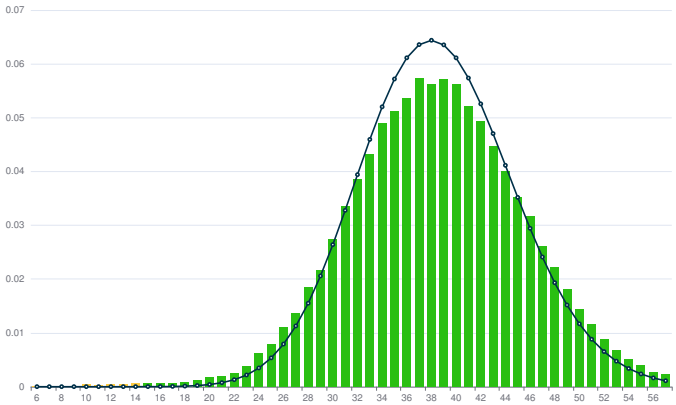
chr19

Mean	37.41
Standard dev.	7.12
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



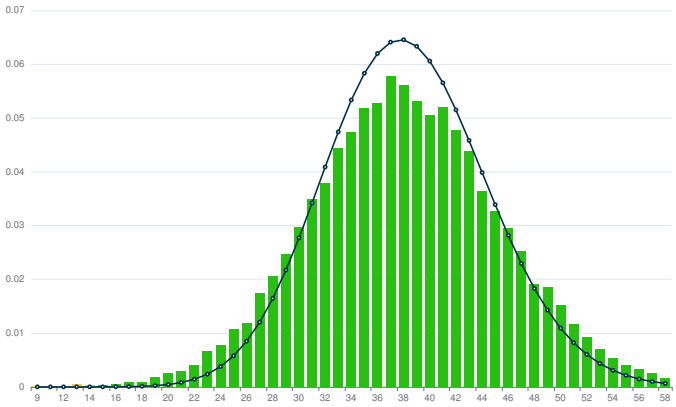
chr20

Mean	38.48
Standard dev.	7.17
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%

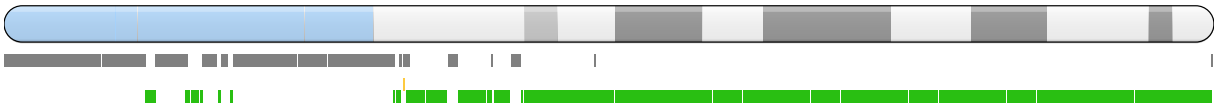


chr21

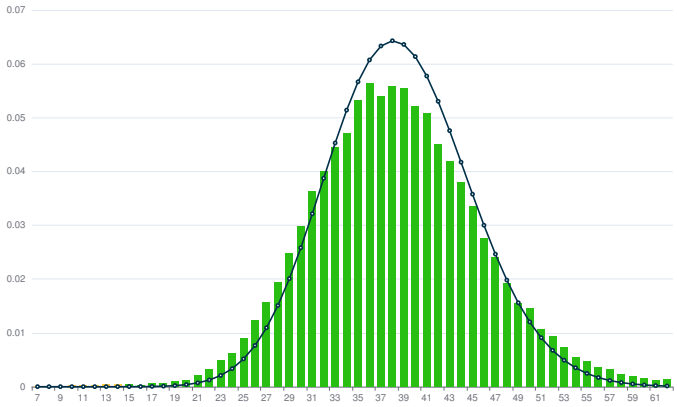
Mean	38.26
Standard dev.	7.65
< 1	0%
[1 - 4[	0%
[4 - 15[	0.1%
≥ 15	99.9%



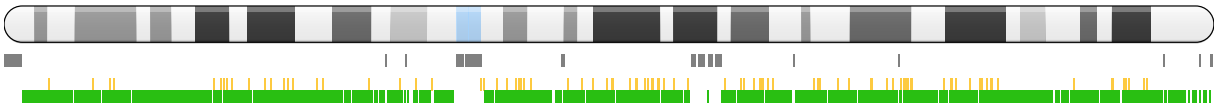
chr22



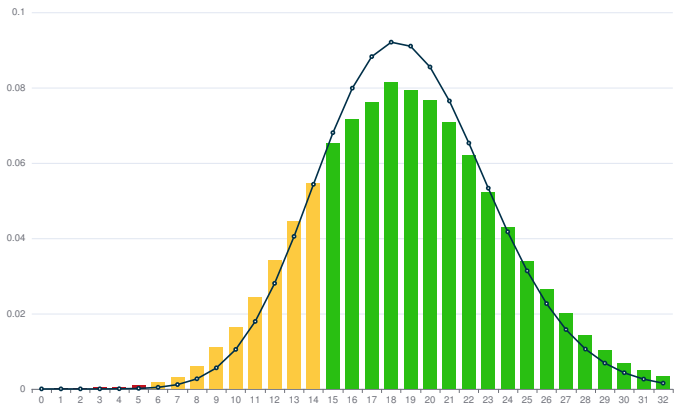
Mean	38.58
Standard dev.	8
< 1	0%
[1 - 4[	0%
[4 - 15[	0.2%
≥ 15	99.8%



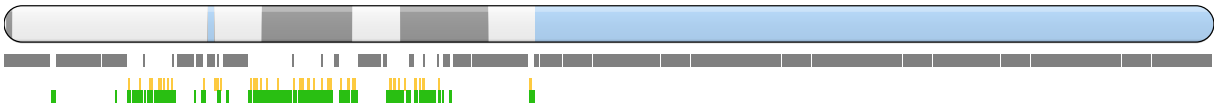
chrX



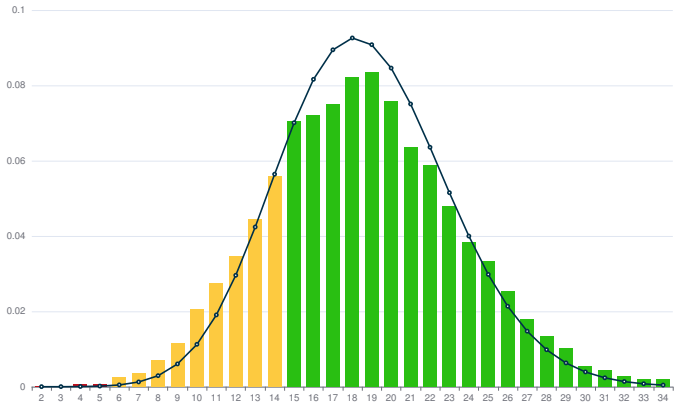
Mean	18.78
Standard dev.	5
< 1	0%
[1 - 4[	0.1%
[4 - 15[	19.7%
≥ 15	80.3%



chrY



Mean	18.63
Standard dev.	5.23
< 1	0%
[1 - 4[	0%
[4 - 15[	20.9%
≥ 15	79.1%



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.