Whole Genome Sequencing Report

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1 Interprétation

LAL-T surexprimant l'oncogène ***TLX1*** en raison d'une translocation ***TRDJ2::TLX1*** (détournement de l'enhanceur de *TRD*).

Mutations tronquantes

— ***NOTCH1*** (NP_060087.3:p.Phe1592TrpfsTer26 57%),
— ***RB1*** (chr13:47,625,834-47,715,009_del 93%),
— ***BCL11B*** (chr14:93,406,942-93,406,996_del 94%),
— ***USP6*** (NP_004496.2:p.Arg656Ter 37%),
— ***WDFY3*** (NP_055806.2:p.Arg86Ter 40%) enzyme de la voie des inositol-phosphate.

Mutations faux-sens

— ***KRAS*** (hotspot NP_004976.2:p.Gly12Ser 26%),
— ***APC*** (NP_000029.2:p.Asp1822Val 72%, WNT Signaling Pathway),
— ***FOXR1*** (NP_859072.1:p.Arg222His 47%),
— ***FOXG1*** (NP_005240.3:p.Thr376Met 62%)

Insertion

— Insertion de 78nt en chr6:156,372,179 dans un intron de ***TIAM2*** (69%).

Délétions

— 9p de 2.5 et 0.7 mb (chr9:20,216,421-22,648,725 chr9:21,582,154-22,297,618) impliquant ***CDKN2A*** (délétion homozygote).
— 18p impliquant ***PTPN2*** (chr18:12,939,006-13,057,758 96%).
— 22q de 154 kb (chr22:46,566,797-46,720,450) impliquant ***PPARA***.

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

2 Sample identity

PARACHINI

3 Alignement

Diagnostic sample

Id	PARACHINI
Time Point	diag
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/07/12 05h18
Number Of Reads	10.9 M
Yield Gb	53.36
Mean Coverage	17.12
N50	7 k
Median Length	4696
Mean Length	4917
Median Identity	99.38
Mean Identity	111.26
Run(s)	7f1dc: 52% 709b3: 48%

MRD sample

Id	PARACHINI
Time Point	mrd
Reference Genome	hs1
Bam Type	WGS
Modified Date (UTC)	2024/07/09 16h23
Number Of Reads	6 M
Yield Gb	32.69
Mean Coverage	10.49
N50	7.7 k
Median Length	5462
Mean Length	5485
Median Identity	99.15
Mean Identity	97.86
Run(s)	5d4f5: 100%

Values computed by cramino v0.14.5

3.1 Normalized read count by chromosome

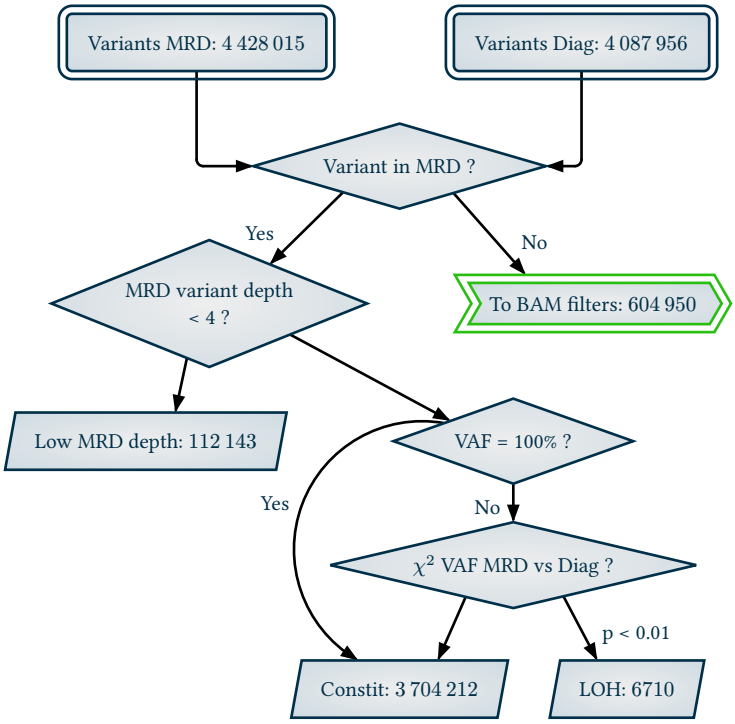
	chr1	chr2	chr3	chr4	chr5	chr6	chr7	chr8	chr9	chr10	chr11	chr12	chr13
diag	1.01	1.02	1.01	0.99	1.01	1.01	1.01	1	0.89	1.02	1	1.02	0.93
mrd	1.02	1.01	0.99	0.95	1	1	1	1	0.9	1.03	1	1.01	0.9

	chr14	chr15	chr16	chr17	chr18	chr19	chr20	chr21	chr22	chrX	chrY	chrM
diag	0.99	0.98	0.97	1	0.99	0.95	1	1.04	0.97	0.51	0.39	98.62
mrd	0.99	0.98	1	1.05	0.97	1.02	1.04	1.02	1.01	0.49	0.36	88.19

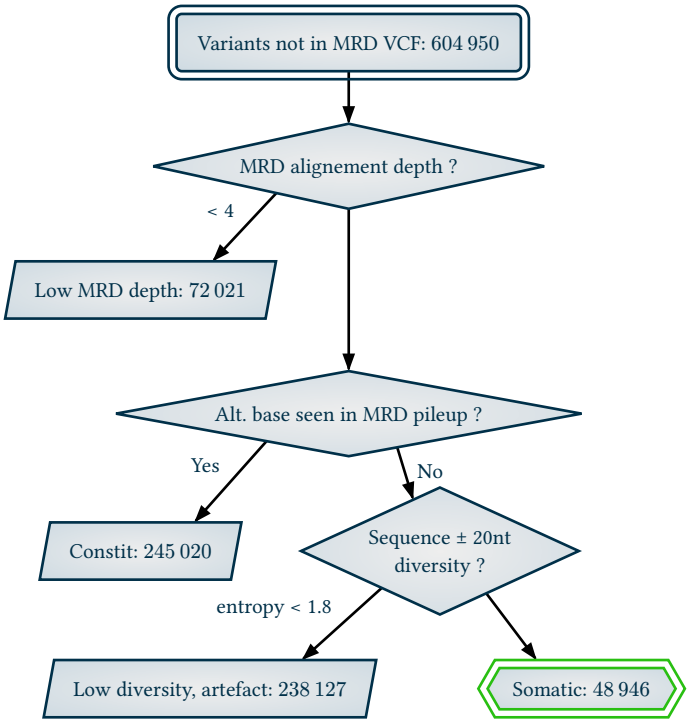
4 Variants

4.1 Variants calling

VCF filters

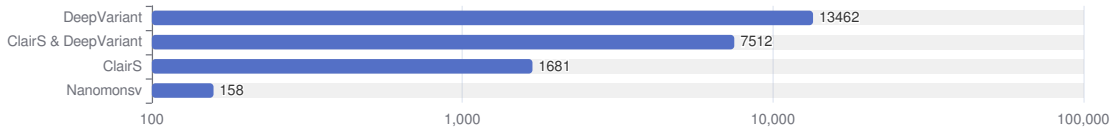


BAM filters

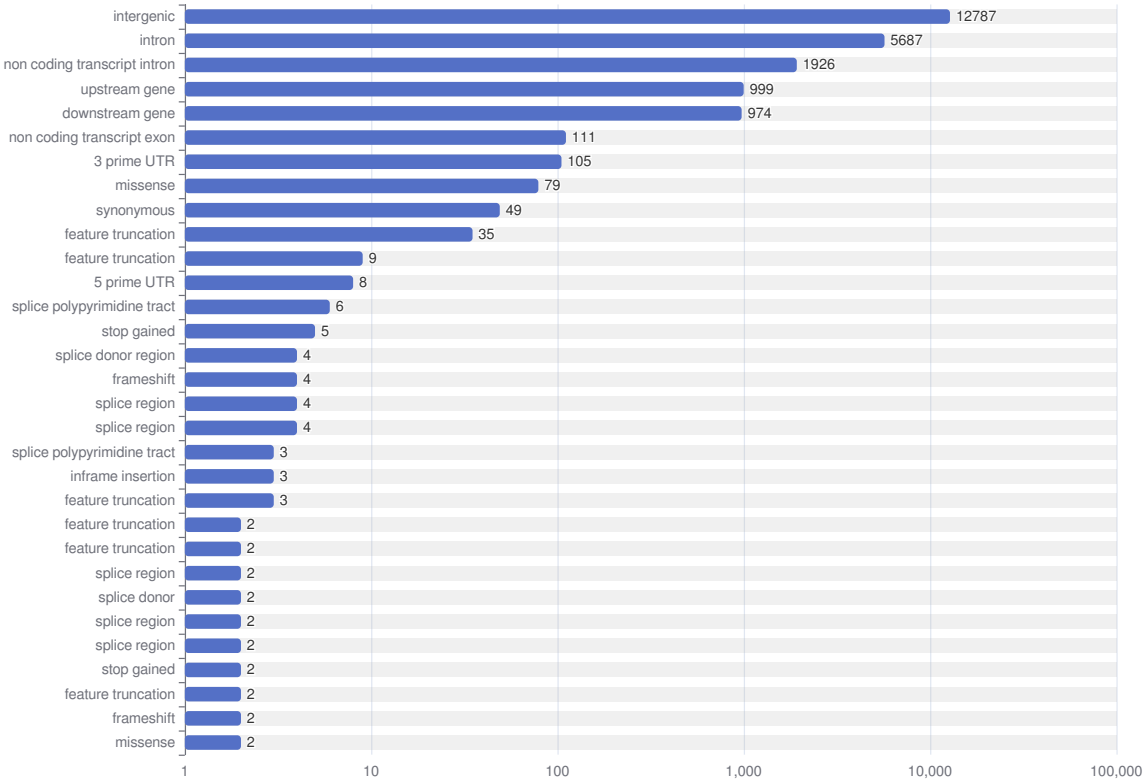


4.2 Somatic variants

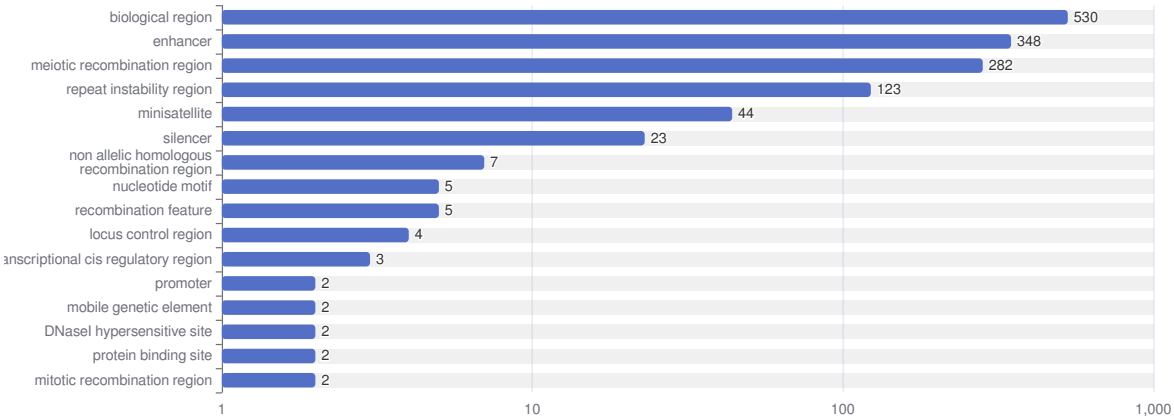
Callers



Consequences (VEP)



NCBI features



4.3 Selected Variants

Pathogenics

chr9:20,216,421 G›<DEL>
intron variant ***SLC24A2***
VAF: 27.27% Nanomonsv: TR: 22, VR: 6, SVTYPE: DEL, SVLEN: −2432304, END: 22648725, SVINSLEN: 19, SVINSSEQ: CTTCCTTATTTGGAATCCA

chr9:21,582,154 a›<DEL>
intergenic variant
VAF: 86.67% Nanomonsv: TR: 15, VR: 13, SVTYPE: DEL, SVLEN: −715464, END: 22297618, SVINSLEN: 4, SVINSSEQ: GGTG

chr9:148,734,014 G›GT
frameshift variant ***NOTCH1***
NM_017617.5:c.4776_4777insA
NP_060087.3:p.Leu1593ThrfsTer17
VAF: 66.67% DeepVariant: Qual: 6.9, GT: 0/1, GQ: 7, DP: 6, AD: [2, 4], VAF: 0.666667, PL: [5, 0, 22]

chr9:148,734,016 A›ATCCCC
frameshift variant ***NOTCH1***
NM_017617.5:c.4774_4775insGGGGA
NP_060087.3:p.Phe1592TrpfsTer26
VAF: 57.14% DeepVariant: Qual: 12.7, GT: 0/1, GQ: 13, DP: 7, AD: [2, 4], VAF: 0.571429, PL: [12, 0, 30]

chr9:148,734,017 A›C
missense variant ***NOTCH1***
NM_017617.5:c.4774T>G
NP_060087.3:p.Phe1592Val
VAF: 71.43% DeepVariant: Qual: 18.3, GT: 0/1, GQ: 18, DP: 7, AD: [2, 5], VAF: 0.714286, PL: [18, 0, 34]

chr9:148,734,019 T›A
missense variant ***NOTCH1***
NM_017617.5:c.4772A>T
NP_060087.3:p.His1591Leu
VAF: 71.43% DeepVariant: Qual: 18.8, GT: 0/1, GQ: 19, DP: 7, AD: [2, 5], VAF: 0.714286, PL: [18, 0, 31]

chr10:102,012,779 c›[chr14:16656857[CGCGTGTTT
upstream gene variant ***TLX1***
VAF: 16.67% Nanomonsv: TR: 30, VR: 5, SVTYPE: BND, SVINSLEN: 8, SVINSSEQ: CGCGTGTT , MATEID: r_18_1

chr10:102,014,479 C›CCC[chr14:16666805[
upstream gene variant ***TLX1***
VAF: 11.9% Nanomonsv: TR: 42, VR: 5, SVTYPE: BND, SVINSLEN: 2, SVINSSEQ: CC , MATEID: r_19_1

chr12:25,116,561 C›T
missense variant ***KRAS***
NM_004985.5:c.34G>A
NP_004976.2:p.Gly12Ser
VAF: 26.09% Cosmic: 2118 ClairS: Qual: 16.234, GT: 0/1, GQ: 16, DP: 23, AF: 0.2609, AD: [0, 6], NAF: 0, NDP: 10, NAD: [0, 0], AU: 0, CU: 17, GU: 0, TU: 6, NAU: 0, NCU: 10, NGU: 0, NTU: 0, H, FAU: 0, FCU: 10, FGU: 0, FTU: 4, RAU: 0, RCU: 7, RGU: 0, RTU: 2

chr14:16,656,857 T›[chr10:102012779[AACACGCGT
downstream gene variant ***TRDJ2***
VAF: 16.67% Nanomonsv: TR: 30, VR: 5, SVTYPE: BND, SVINSLEN: 8, SVINSSEQ: `AACACGCG` , MATEID: r_18_0

chr14:16,666,805 G›]chr10:102014479]GGG
downstream gene variant ***TRDC***
VAF: 11.9% Nanomonsv: TR: 42, VR: 5, SVTYPE: BND, SVINSLEN: 2, SVINSSEQ: `GG` , MATEID: r_19_0

Likely Pathogenics

chr4:47,432,169 C›[chr4:47432198[T
upstream gene variant ***COMMD8***
VAF: 19.05% Nanomonsv: TR: 21, VR: 4, SVTYPE: BND, MATEID: r_126_1

chr4:47,432,198 T›[chr4:47432169[T
upstream gene variant ***COMMD8***
VAF: 19.05% Nanomonsv: TR: 21, VR: 4, SVTYPE: BND, MATEID: r_126_0

chr4:88,179,944 G›A
stop gained ***WDFY3***
NM_014991.6:c.256C>T
NP_055806.2:p.Arg86Ter

VAF: 40% Cosmic: 1

DeepVariant:

Qual: 19.4,

GT: 0/1, GQ: 19, DP: 5, AD: [3, 2], VAF: 0.4, PL: [19, 0, 39]

chr5:113,351,591 A›T
missense variant ***APC***
NM_000038.6:c.5465A>T
NP_000029.2:p.Asp1822Val

VAF: 71.88%

ClairS:

Qual: 15.625,

GT: 0/1, GQ: 15, DP: 16, AF: 0.6875, AD: [0, 11], NAF: 0, NDP: 5, NAD: [0, 0], AU: 5, CU: 0, GU: 0, TU: 11, NAU: 5, NCU: 0, NGU: 0, NTU: 0, H, FAU: 4, FCU: 0, FGU: 0, FTU: 3, RAU: 1, RCU: 0, RGU: 0, RTU: 8

DeepVariant:

Qual: 26.7,

GT: 0/1, GQ: 27, DP: 16, AD: [4, 12], VAF: 0.75, PL: [26, 0, 42]

chr6:156,372,179 C›CTATGATTATCTGTATATTCTCAATCT...
intron variant ***TIAM2***

VAF: 68.75%

Nanomonsv:

TR: 16, VR: 11, SVTYPE: INS, END: 156372179, SVINSLEN: 78, SVINSSEQ:

```
TATGATTATCTGTATATTCTCAATCTATAGCACACTGCGAAGGATATAGTACTGGCTTAA
TAAGTTTGATGATTAATT
```

chr11:119,000,941 G›A
missense variant ***FOXR1***
NM_181721.3:c.665G>A
NP_859072.1:p.Arg222His

VAF: 52.25%

ClairS:

Qual: 19.848,

GT: 0/1, GQ: 19, DP: 14, AF: 0.5714, AD: [0, 8], NAF: 0, NDP: 17, NAD: [0, 0], AU: 8, CU: 0, GU: 6, TU: 0, NAU: 0, NCU: 0, NGU: 17, NTU: 0, FAU: 3, FCU: 0, FGU: 2, FTU: 0, RAU: 5, RCU: 0, RGU: 4, RTU: 0

DeepVariant:

Qual: 24.9,

GT: 0/1, GQ: 25, DP: 19, AD: [10, 9], VAF: 0.473684, PL: [24, 0, 47]

chr13:47,625,834 C›<DEL>
intron variant ***RB1***

VAF: 93.33%

Nanomonsv:

TR: 15, VR: 14, SVTYPE: DEL, SVLEN: −89175, END: 47715009, SVINSLEN: 13, SVINSSEQ:

```
CGTCACCCCCCAA
```

chr14:22,966,339 C>T
missense variant ***FOXG1***
NM_005249.5:c.1127C>T
NP_005240.3:p.Thr376Met

VAF: 61.54% Cosmic: 3

DeepVariant:

Qual: 26.4,

GT: 0/1, GQ: 26, DP: 13, AD: [5, 8], VAF: 0.615385, PL: [26, 0, 43]

ClairS:

Qual: 14.974,

GT: 0/1, GQ: 14, DP: 13, AF: 0.6154, AD: [0, 8], NAF: 0, NDP: 9, NAD: [0, 0], AU: 0, CU: 5, GU: 0, TU: 8, NAU: 0, NCU: 9, NGU: 0, NTU: 0, FAU: 0, FCU: 2, FGU: 0, FTU: 5, RAU: 0, RCU: 3, RGU: 0, RTU: 3

chr14:93,406,942 A><DEL>
feature truncation, frameshift variant ***BCL11B***

VAF: 94.12%

Nanomonsv:

TR: 17, VR: 16, SVTYPE: DEL, SVLEN: −54, END: 93406996

chr17:5,038,209 C>T
stop gained ***USP6***
NM_004505.4:c.1966C>T
NP_004496.2:p.Arg656Ter

VAF: 37.09% GnomAD: 0.0000195

DeepVariant:

Qual: 20.5,

GT: 0/1, GQ: 21, DP: 14, AD: [9, 5], VAF: 0.357143, PL: [20, 0, 45]

ClairS:

Qual: 13.366,

GT: 0/1, GQ: 13, DP: 13, AF: 0.3846, AD: [0, 5], NAF: 0, NDP: 13, NAD: [0, 0], AU: 0, CU: 8, GU: 0, TU: 5, NAU: 0, NCU: 13, NGU: 0, NTU: 0, H, FAU: 0, FCU: 2, FGU: 0, FTU: 2, RAU: 0, RCU: 6, RGU: 0, RTU: 3

chr18:12,939,006 c›<DEL>
intergenic variant

VAF: 96.15%

Nanomonsv:

TR: 26, VR: 25, SVTYPE: DEL, SVLEN: −118752, END: 13057758, SVINSLEN: 3, SVINSSEQ:

```
CCC
```

chr22:46,566,797 G›<DEL>
upstream gene variant ***MIRLET7BHG***

VAF: 26.92%

Nanomonsv:

TR: 26, VR: 7, SVTYPE: DEL, SVLEN: −153653, END: 46720450, SVINSLEN: 4, SVINSSEQ:

```
TAGA
```

Variants of uncertain significance

chr1:27,859,148 T›TTAAGTGAACAGATTTATAAGGAGATA...
intron variant ***EYA3***

VAF: 60%

Nanomonsv:

TR: 20, VR: 12, SVTYPE: INS, END: 27859148, SVINSLEN: 143, SVINSSEQ:

```
TAAGTGAACAGATTTATAAGGAGATAAACAACATTGGCAAAGGAAACAAACACTCGTTTT
GCTTTTTTGTGTGGGATAGCTACATTTACACTTGGTTAAAAACAAAACATTTGAACATCT
TTCTGTTTCAACTTGAACATGAT
```

chr1:32,042,473 C>T
missense variant ***TXLNA***
NM_175852.4:c.554C>T
NP_787048.1:p.Pro185Leu

VAF: 51.27% Cosmic: 2

DeepVariant:

Qual: 23.9,

GT: 0/1, GQ: 24, DP: 25, AD: [13, 12], VAF: 0.48, PL: [23, 0, 51]

ClairS:

Qual: 17.736,

GT: 0/1, GQ: 17, DP: 22, AF: 0.5455, AD: [0, 12], NAF: 0, NDP: 6, NAD: [0, 0], AU: 0, CU: 10, GU: 0, TU: 12, NAU: 0, NCU: 6, NGU: 0, NTU: 0, H, FAU: 0, FCU: 4, FGU: 0, FTU: 5, RAU: 0, RCU: 6, RGU: 0, RTU: 7

chr1:93,910,950 C>T
stop gained ***ABCA4***
NM_000350.3:c.1767G>A
NP_000341.2:p.Trp589Ter

VAF: 39.61%

DeepVariant:

Qual: 34.9,

GT: 0/1, GQ: 35, DP: 14, AD: [8, 6], VAF: 0.428571, PL: [34, 0, 62]

ClairS:

Qual: 13.459,

GT: 0/1, GQ: 13, DP: 11, AF: 0.3636, AD: [0, 4], NAF: 0, NDP: 12, NAD: [0, 0], AU: 0, CU: 7, GU: 0, TU: 4, NAU: 0, NCU: 12, NGU: 0, NTU: 0, H, FAU: 0, FCU: 3, FGU: 0, FTU: 3, RAU: 0, RCU: 4, RGU: 0, RTU: 1

chr1:175,656,182 c›cACACACATCATATATATATTTATATA...
intergenic variant
VAF: 41.67% Nanomonsv: TR: 12, VR: 5, SVTYPE: INS, END: 175656182, SVINSLEN: 59, SVINSSEQ: ACACACATCATATATATATTTATATATAAAACAACAGATGTCATACATATACATATATA

chr1:201,157,957 C›A
missense variant ***LMOD1***
NM_012134.3:c.811G>T
NP_036266.2:p.Val271Phe
VAF: 48.53% DeepVariant: Qual: 33.6, GT: 0/1, GQ: 34, DP: 17, AD: [9, 8], VAF: 0.470588, PL: [33, 0, 61] ClairS: Qual: 14.847, GT: 0/1, GQ: 14, DP: 16, AF: 0.5, AD: [0, 8], NAF: 0, NDP: 8, NAD: [0, 0], AU: 8, CU: 8, GU: 0, TU: 0, NAU: 0, NCU: 8, NGU: 0, NTU: 0, H, FAU: 4, FCU: 4, FGU: 0, FTU: 0, RAU: 4, RCU: 4, RGU: 0, RTU: 0

chr2:169,689,760 T›TAG
frameshift variant ***LRP2***
NM_004525.3:c.5984_5985insCT
NP_004516.2:p.Val1996Ter
VAF: 54.55% DeepVariant: Qual: 25.5, GT: 0/1, GQ: 26, DP: 11, AD: [4, 6], VAF: 0.545455, PL: [25, 0, 47]

chr3:112,752,913 t›tTAAAAAAATTTATGCCATTCTCAGTA...

intergenic variant

VAF: 58.33%

Nanomonsv:

TR: 12, VR: 7, SVTYPE: INS, END: 112752913, SVINSLEN: 630, SVINSSEQ:

```
TAAAAAAATTTATGCCATTCTCAGTAAACTATCGCAAGAACAAAAAACCAAACACCGCAT
ATTCTCACTCATAGGTGGGAATTGAACAATGAGATCACATGGACACAGGAAGGGGAATAT
CACACTCTGGGGACTGTGGTGGGGTCGGGGGAGGGGGGAGGGATAGCATTGGGAGATATA
CCTAATGCTAGATGACACGTTAGTGGGTGCAGCGCACCAGCATGGCACATGTATACATAT
GTAACTAACCTGCACAATGTGCACATGTACCCTAAAACTTAGAGTATAATAAAAAAAAAA
ATTAAAAAAATAAAAAAATAAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGAACAGAT
ATATGACCTAAGTTCCAACAATCAGATATGACTTTAAGAGACATGAATGCATAAACAAGA
CAAGCAAGAAACCTGTTCTATATGGGGGGAAAGAATAGTGGTAGAAGCCTCCCGTTCTTC
AGAGGCGGCAGTAATATTTTCACTAGCACATTTTCCCAGCATAAGCACTGTTTCTGTAAT
TAGCCTTTAGCCTGGCTCTGAGTCTCCTTGAGATTTTGTAAGCTTTCTAATAGTCTGAAT
AAATTCATTTTCTGTGTAAAAAAAAAAAAA
```

chr3:113,414,714 c›<DEL>

intergenic variant

VAF: 50%

Nanomonsv:

TR: 16, VR: 8, SVTYPE: DEL, SVLEN: −282, END: 113414996

chr3:142,622,961 a›a]chr3:142622996]

VAF: 18.75%

Nanomonsv:

TR: 16, VR: 3, SVTYPE: BND, MATEID: r_115_1

chr3:142,622,996 a›a]chr3:142622961]

VAF: 18.75%

Nanomonsv:

TR: 16, VR: 3, SVTYPE: BND, MATEID: r_115_0

chr3:165,774,326 a›<DEL>
intergenic variant

VAF: 33.33%

Nanomonsv:

TR: 21, VR: 7, SVTYPE: DEL, SVLEN: −6248, END: 165780574, SVINSLEN: 4, SVINSSEQ:

```
CAGT
```

chr4:31,479,643 a›aTTTCGGACATGAAGTCCTTGCCCACG...
intergenic variant

VAF: 46.15%

Nanomonsv:

TR: 13, VR: 6, SVTYPE: INS, END: 31479643, SVINSLEN: 437, SVINSSEQ:

```
TTTCGGACATGAAGTCCTTGCCCACGCCTATGTCCTGAATGGTAATGCCTAGGTTTTCTT
CTAGGGTTTTTATGGTTTTAGGTTTAACGTTTAAATCTTTAATCCATCTTGAATTGATTT
TTGTATAAGGTGTAAGGAAGGGATCCAGTTTCAGCTTTCTACATATGGCTAGCCAGTTTT
CCCAGCACCATTTATTAAATAGGGAATCCTTTCCCCATTGCTTGTTTTTCTCAGGTTTGT
CAAAGATCAGATAGTTGTAGATATGCGGCATTATTTCTGAGGGCTCTGTTCTGTTCCATT
GATCTATATCTCTGTTTTGGCACCAGTACCATGCTGTTTTGGTTACTGTAGCCTTGTAGT
ATAGTTTGAAGTCAGGTAGTGTGATGCCTCCAGCTTTGTTCTTTTGGCTTAGGATTGACT
TGGCAATGCGGGCTCTT
```

chr4:44,261,800 g›g]chr4:44261841]
feature truncation, intron variant ***KCTD8***

VAF: 20%

Nanomonsv:

TR: 15, VR: 3, SVTYPE: BND, MATEID: r_124_1

chr4:44,261,841 g›g]chr4:44261800]
feature truncation, intron variant ***KCTD8***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, MATEID: r_124_0

chr5:146,663,365 C›T
missense variant ***LARS1***
NM_016460.4:c.2593G>A
NP_057544.2:p.Asp865Asn
VAF: 54.55% DeepVariant: Qual: 22.6, GT: 0/1, GQ: 23, DP: 11, AD: [5, 6], VAF: 0.545455, PL: [22, 0, 49] ClairS: Qual: 7.42, GT: 0/1, GQ: 7, DP: 11, AF: 0.5455, AD: [0, 6], NAF: 0, NDP: 4, NAD: [0, 0], AU: 0, CU: 5, GU: 0, TU: 6, NAU: 0, NCU: 4, NGU: 0, NTU: 0, H, FAU: 0, FCU: 1, FGU: 0, FTU: 3, RAU: 0, RCU: 4, RGU: 0, RTU: 3

chr6:3,178,742 C›CCTCCCACTCGAGCACCCTGTCTCCCA...
intron variant ***SLC22A23***
VAF: 38.1% Nanomonsv: TR: 21, VR: 8, SVTYPE: INS, END: 3178742, SVINSLEN: 60, SVINSSEQ: CTCCCACTCGAGCACCCTGTCTCCCAGGGAGCACCCTGTCTCCCACTCGAGCACCCTGTC

chr6:38,432,162 T›TGGGCCATCTTTTTTTTTTTTTTTTT...

intron variant ***BTBD9***

VAF: 42.11%

Nanomonsv:

TR: 19, VR: 8, SVTYPE: INS, END: 38432162, SVINSLEN: 285, SVINSSEQ:

```
GGGCCATCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGAGACGGAGTCTCGCTC
TGTCGCCCAGGCTGGAGTGCAGTGGCGGGATCTCGGCTCACTGCAAGCTCCGCCTCCCGG
GTTCACGCCATTCTCCTGCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCGCCCGCCACT
ACGCCCGGCTAATTTTTTGTATTTTTAGTAGAGACGGGGTTTCACCGTTTTAGCCGGGAT
GGTCTCGATCTCCTGACCTCGTGATCCGCCCGCCTCGGCCTCCCG
```

chr7:159,116,887 T›TCTACCACTAAACCACAGCCAAAGTAC...

intron variant ***PTPRN2***

VAF: 45%

Nanomonsv:

TR: 20, VR: 9, SVTYPE: INS, END: 159116887, SVINSLEN: 61, SVINSSEQ:

```
CTACCACTAAACCACAGCCAAAGTACACTGAGGGACTACACATTACCTCCCTCTATCTAC
C
```

chr8:2,916,848 a›a]chr8:2917023]

feature truncation, intron variant ***CSMD1***

VAF: 15.79%

Nanomonsv:

TR: 19, VR: 3, SVTYPE: BND, MATEID: r_173_1

chr8:2,917,023 a›a]chr8:2916848]

feature truncation, intron variant ***CSMD1***

VAF: 15.79%

Nanomonsv:

TR: 19, VR: 3, SVTYPE: BND, MATEID: r_173_0

chr8:88,530,561 t›t]chr8:88530576]
feature truncation, intron variant ***CNBD1***
VAF: 18.75% Nanomonsv: TR: 16, VR: 3, SVTYPE: BND, MATEID: r_175_0

chr8:88,530,576 g›g]chr8:88530561]
feature truncation, intron variant ***CNBD1***
VAF: 18.75% Nanomonsv: TR: 16, VR: 3, SVTYPE: BND, MATEID: r_175_1

chr9:110,612,486 A›[chr9:110612502[CA
feature truncation, intron variant ***GABBR2***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, SVINSLEN: 1, SVINSSEQ: C , MATEID: r_188_1

chr9:110,612,502 A›[chr9:110612486[GA
feature truncation, intron variant ***GABBR2***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, SVINSLEN: 1, SVINSSEQ: G , MATEID: r_188_0

chr9:125,483,156 C>T
stop gained ***PRPF4***
NM_004697.5:c.679C>T
NP_004688.2:p.Gln227Ter

VAF: 18.18%

DeepVariant:

Qual: 4.8,

GT: 0/1, GQ: 5, DP: 11, AD: [9, 2], VAF: 0.181818, PL: [3, 0, 34]

chr11:124,325,383 g>gTATATAATATGTATCTATAGATACAT...
intergenic variant

VAF: 44.44%

Nanomonsv:

TR: 18, VR: 8, SVTYPE: INS, END: 124325383, SVINSLEN: 57, SVINSSEQ:

TATATAATATGTATCTATAGATACATATTATATAATATGTATCTATAGATACATATT

chr12:10,302,595 G>T
missense variant ***KLRC3***
NM_002261.3:c.604C>A
NP_002252.2:p.His202Asn

VAF: 23.81%

ClairS:

Qual: 7.586,

GT: 0/1, GQ: 7, DP: 21, AF: 0.2381, AD: [0, 5], NAF: 0, NDP: 11, NAD: [0, 0], AU: 0, CU: 0, GU: 16, TU: 5, NAU: 0, NCU: 0, NGU: 11, NTU: 0, H, FAU: 0, FCU: 0, FGU: 7, FTU: 3, RAU: 0, RCU: 0, RGU: 9, RTU: 2

chr12:84,291,772 A›<DEL>
intergenic variant

VAF: 57.14%

Nanomonsv:

TR: 14, VR: 8, SVTYPE: DEL, SVLEN: −110, END: 84291882, SVINSLEN: 10, SVINSSEQ:

```
CCCCTTGAGA
```

chr13:33,455,622 a›aGTGGATTTGATGAAGTGCTCTGCCTG...
intergenic variant

VAF: 78.95%

Nanomonsv:

TR: 19, VR: 15, SVTYPE: INS, END: 33455623, SVINSLEN: 86, SVINSSEQ:

```
GTGGATTTGATGAAGTGCTCTGCCTGTATCATCTGCATTTTATCACTGCGTCGGCGTCAG
CCAAACCCTCTTCCCTGATCAGAACT
```

chr13:52,876,198 T›<DEL>
intergenic variant

VAF: 76.47%

Nanomonsv:

TR: 17, VR: 13, SVTYPE: DEL, SVLEN: −5479, END: 52881677

chr13:68,318,688 t›<DEL>
intergenic variant

VAF: 100%

Nanomonsv:

TR: 10, VR: 10, SVTYPE: DEL, SVLEN: −157, END: 68318845

chr14:40,560,211 a›aTATATTAATTATAATATAATTATATA...
intron variant, non coding transcript variant ***LINC00871***

VAF: 53.33%

Nanomonsv:

TR: 15, VR: 8, SVTYPE: INS, END: 40560211, SVINSLEN: 130, SVINSSEQ:

```
TATATTAATTATAATATAATTATATATTATAATTATATATATAATATAATATAATATAAT
ATTAACAATTTAATATAATATTAACAATATAAATAATATATTAATAATAATATAATATTA
ACAATTAATA
```

chr14:94,110,028 A›T
missense variant ***EML1***
NM_004434.3:c.467A>T
NP_004425.2:p.Asn156Ile

VAF: 100%

DeepVariant:

Qual: 44.8,

GT: 1/1, GQ: 33, DP: 10, AD: [0, 10], VAF: 1, PL: [44, 32, 0]

ClairS:

Qual: 14.564,

GT: 1/1, GQ: 14, DP: 9, AF: 1, AD: [0, 9], NAF: 0, NDP: 11, NAD: [0, 0], AU: 0, CU: 0, GU: 0, TU: 9, NAU: 11, NCU: 0, NGU: 0, NTU: 0, FAU: 0, FCU: 0, FGU: 0, FTU: 5, RAU: 0, RCU: 0, RGU: 0, RTU: 4

chr15:55,492,467 a›a]chr15:55492498]
downstream gene variant ***MYZAP***

VAF: 20%

Nanomonsv:

TR: 15, VR: 3, SVTYPE: BND, MATEID: r_68_1

chr15:55,492,498 c›c]chr15:55492467]
downstream gene variant ***MYZAP***
VAF: 20% Nanomonsv: TR: 15, VR: 3, SVTYPE: BND, MATEID: r_68_0

chr15:71,194,016 T›TAGAGGCTGTGACAGAGGCTGTGACAG...
frameshift variant, stop gained ***LOC124903571***
XM_047433430.1:c.716_717insCAGAGGCTGTGACAGAGACT...
XP_047289386.1:p.Glu239AspfsTer124
VAF: 38.89% DeepVariant: Qual: 27.6, GT: 0/1, GQ: 28, DP: 18, AD: [9, 7], VAF: 0.388889, PL: [27, 0, 51]

chr15:74,130,405 C›<DEL>
intron variant ***ETFA***
VAF: 41.67% Nanomonsv: TR: 24, VR: 10, SVTYPE: DEL, SVLEN: −57, END: 74130462

chr15:74,132,775 c›cGCCCC[chr13:42714455[
feature truncation, intron variant ***ETFA***
VAF: 20.59% Nanomonsv: TR: 34, VR: 7, SVTYPE: BND, SVINSLEN: 5, SVINSSEQ: GCCCC , MATEID: r_41_0

chr16:59,842,589 A›C
intron variant ***FTO***
NM_001080432.3:c.1365-67182A>C

VAF: 25% GnomAD: 0.000321

ClairS:

Qual: 6.252,

GT: 0/1, GQ: 6, DP: 12, AF: 0.25, AD: [0, 3], NAF: 0, NDP: 8, NAD: [0, 0], AU: 9, CU: 3, GU: 0, TU: 0, NAU: 8, NCU: 0, NGU: 0, NTU: 0, FAU: 4, FCU: 0, FGU: 0, FTU: 0, RAU: 5, RCU: 3, RGU: 0, RTU: 0

chr16:94,783,800 G›A
missense variant ***CTU2***
NM_001012759.3:c.757G>A
NP_001012777.1:p.Val253Met

VAF: 31.67%

DeepVariant:

Qual: 25.6,

GT: 0/1, GQ: 26, DP: 10, AD: [7, 3], VAF: 0.3, PL: [25, 0, 49]

ClairS:

Qual: 7.38,

GT: 0/1, GQ: 7, DP: 9, AF: 0.3333, AD: [0, 3], NAF: 0, NDP: 5, NAD: [0, 0], AU: 3, CU: 0, GU: 6, TU: 0, NAU: 0, NCU: 0, NGU: 5, NTU: 0, H, FAU: 2, FCU: 0, FGU: 3, FTU: 0, RAU: 1, RCU: 0, RGU: 3, RTU: 0

chr17:32,153,330 G›GAAA]chr17:32153366]
feature truncation, intron variant ***NF1***

VAF: 14.29%

Nanomonsv:

TR: 21, VR: 3, SVTYPE: BND, SVINSLEN: 3, SVINSSEQ:

AAA

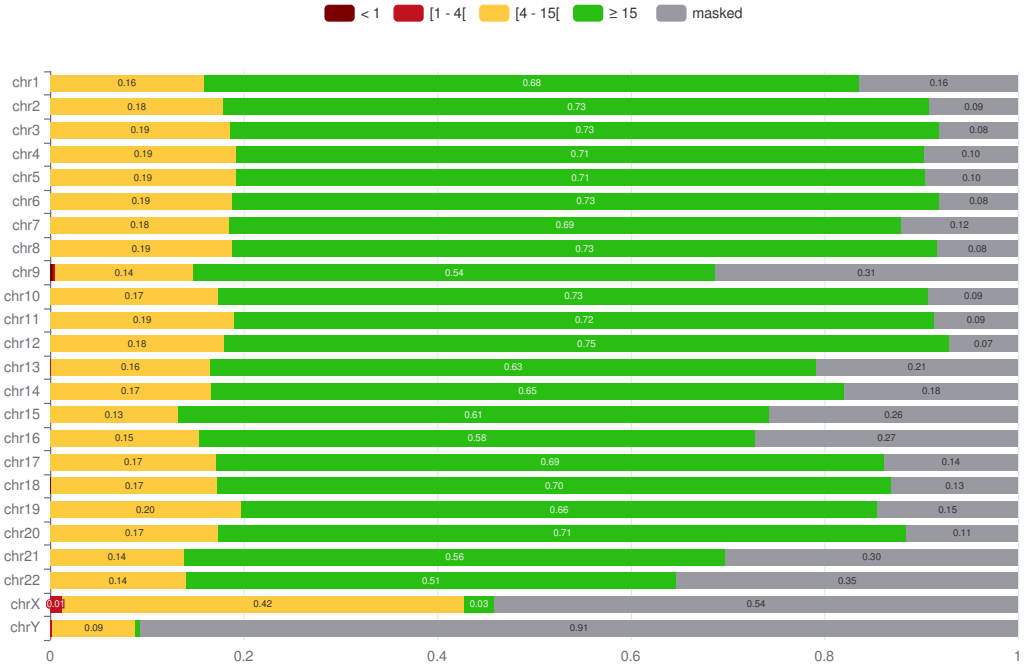
, MATEID: r_79_1

chr17:32,153,366 a›aTTT]chr17:32153330]
feature truncation, intron variant ***NF1***
VAF: 14.29% Nanomonsv: TR: 21, VR: 3, SVTYPE: BND, SVINSLEN: 3, SVINSSEQ: `TTT` , MATEID: r_79_0

chr20:25,194,942 T›TCCTCAGGTGGATGCCCCTCAGGTGGA...
intergenic variant
VAF: 62.5% Nanomonsv: TR: 24, VR: 15, SVTYPE: INS, END: 25194942, SVINSLEN: 76, SVINSSEQ: `CCTCAGGTGGATGCCCCTCAGGTGGATTCCCCTCAGGTGGATGCCCCTCAGGTGGATTCC CCTCAGGTGGATTCCC`

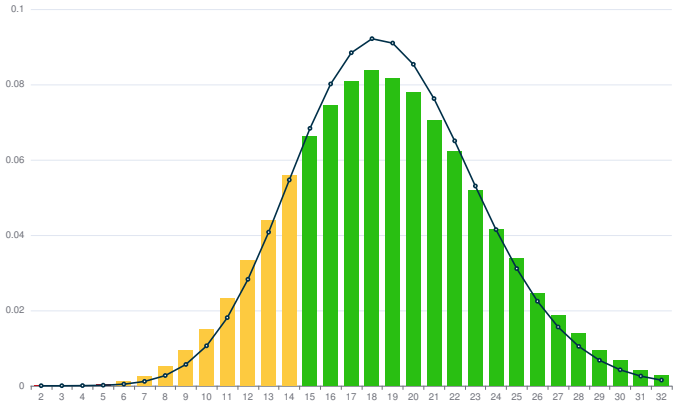
5 Coverage by chromosome

5.1 Proportion at given depth by chromosome

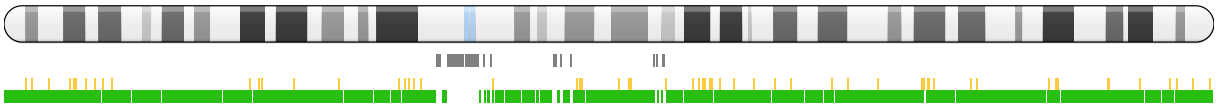


chr1

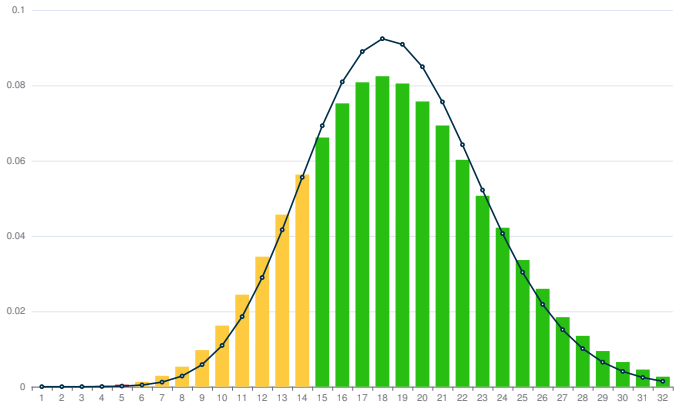
Mean	18.76
Standard dev.	4.81
< 1	0%
[1 - 4[	0%
[4 - 15[	19%
≥ 15	81%



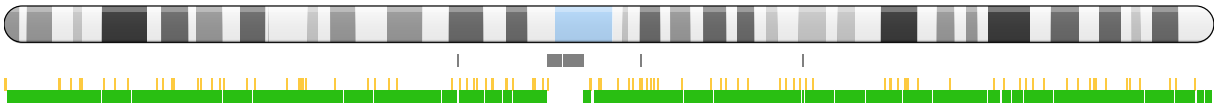
chr2



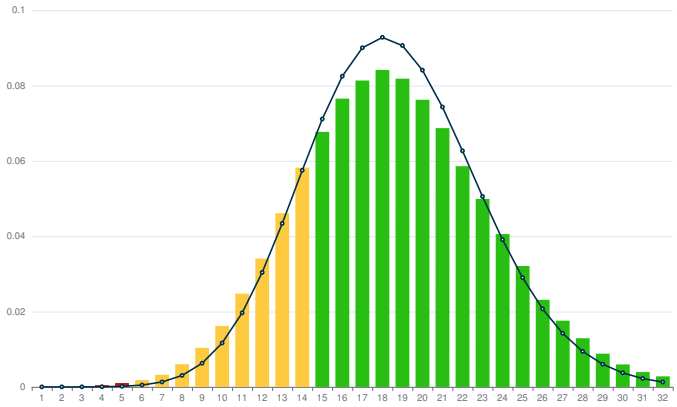
Mean	18.69
Standard dev.	4.85
< 1	0%
[1 - 4[	0%
[4 - 15[	19.7%
≥ 15	80.3%



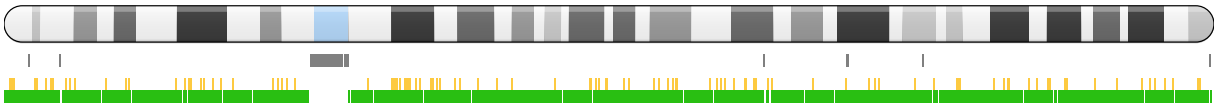
chr3



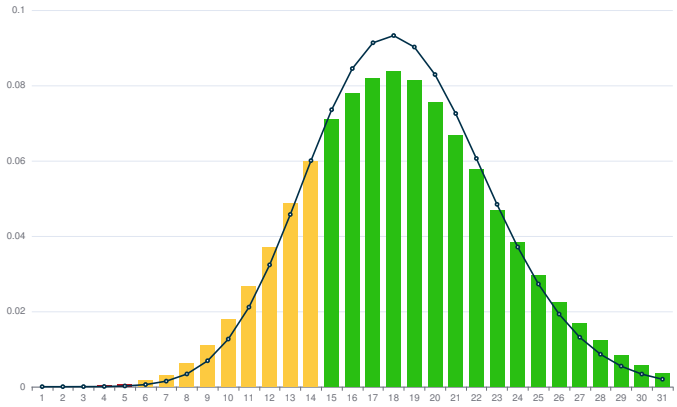
Mean	18.56
Standard dev.	4.85
< 1	0%
[1 - 4[	0%
[4 - 15[	20.2%
≥ 15	79.7%



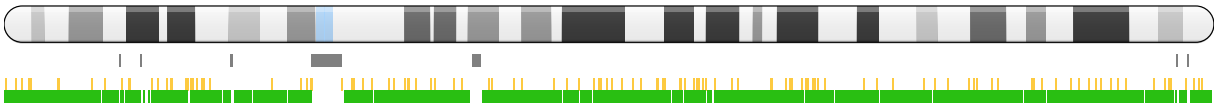
chr4



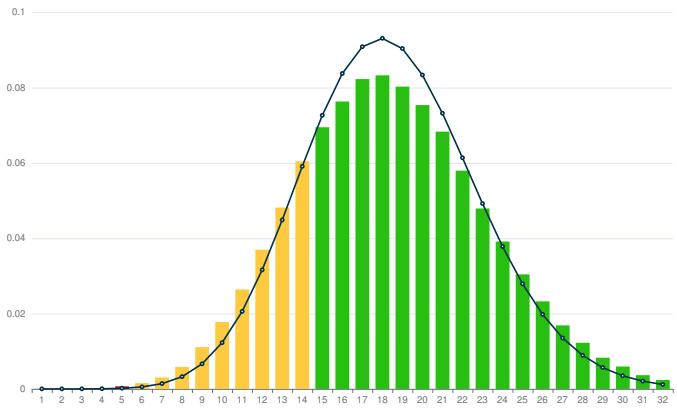
Mean	18.38
Standard dev.	4.81
< 1	0%
[1 - 4[	0%
[4 - 15[	21.3%
≥ 15	78.7%



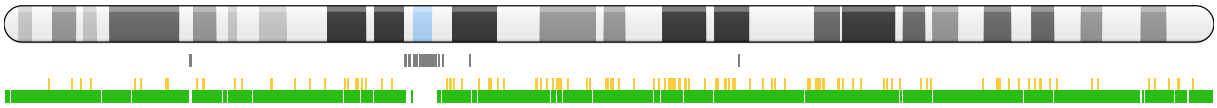
chr5



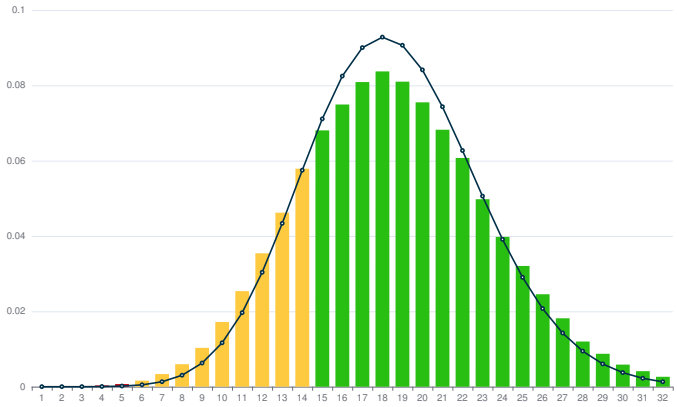
Mean	18.44
Standard dev.	4.91
< 1	0%
[1 - 4[	0%
[4 - 15[	21.2%
≥ 15	78.8%



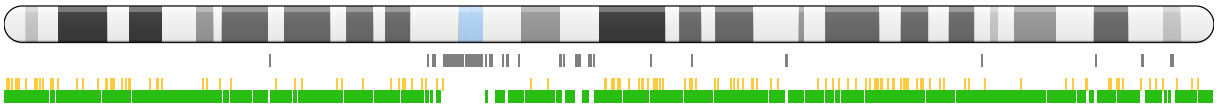
chr6



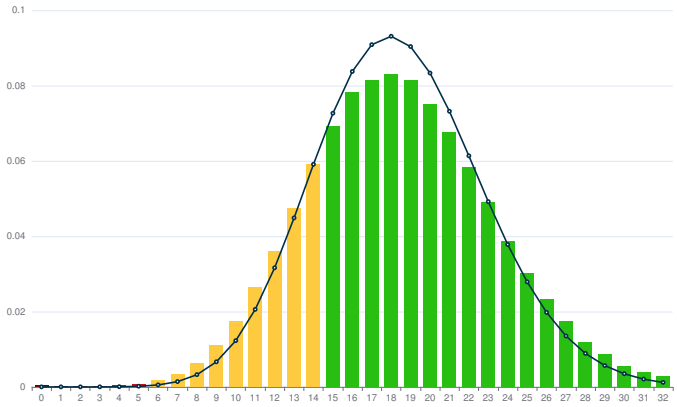
Mean	18.56
Standard dev.	4.86
< 1	0%
[1 - 4[	0%
[4 - 15[	20.4%
≥ 15	79.5%



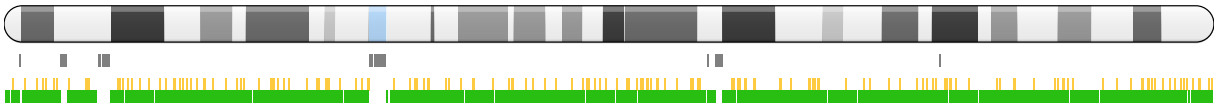
chr7



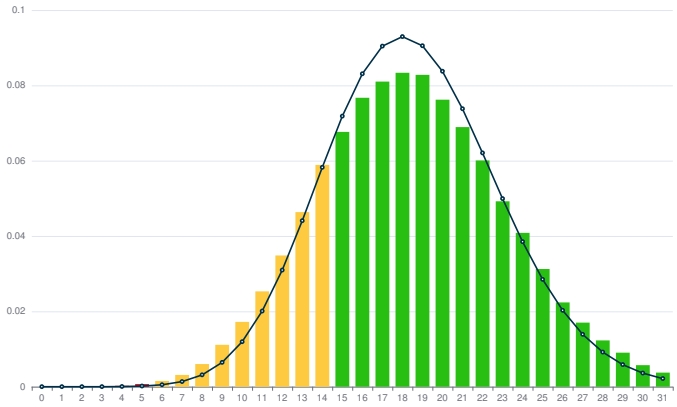
Mean	18.44
Standard dev.	4.88
< 1	0%
[1 - 4[	0%
[4 - 15[	20.9%
≥ 15	79%



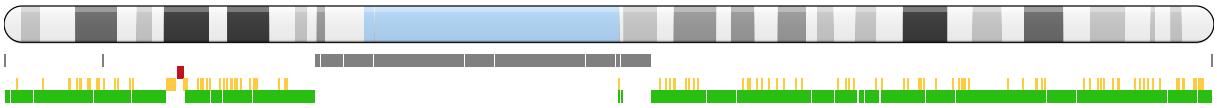
chr8



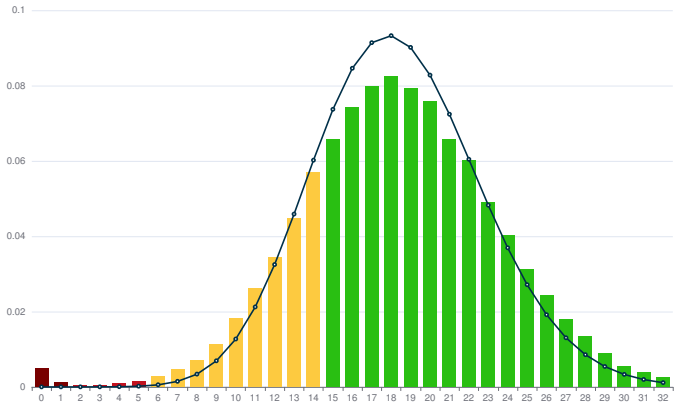
Mean	18.5
Standard dev.	4.8
< 1	0%
[1 - 4[	0%
[4 - 15[	20.5%
≥ 15	79.5%



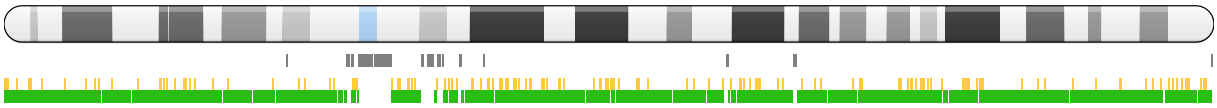
chr9



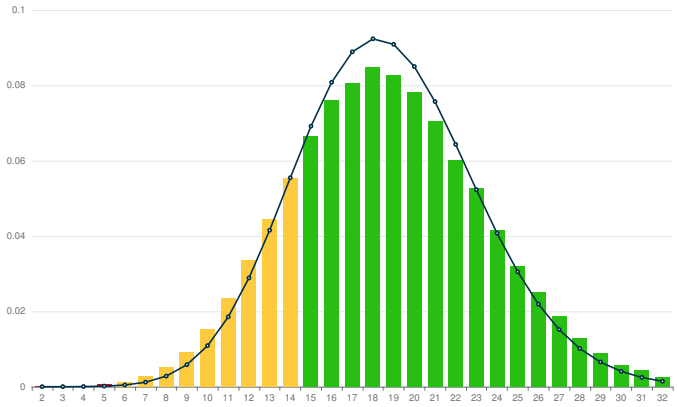
Mean	18.37
Standard dev.	5.17
< 1	0.5%
[1 - 4[	0.2%
[4 - 15[	20.9%
≥ 15	78.4%



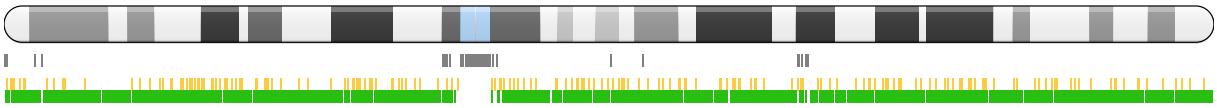
chr10



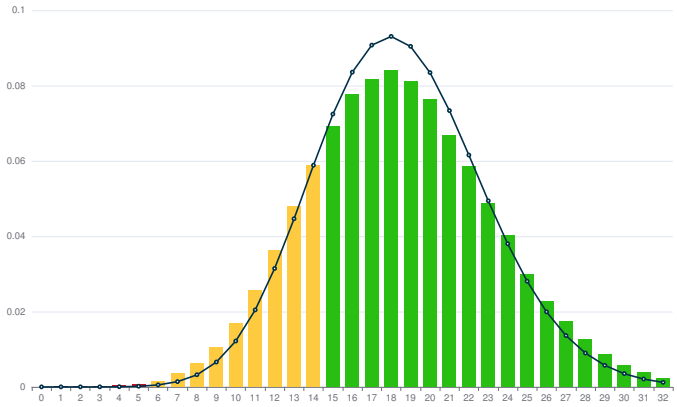
Mean	18.7
Standard dev.	4.78
< 1	0%
[1 - 4[	0%
[4 - 15[	19.1%
≥ 15	80.8%



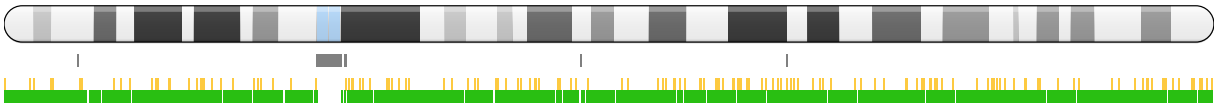
chr11



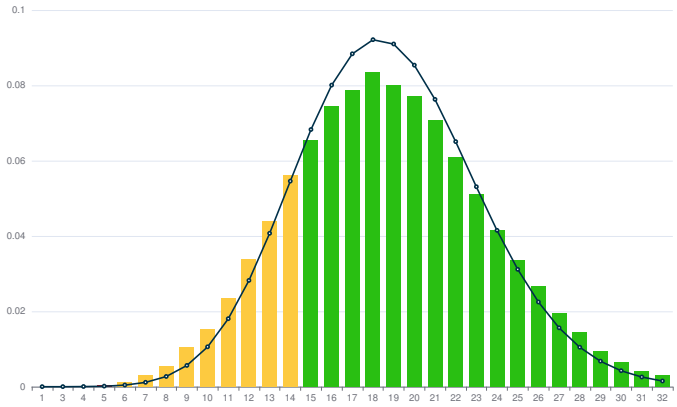
Mean	18.46
Standard dev.	4.82
< 1	0%
[1 - 4[	0%
[4 - 15[	20.8%
≥ 15	79.2%



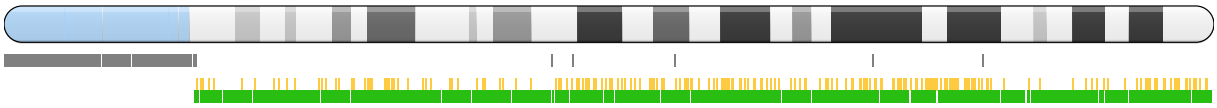
chr12



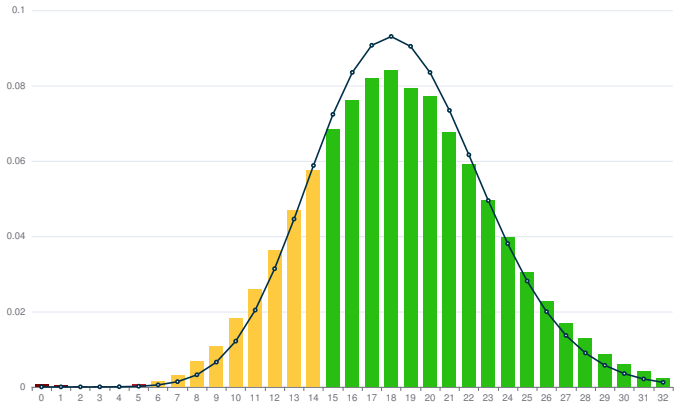
Mean	18.76
Standard dev.	4.88
< 1	0%
[1 - 4[	0%
[4 - 15[	19.4%
≥ 15	80.6%



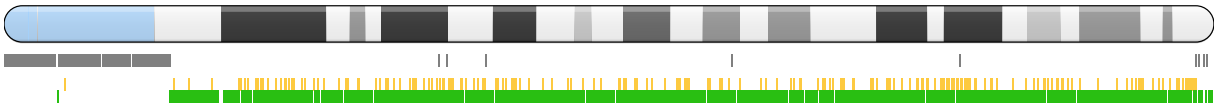
chr13



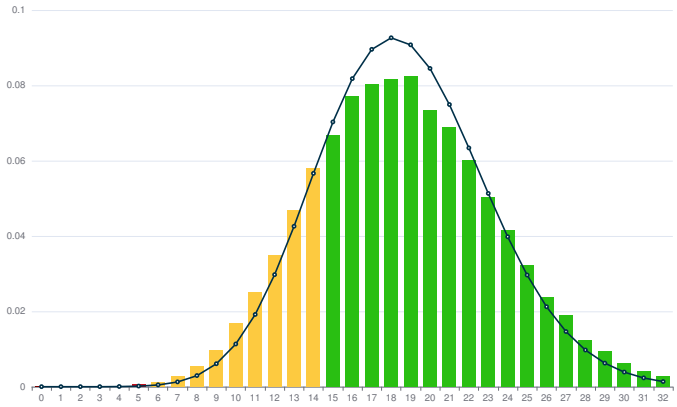
Mean	18.47
Standard dev.	4.87
< 1	0.1%
[1 - 4[	0%
[4 - 15[	20.8%
≥ 15	79.1%



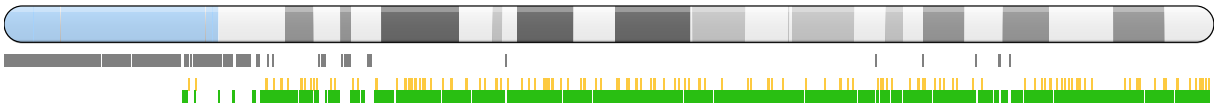
chr14



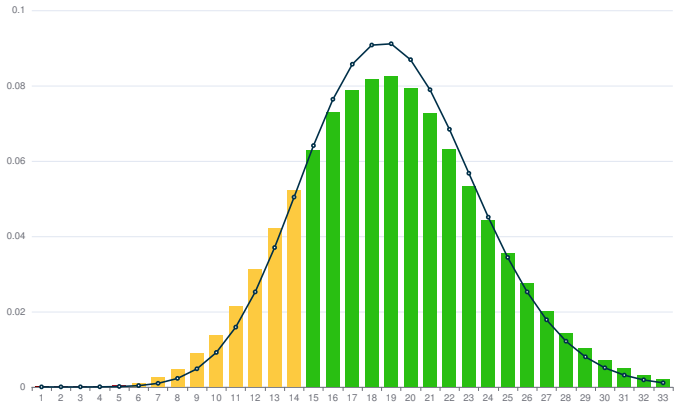
Mean	18.62
Standard dev.	4.87
< 1	0%
[1 - 4[	0%
[4 - 15[	20.2%
≥ 15	79.8%



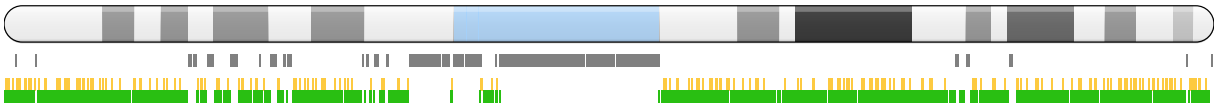
chr15



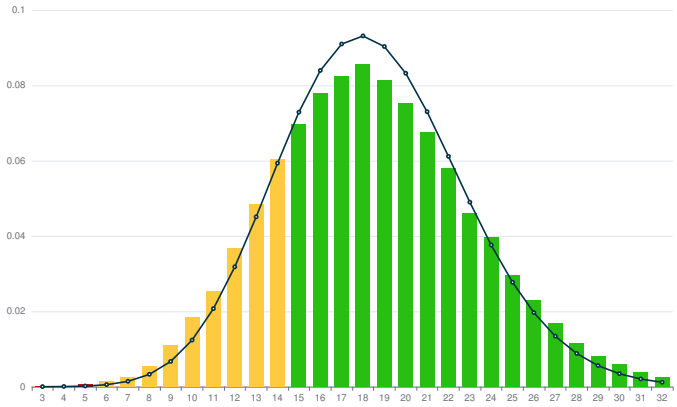
Mean	19.07
Standard dev.	5.1
< 1	0%
[1 - 4[	0%
[4 - 15[	17.8%
≥ 15	82.2%



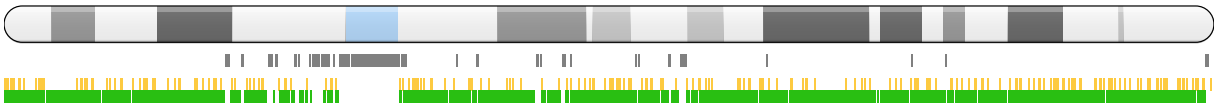
chr16



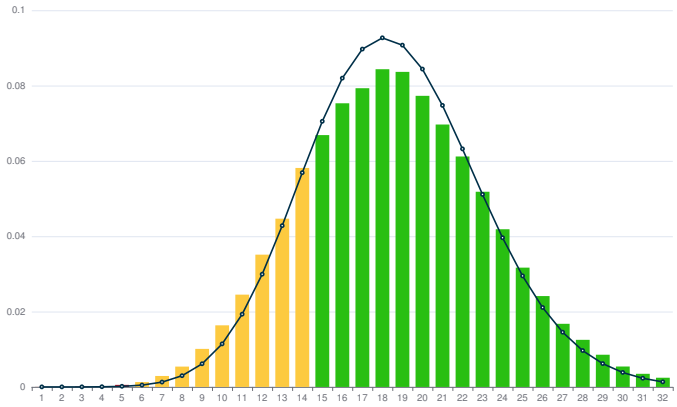
Mean	18.43
Standard dev.	4.81
< 1	0%
[1 - 4[	0%
[4 - 15[	21.1%
≥ 15	78.9%



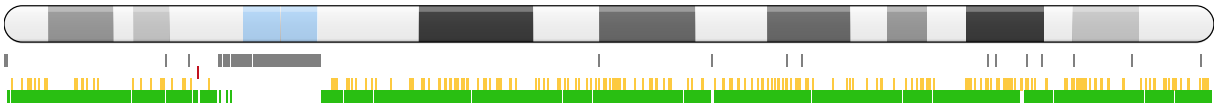
chr17



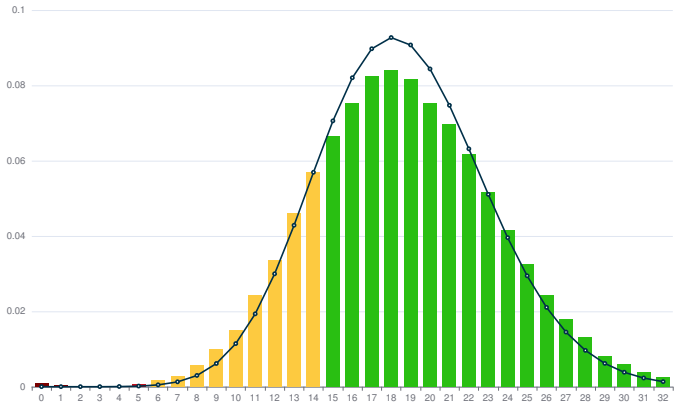
Mean	18.6
Standard dev.	4.8
< 1	0%
[1 - 4[	0%
[4 - 15[	19.9%
≥ 15	80.1%



chr18

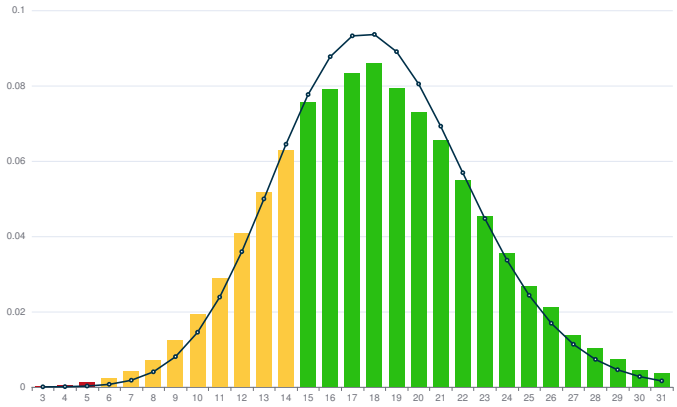


Mean	18.6
Standard dev.	4.83
< 1	0.1%
[1 - 4[	0.1%
[4 - 15[	19.7%
≥ 15	80.1%

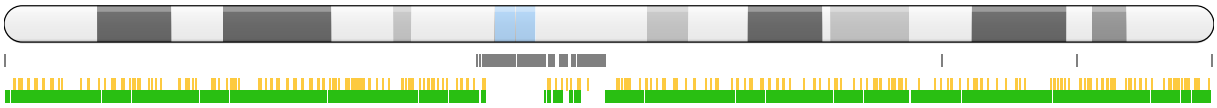


chr19

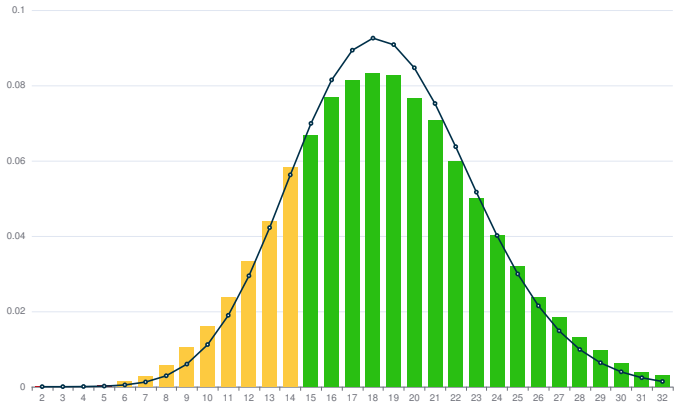
Mean	18.07
Standard dev.	4.77
< 1	0%
[1 - 4[	0%
[4 - 15[	23%
≥ 15	76.9%



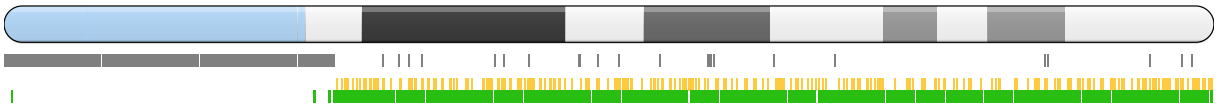
chr20



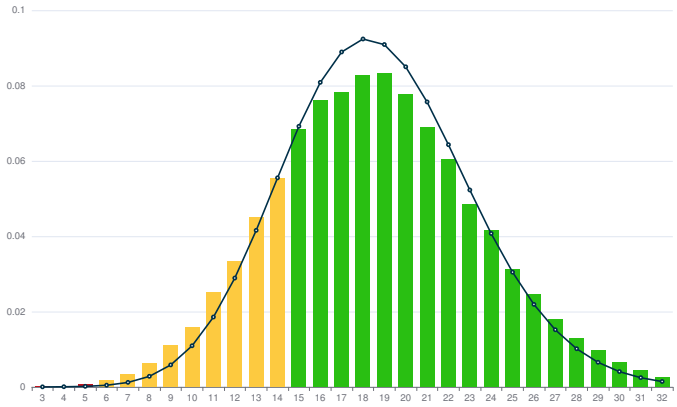
Mean	18.65
Standard dev.	4.83
< 1	0%
[1 - 4[	0%
[4 - 15[	19.7%
≥ 15	80.3%



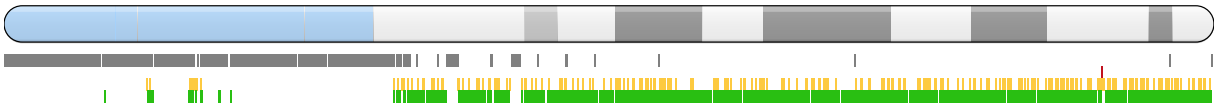
chr21



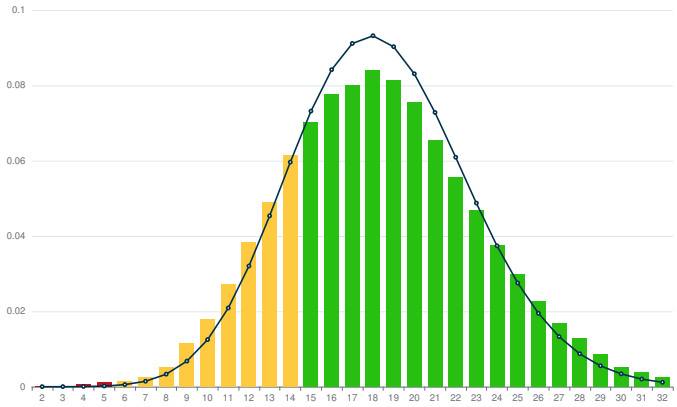
Mean	18.7
Standard dev.	5.19
< 1	0%
[1 - 4[	0%
[4 - 15[	19.8%
≥ 15	80.2%



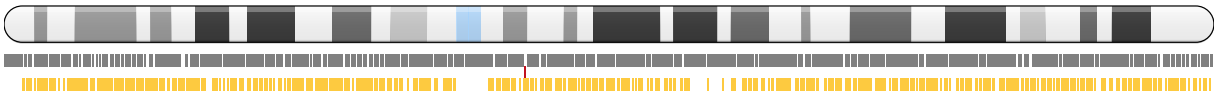
chr22



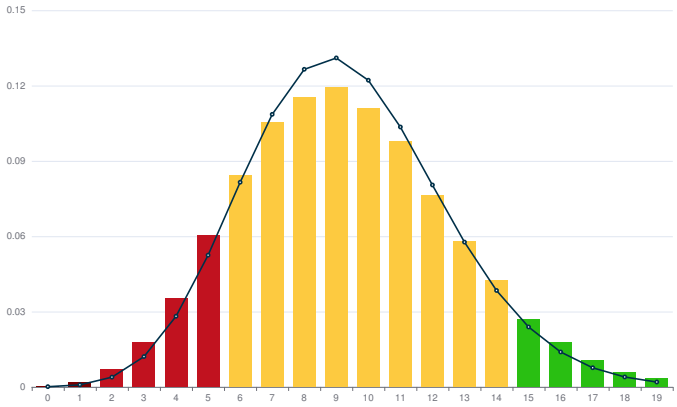
Mean	18.41
Standard dev.	4.95
< 1	0%
[1 - 4[	0%
[4 - 15[	21.6%
≥ 15	78.3%



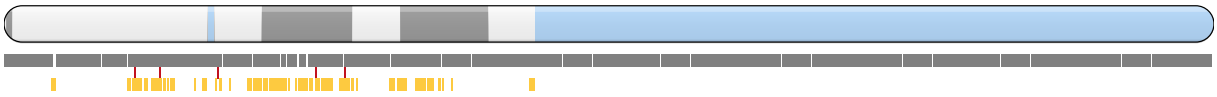
chrX



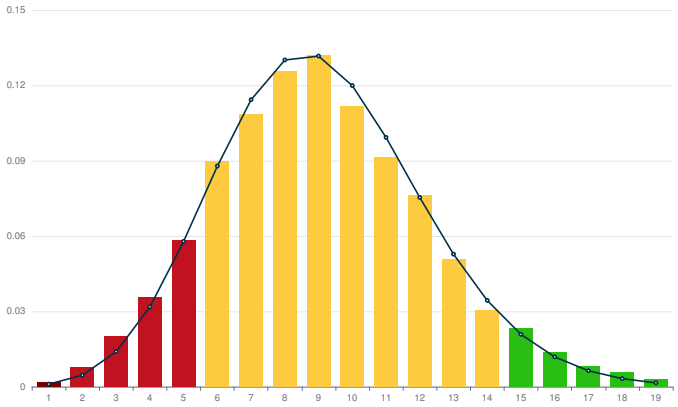
Mean	9.32
Standard dev.	3.37
< 1	0%
[1 - 4[	2.6%
[4 - 15[	90.5%
≥ 15	6.9%



chrY



Mean	9.11
Standard dev.	3.27
< 1	0%
[1 - 4[	3%
[4 - 15[	91.1%
≥ 15	5.9%



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.