

# somaticGermline TCRBOA6 - Report

Autor

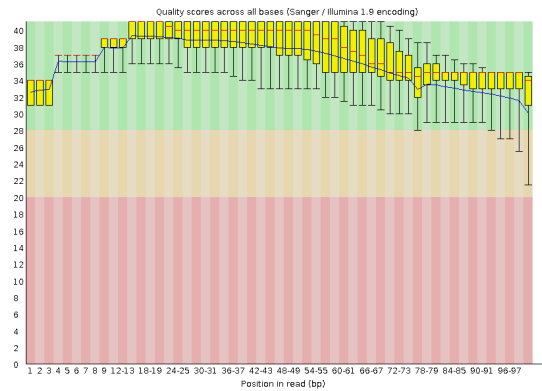
12. Oktober 2018

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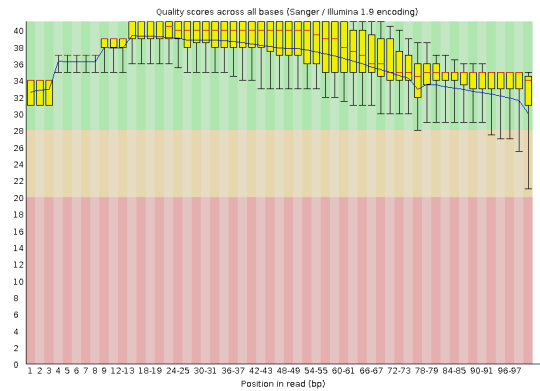
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# 1 Qualität der Genomsequenzierung

## 1.1 Raw Quality

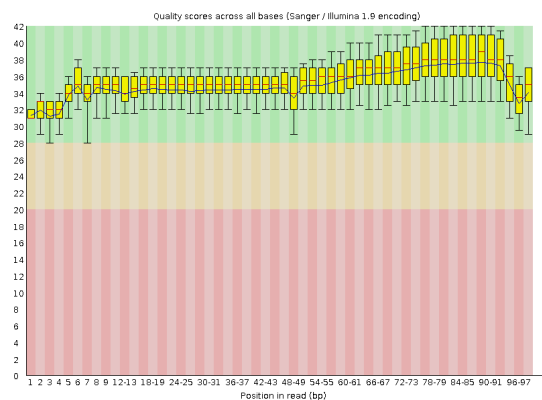


(a) Tumor Qualität

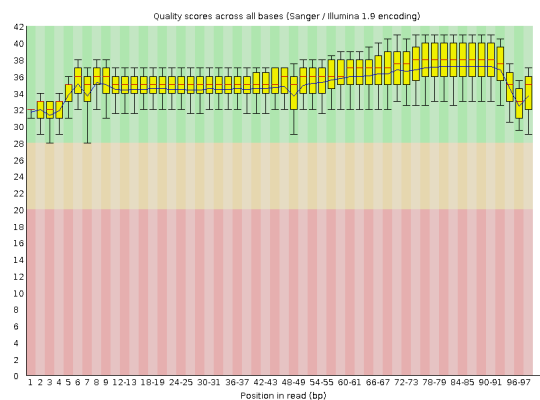


(b) Keimbahn Qualität

## 1.2 Base Quality Score Recalibration (BQSR)



(c) Tumor Qualität nach BQSR



(d) Keimbahn Qualität nach BQSR

## 1.3 Zusammenfassung

- Agilent SureSelect V6
- Paired end 100bp
- TD: 110 Mio. Reads
- GD: 105 Mio. Reads
- Gute Qualität der Reads

## 2 Coverage

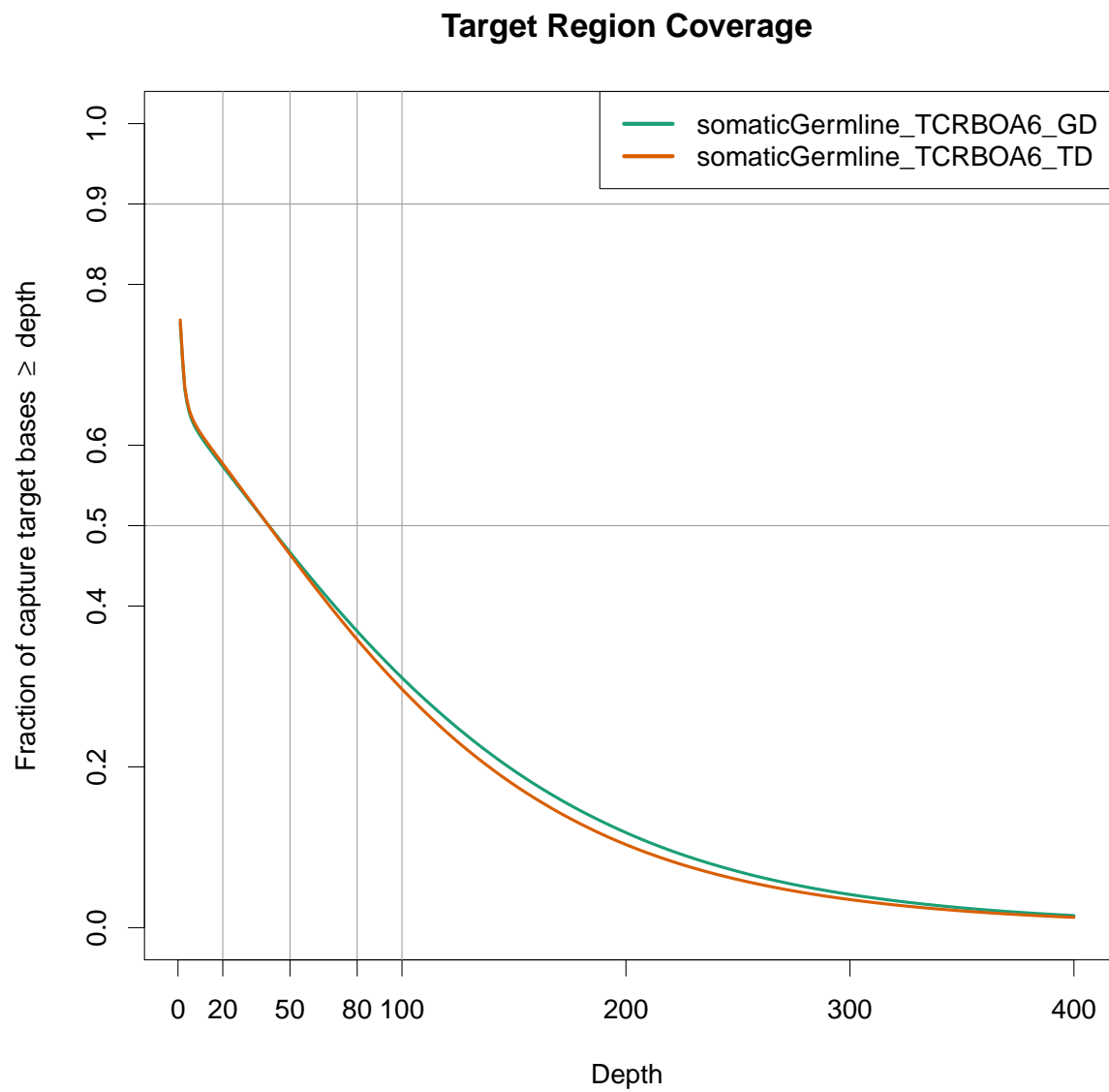


Abbildung 1: Coverage

### 2.1 Mean Coverage

```
## [1] "Mean Coverage somaticGermline_TCRBOA6_GD : 79.0732583"  
## [1] "Mean Coverage somaticGermline_TCRBOA6_TD : 75.364886"
```

## 3 Mutationsanalyse

### 3.1 Informationen zur Analyse

- Aligned zum Referenzgenom UCSC hg19
- Einschlusskriterien der Mutation
  - Mindestens 8 Reads pro Base
  - Seltene Mutationen (Minor-Allele Frequency (MAF)  $< 0.001$ , basierend auf gnomAD exome, ExAC, ESP6500 und 1000g)
  - Keine “Black-listed“ Gene/Sequenzen
  - Variant Allele Frequency (VAF)  $> 10\%$
- Analyse der Mutationen
  - Annotation bekannter Mutationen (Cosmic, Clinvar, dbSNP)
  - Ranking der Wichtigkeit (RVIS Score)
  - Strukturanalyse der mutierten Proteine (Condel, CADD)

### 3.2 Somatische Mutationen und Loss of Heterozygosity (LoH)

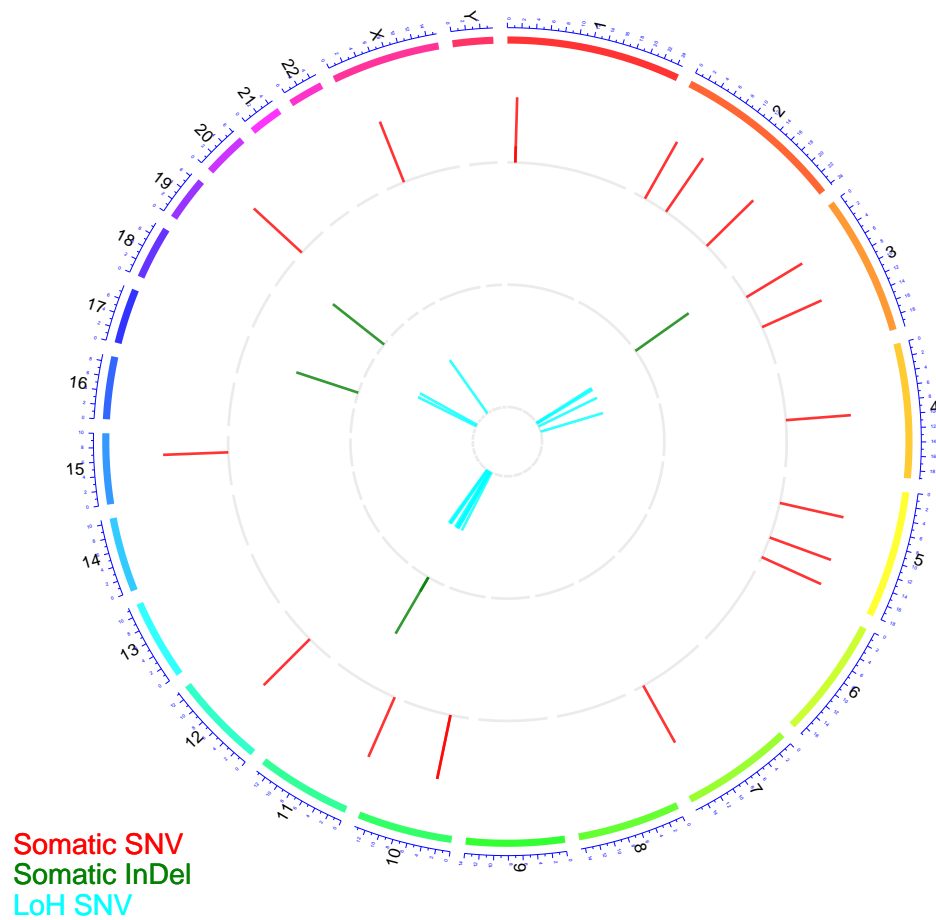


Abbildung 2: Circos Plot

Tabelle 1: Zusammenfassung der identifizierten Mutationen

Mutationstyp	Number of exonic	Zygotizität	TS	OG	HS
somatic SNV	1	homozygot	0	0	0
somatic SNV	17	heterozygot	0	0	0
LoH SNV	16	-	0	0	0
somatic InDel	0	homozygot	0	0	0
somatic InDel	4	heterozygot	2	0	0
LoH InDel	0	-	0	0	0

- 22 somatische Mutationen (exonisch)
- 16 Loss of Heterozygotizität (LoH)
- Insgesamt 38 Mutationen
- Mutationslast 1.49/Mb

Tabelle 2: Tumorsuppressoren und Onkogene - Überblick

Symbol	Gene Name	TSG	OG	HS
VHL	von Hippel-Lindau tumor suppressor	1	0	0
MEN1	menin 1	1	0	0

### 3.3 Tumorsuppressoren und Onkogene

Tabelle 3: Tumorsuppressoren und Onkogene

Symbol	Gene Name	Exonic Function	Aminoacid Change	VAF	Zygosity	Reads	TSG	OG	HS	TARGET	MAF	CADD	Condel	CLINSIG	COSMIC
VHL	von Hippel-Lindau tumor suppressor	frameshift deletion	p.His125fs	51.49%	het	52 10:	1	0	0		NA	NA	NA	NA	NA
MEN1	menin 1	frameshift insertion		55.36%	het	62 11:	1	0	0		NA	NA	NA		NA

### 3.4 Somatische Mutationen (top20 nach VAF)

Tabelle 4: somatische Mutationen

Symbol	Gene Name	Exonic Function	Aminoacid Change	VAF	Zygosity	Reads	TSG	OG	HS	TARGET	MAF	CADD	Condel	CLINSIG	COSMIC
GPR156	G protein-coupled receptor 156	nonsynonymous SNV	p.Ala608Val	75.76%	hom	25   33	0	0	0	.	NA	20.900	N	NA	NA
DOCK3	dedicator of cytokinesis 3	nonsynonymous SNV	p.Leu1633Phe	66.67%	het	28   42	0	0	0	.	0.00e+	19.080	N	NA	NA
MEN1	menin 1	frameshift insertion		55.36%	het	62   111	1	0	0		NA	NA	NA		NA
VHL	von Hippel-Lindau tumor suppressor	frameshift deletion	p.His125fs	51.49%	het	52   101	1	0	0		NA	NA	NA	NA	NA
FAM228B	family with sequence similarity 228 member B	unknown	p.Leu316*	43.28%	het	29   67	0	0	0	.	NA	35.000	N	NA	NA
SNX18	sorting nexin 18	nonsynonymous SNV	p.Ser613Phe	40%	het	24   60	0	0	0	.	NA	11.510	N	NA	NA
PLEKHM2	pleckstrin homology and RUN domain containing M2	nonsynonymous SNV	p.Arg830Trp	40.24%	het	134   131	0	0	0	.	9.31e-06	34.000	D	NA	ID=COSM6749990, COSM6749991
UNC5C	unc-5 netrin receptor C	nonsynonymous SNV	p.Pro839Ser	38.82%	het	59   151	0	0	0	.	NA	23.800	N	NA	ID=COSM2989103
NEUROD1	neuronal differentiation 1	nonsynonymous SNV	p.Lys39Glu	38.73%	het	67   171	0	0	0	.	NA	10.670	D	NA	NA
CYBB	cytochrome b-245 beta chain	nonsynonymous SNV	p.Gly512Arg	35.59%	het	63   117	0	0	0	.	NA	32.000	D	NA	NA



Tabelle 4: somatische Mutationen (*continued*)

Symbol	Gene Name	Exonic Function	Aminoacid Change	VAF	Zygosity	Reads	TSG	OG	HS	TARGET	MAF	CADD	Condel	CLINSIG	COSMIC
ZC3H10	zinc finger CCCH-type containing 10	nonsynonymou SNV	p.Val181Asp	35.54%	het	43   12'	0	0	0	.	NA	9.774	N	NA	NA
LCP2	lymphocyte cytosolic protein 2	nonsynonymou SNV	p.Ala143Val	34.41%	het	96   28'	0	0	0	.	1.00e- 04	23.000	N	NA	NA
CEACAM8	carcinoembryo antigen related cell adhesion molecule 8	frameshift deletion	p.Gln16fs	34.04%	het	16   48	0	0	0	.	NA	NA	NA	NA	NA
ATP6V0A4	ATPase H+ transporting V0 subunit a4	nonsynonymou SNV	p.Ala706Ser	32.88%	het	24   73	0	0	0	.	NA	1.999	N	NA	NA
MEGF10	multiple EGF like domains 10	nonsynonymou SNV	p.Ala726Val	32.58%	het	43   13'	0	0	0	.	NA	24.800	N	NA	NA
TMC2	transmembran channel like 2	stopgain	p.Lys165*	31.64%	het	56   17'	0	0	0	.	NA	37.000	NA	NA	NA
TTC31	tetratricopeptic repeat domain 31	nonsynonymou SNV	p.Glu199Gly	28.47%	het	39   13'	0	0	0	.	NA	23.100	N	NA	NA
ANKRD30A	ankyrin repeat domain 30A	nonsynonymou SNV	p.Cys873Tyr	28.12%	het	9   32	0	0	0	.	NA	6.906	N	NA	NA
LCTL	lactase like	nonsynonymou SNV	p.Thr36Ile	26.57%	het	38   14'	0	0	0	.	NA	23.700	N	NA	NA
MUC2	mucin 2, oligomeric mucus/gel- forming	nonsynonymou SNV	p.Ser1698Thr	16.33%	het	8   51	0	0	0	.	NA	0.646	N	NA	ID=COSM4184070, COSM4184071

### 3.5 LoH

Tabelle 5: LoH

Symbol	Gene Name	Exonic Function	Aminoacid Change	MAF_Normal	MAF_Tumor	Reads_Normal	Reads_Tumor	TSG	OG	H5	TARGET	MAF	CADD	Condel	CLINSIG	COSMIC
SLC22A13	solute carrier family 22 member 13	nonsynonymot SNV	p.Ala77Val	48.47%	78.72%	79 16	74 94	0	0	0	.	8.06e-05	3.410	D	NA	NA
ARIH2OS	ariadne RBR E3 ubiquitin protein ligase 2 opposite strand	nonsynonymot SNV	p.Ser166Pro	47.06%	76.74%	32 68	33 43	0	0	0	.	2.70e-05	13.200	N	NA	NA
NFKBIZ	NFKB inhibitor zeta	nonsynonymot SNV	p.Leu545Pro	40%	77.78%	12 30	14 18	0	0	0	.	9.00e-04	27.200	N	NA	NA
LSG1	large 60S subunit nuclear export GTPase 1	nonsynonymot SNV	p.Leu510Phe	50.38%	78.82%	67 13	67 85	0	0	0	.	0.00e+	23.300	D	NA	NA
ABTB2	ankyrin repeat and BTB domain containing 2	nonsynonymot SNV	p.Arg452Gln	54.84%	90.24%	17 31	37 41	0	0	0	.	9.07e-06	29.300	N	NA	NA
TNKS1BP1	tankyrase 1 binding protein 1	nonsynonymot SNV	p.Arg427Gln	48.21%	75.36%	54 11	52 69	0	0	0	.	2.00e-04	34.000	N	NA	ID=COSM1229944
MPEG1	macrophage expressed 1	nonsynonymot SNV	p.Gln694Arg	52.17%	75.86%	84 16	88 11	0	0	0	.	6.27e-05	6.974	N	NA	NA
LTBP3	latent transforming growth factor beta binding protein 3	nonsynonymot SNV	p.Pro488Ser	52.48%	82.86%	74 14	58 70	0	0	0	.	NA	12.940	D	NA	NA
ACY3	aminoacylase 3	nonsynonymot SNV	p.Thr277Arg	53.51%	77.98%	99 18	85 10	0	0	0	.	8.96e-06	23.600	D	NA	NA
MYO7A	myosin VIIA	nonsynonymot SNV	p.Val411Ala	41.33%	79.59%	81 19	78 99	0	0	0	.	5.44e-05	26.000	D	Uncer si-gni-fi-can-ce	NA

ALKBH8	alkB homolog 8, tRNA methyltransferase	nonsynonymous SNV	p.Ser149Cys	54.35%	88.46%	25 46	46 52	0	0	0	.	1.80e-05	24.500	N	NA	NA
ANKK1	ankyrin repeat and kinase domain containing 1	nonsynonymous SNV	p.Arg295Cys	44.3%	78.26%	35 81	36 46	0	0	0	.	8.96e-06	14.800	N	NA	NA
NECTIN1	nectin cell adhesion molecule 1	nonsynonymous SNV	p.Gly480Ser	45.13%	75.81%	88 190	94 121	0	0	0	.	9.87e-05	19.050	N	NA	NA
ZNF521	zinc finger protein 521	nonsynonymous SNV	p.Glu484Lys	47.55%	85.12%	68 141	103 111	0	0	0	.	1.80e-05	21.900	N	NA	ID=COSM6830919
LIPG	lipase G, endothelial type	nonsynonymous SNV	p.Ser95Arg	49.12%	78.38%	28 57	29 37	0	0	0	.	3.59e-05	23.400	D	NA	NA
BRWD1	bromodomain and WD repeat domain containing 1	nonsynonymous SNV	p.Thr1205Ile	46.34%	88.24%	19 41	30 34	0	0	0	.	2.70e-05	25.300	N	NA	NA

### 3.6 Funktionelle Analysen

#### GO

Tabelle 6: Ergebnisse GO Analyse, top 20

Term	Count	Size	p-value	adj.P.Val
columnar/cuboidal epithelial cell differentiation	3	104	7.94e-04	1e+00
sensory perception of sound	3	137	1.62e-03	1e+00
sensory perception of mechanical stimulus	3	153	2.21e-03	1e+00
digestion	3	172	3.27e-03	1e+00
homeostatic process	7	1621	1.97e-02	1e+00
anatomical structure homeostasis	3	372	2.54e-02	1e+00
response to peptide hormone	3	401	3.30e-02	1e+00
epithelial cell differentiation	4	720	3.57e-02	1e+00
response to peptide	3	448	4.34e-02	1e+00
negative regulation of intracellular signal transduction	3	468	4.66e-02	1e+00
response to abiotic stimulus	5	1153	4.80e-02	1e+00

## Consensus

Tabelle 7: Ergebnisse Consensus Analyse, top 20

Term	Count	Size	p-value	adj.P.Val	Symbol
NA	NA	NA	NA	NA	NULL

## Reactome

Tabelle 8: Ergebnisse Reactome Analyse, top 20

Term	Count	Size	p-value	adj.P.Val
NA	NA	NA	NA	NA

## Hallmarks of Cancer

Tabelle 9: Ergebnisse Hallmarks Analyse, top 20

Term	Count	Size	p-value	adj.P.Val
NA	NA	NA	NA	NA

### 3.7 Wichtige Signalwege

```
## [1] "Keine Mutationen in wichtigen Signalwegen!"
```



## 4 Copy Number Variation

### 4.1 Anzahl CNVs

```
## [1] "#CNVs: 152"
```

### 4.2 CNV Plots

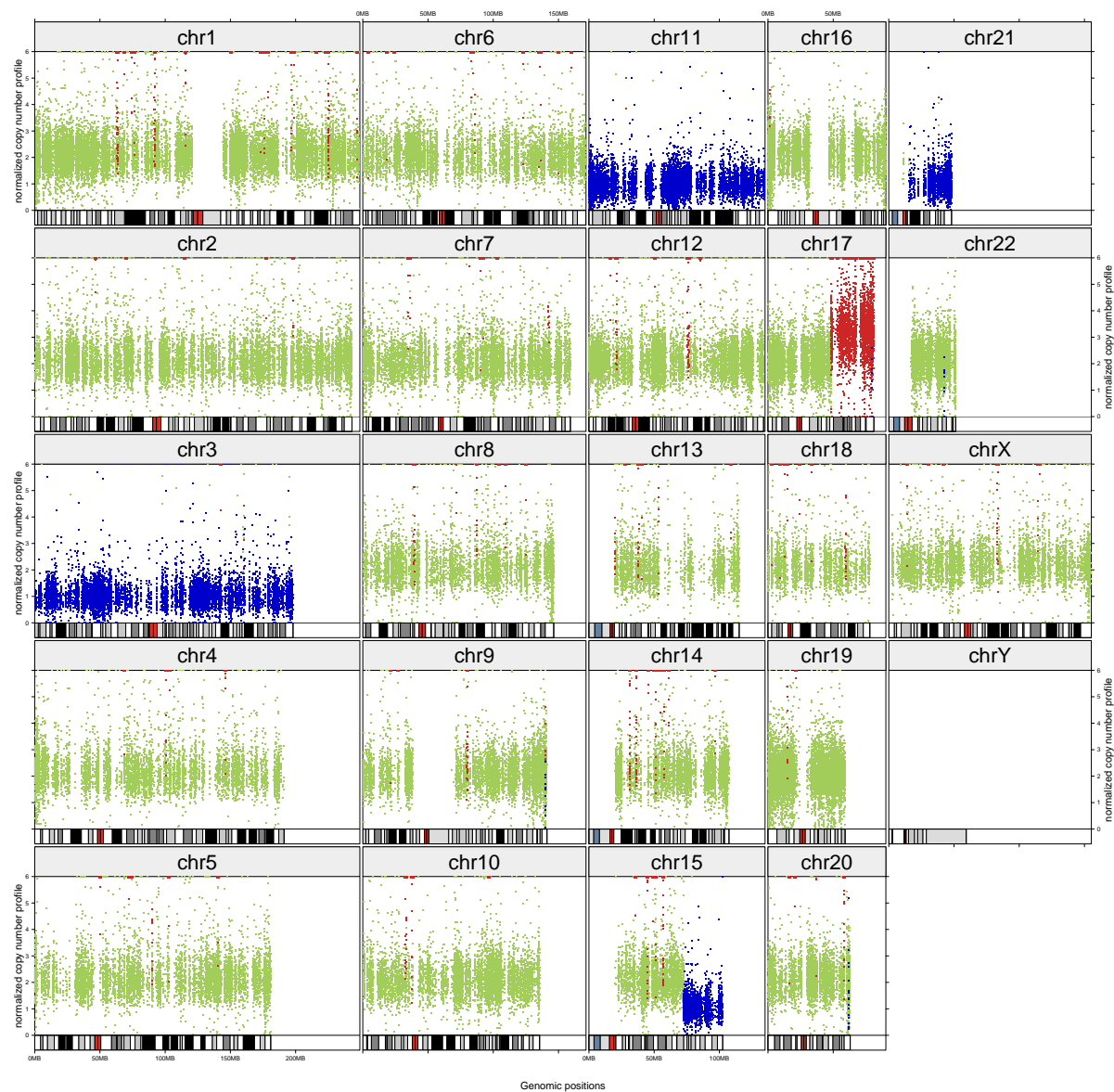


Abbildung 3: Copy Number Variation

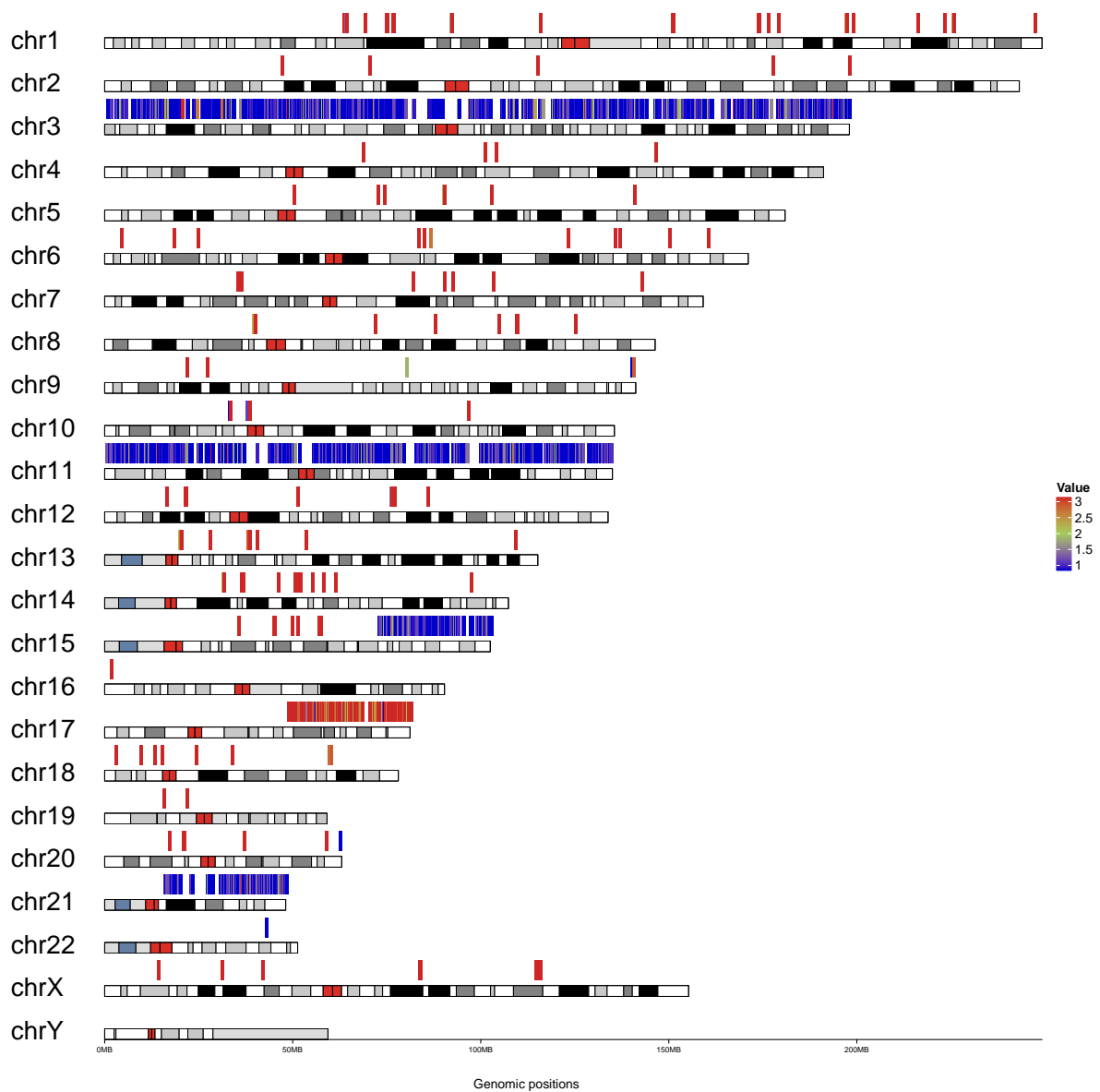


Abbildung 4: Copy Number Variation - Ideogram

### 4.3 Tumorsuppressoren

Tabelle 10: Tumorsuppressoren

chr	copy.number	status	TumorSuppressor
3	1	loss	VHL
3	1	loss	MLH1,TGFBR2,BAP1,RYBP,SETD2,SHQ1,PBRM1
3	1	loss	ATR
11	1	loss	MEN1
11	1	loss	ATM,CBL,CHEK1,KMT2A,SDHD
15	1	loss	BLM
17	3	gain	RAD51C,AXIN2,SPOP,RNF43
21	1	loss	RUNX1
21	1	loss	RUNX1

#### 4.4 Onkogene

Tabelle 11: Onkogene

chr	copy.number	status	Oncogene
3	1	loss	RAF1
3	1	loss	RHOA,CTNNB1,MYD88
3	1	loss	PIK3CB
3	1	loss	PIK3CA,PRKCI
3	1	loss	BCL6
11	1	loss	HRAS,IGF2,RRAS2
11	1	loss	CCND1,FGF3,FGF4,FGF19
11	1	loss	YAP1
15	1	loss	IDH2,IGF1R,NTRK3
17	3	gain	PPM1D
17	3	gain	RPTOR
19	3	gain	BRD4
21	1	loss	ERG
21	1	loss	ERG
21	1	loss	ERG
21	1	loss	TMPRSS2,U2AF1

## 4.5 Funktionelle Analyse der CNVs

### GAIN

Tabelle 12: Ergebnisse GO Analyse - GAIN, top 20

Term	Count	Size	p-value	adj.P.Val
axon extension	3	100	1.92e-02	1e+00
establishment of cell polarity	3	103	2.02e-02	1e+00
regulation of epithelial cell proliferation	5	289	2.40e-02	1e+00
negative regulation of epithelial cell proliferation	3	116	2.83e-02	1e+00
formation of primary germ layer	3	119	3.09e-02	1e+00
transport along microtubule	3	125	3.36e-02	1e+00
microtubule-based transport	3	125	3.36e-02	1e+00
sensory perception of sound	3	137	4.01e-02	1e+00
establishment of protein localization to plasma membrane	3	138	4.40e-02	1e+00
neuron projection extension	3	140	4.48e-02	1e+00
epithelial cell proliferation	5	343	4.48e-02	1e+00
cytoskeleton-dependent intracellular transport	3	142	4.64e-02	1e+00

## LOSS

Tabelle 13: Ergebnisse GO Analyse - LOSS, top 20

Term	Count	Size	p-value	adj.P.Val
detection of chemical stimulus involved in sensory perception of smell	175	426	2.52e-26	3.90e-22
sensory perception of smell	182	453	1.99e-25	1.54e-21
detection of chemical stimulus involved in sensory perception	180	470	4.87e-22	2.52e-18
detection of stimulus involved in sensory perception	190	520	6.48e-20	2.51e-16
detection of chemical stimulus	185	505	1.28e-19	3.98e-16
sensory perception of chemical stimulus	189	528	8.02e-19	2.07e-15
detection of stimulus	215	678	4.02e-13	8.90e-10
sensory perception	257	953	5.08e-07	9.83e-04
urate transport	8	10	3.80e-05	6.54e-02
adenylate cyclase-inhibiting dopamine receptor signaling pathway	8	11	4.53e-04	7.02e-01
sodium-independent organic anion transport	13	25	5.49e-04	7.74e-01
positive regulation of triglyceride catabolic process	6	8	2.03e-03	1.00e+00
neurological system process	306	1281	2.84e-03	1.00e+00
behavioral response to cocaine	10	19	3.22e-03	1.00e+00
G-protein coupled purinergic nucleotide receptor signaling pathway	8	14	4.36e-03	1.00e+00
G-protein coupled purinergic receptor signaling pathway	11	23	5.23e-03	1.00e+00
regulation of triglyceride catabolic process	7	12	6.63e-03	1.00e+00
negative regulation of cyclase activity	13	30	6.98e-03	1.00e+00
axon choice point recognition	5	7	7.05e-03	1.00e+00
neuron recognition	14	34	8.87e-03	1.00e+00

## 5 Analyse der Mutationssignaturen

- Nur somatische Mutationen werden berücksichtigt
- Nur Signaturen, die mehr als 1% aller SNVs beinhalten, werden verwendet
- Die Signaturen basieren auf den aktuellen *COSMIC Mutation Signatures* <http://cancer.sanger.ac.uk/cosmic/signatures>
- AC3 wird als *BRCAness* bezeichnet

Tabelle 14: Ergebnisse Mutationssignatur Analyse

Signature	Process	Percentage
AC2	APOBEC	7.64
AC3	defect DNA DSB repair hom. recomb.	15.13
AC4	tobacco mutagens, benzo(a)pyrene	8.00
AC6	defect DNA MMR, found in MSI tumors	6.52
AC12	unknown	12.38
AC15	defect DNA MMR	7.00
AC17	unknown	1.30
AC20	associated w. small indels at repeats	18.73
AC21	unknown	7.82
AC22	aristocholic acid	2.51
AC23	unknown	2.79
AC30	unknown	10.18

## **6 Versionsinfo**

### **6.1 Genome**

- UCSC hg19

### **6.2 Programmversionen**

- FastQC: 0.11.5
- Trimmomatic: 0.36
- BWA: 0.7.15
- bam-readcount: 0.8.0
- samtools 1.4.1
- GATK: 3.6
- picard-tools: 2.9.2
- VarScan: 2.4.3
- annovar 2017-07-17
- bedtools: 2.26.0
- Control-FREEC: 11.0
- Java: 1.8.0\_121

### **6.3 Annovar Datenbanken**

- refGene GRCh37 (20170601)
- esp6500siv2\_all (20141222)
- avsnp150 (dbSNP) (20170929)
- clinvar\_20170905 (20171003)
- 1000g2015aug\_all (20150824)
- cosmic84 (20180213)
- exac03 (20151129)
- gnomad\_exome (20170311)
- cadd13 (20170123)