

# somaticGermline TCRBOA6 VCRome - Report

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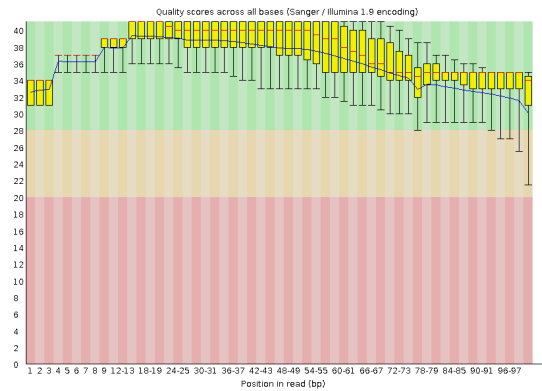
12. Januar 2019

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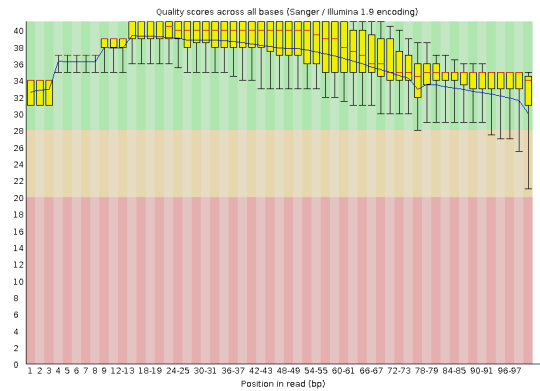
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# 1 Qualität der Genomsequenzierung

## 1.1 Raw Quality

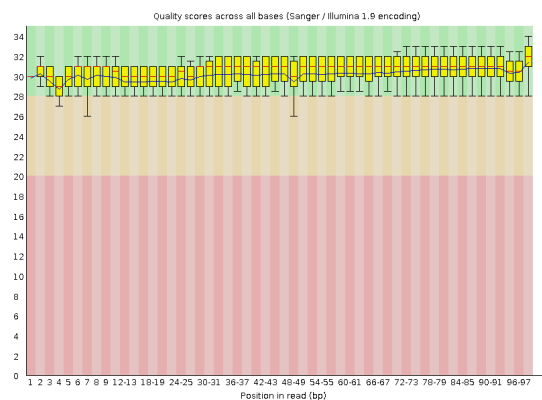


(a) Tumor Qualität

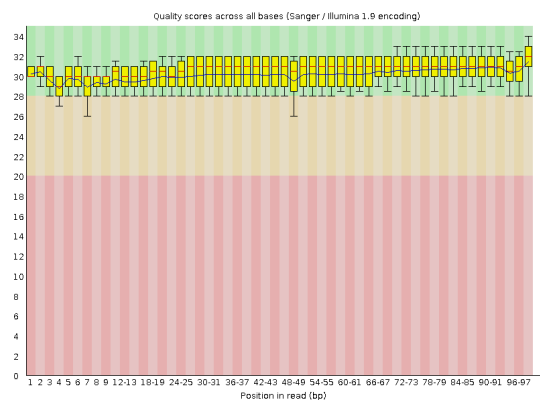


(b) Keimbahn Qualität

## 1.2 Base Quality Score Recalibration (BQSR)



(c) Tumor Qualität nach BQSR



(d) Keimbahn Qualität nach BQSR

## 1.3 Zusammenfassung

- VCRome 2.1
- Paired end 100bp
- TD: 110 Mio. Reads
- GD: 105 Mio. Reads
- Gute Qualität der Reads

## 2 Coverage

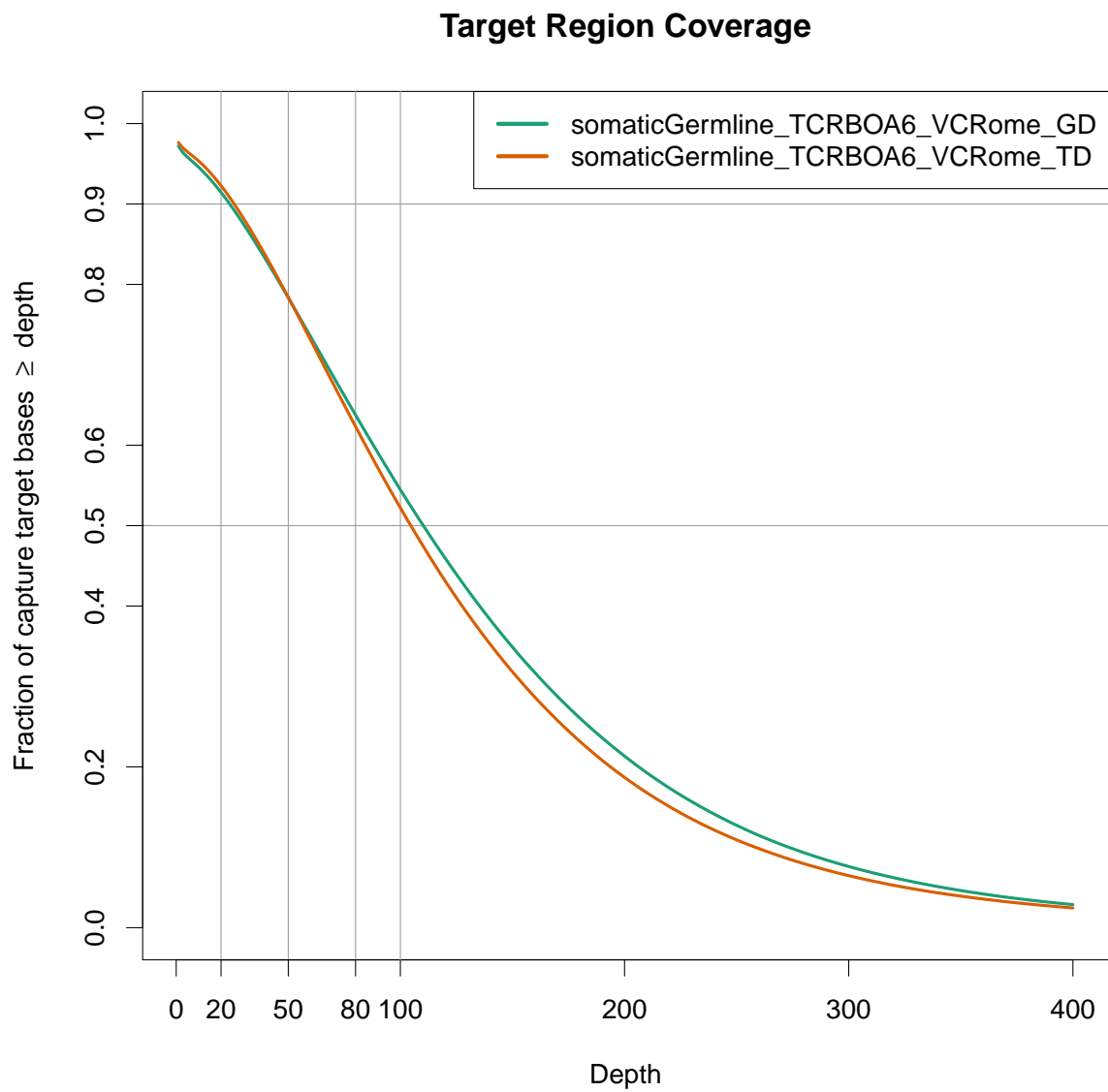


Abbildung 1: Coverage

### 2.1 Mean Coverage

```
## [1] "Mean Coverage somaticGermline_TCRBOA6_VCRome_GD : 135.2431552"  
## [1] "Mean Coverage somaticGermline_TCRBOA6_VCRome_TD : 128.9476502"
```

## 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)

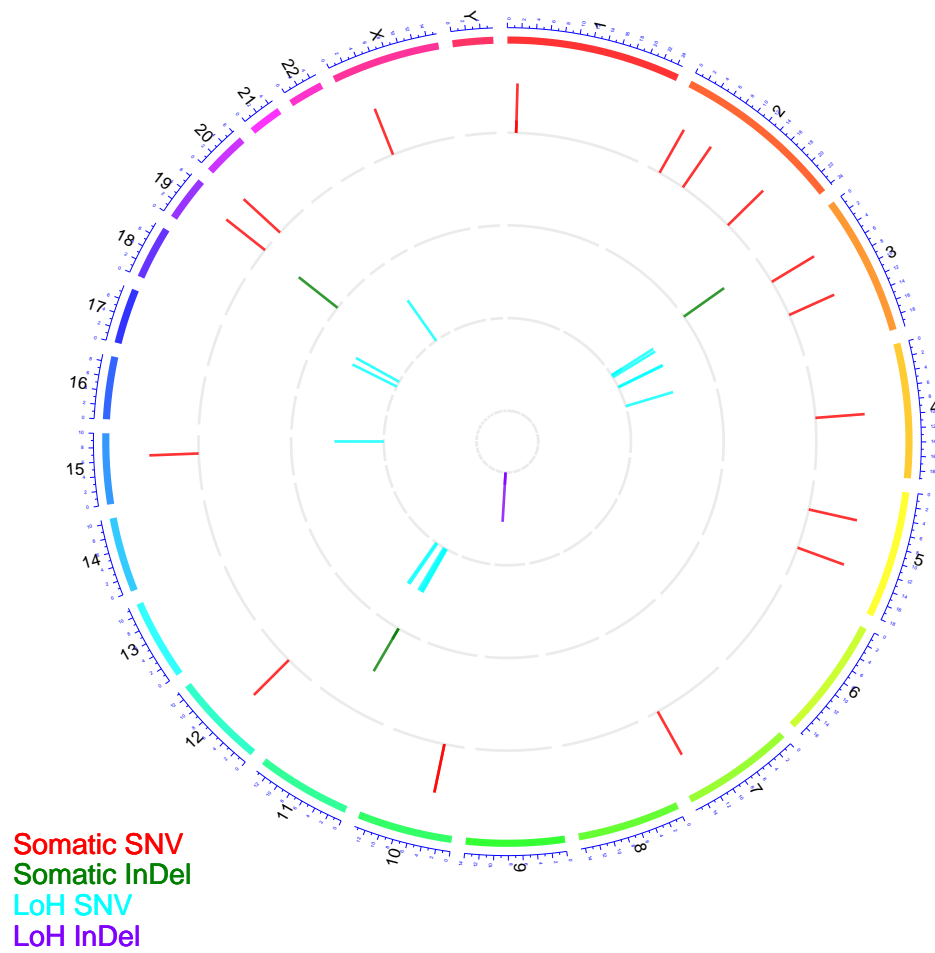


Abbildung 2: Circos Plot

Tabelle 1: Zusammenfassung der identifizierten Mutationen

Mutationstyp	Number of exonic	Zygotizität	TS	OG	HS
somatic SNV	1	homozygot	0	0	0
somatic SNV	16	heterozygot	0	0	0
LoH SNV	15	-	0	0	0
somatic InDel	0	homozygot	0	0	0
somatic InDel	3	heterozygot	2	0	0
LoH InDel	1	-	0	0	0

- 20 somatische Mutationen (exonisch)
- 16 Loss of Heterozygotizität (LoH)
- Insgesamt 36 Mutationen
- Mutationslast 1.33/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	50.98%	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	50.98%	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	39.22%	het	60   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	nonsynonymous SNV	p.Val181Asp	35.54%	het	43   12	0	0	0	.	NA	9.774	N	NA	NA
CEACAM8	carcinoembryon antigen related cell adhesion molecule 8	frameshift deletion	p.Gln16fs	34.04%	het	16   48	0	0	0	.	NA	NA	NA	NA	NA
CD177	CD177 molecule	unknown	p.Val240Met	33.83%	het	68   20	0	0	0	.	NA	3.844	NA	NA	NA
ATP6V0A4	ATPase H+ transporting V0 subunit a4	nonsynonymous SNV	p.Ala706Ser	32.88%	het	24   73	0	0	0	.	NA	1.999	N	NA	NA
MEGF10	multiple EGF like domains 10	nonsynonymous SNV	p.Ala726Val	32.58%	het	43   13	0	0	0	.	NA	24.800	N	NA	NA
TMC2	transmembrane channel like 2	stopgain	p.Lys165*	31.64%	het	56   17	0	0	0	.	NA	37.000	NA	NA	NA
TTC31	tetratricopeptide repeat domain 31	nonsynonymous SNV	p.Glu199Gly	28.47%	het	39   13	0	0	0	.	NA	23.100	N	NA	NA
ANKRD30A	ankyrin repeat domain 30A	nonsynonymous SNV	p.Cys873Tyr	28.12%	het	9   32	0	0	0	.	NA	6.906	N	NA	NA
LCTL	lactase like	nonsynonymous SNV	p.Thr36Ile	26.57%	het	38   14	0	0	0	.	NA	23.700	N	NA	NA
ANKRD30A	ankyrin repeat domain 30A	nonsynonymous SNV	p.Cys516Tyr	11.46%	het	29   25	0	0	0	.	NA	0.001	N	NA	NA

### 3.5 LoH

Tabelle 5: LoH

Symbol	Gene Name	Exonic Function	Aminoacid Change	MAF	MAF	Reads	Reads	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	13.20	N	NA	NA
FILIP1L	filamin A interacting protein 1 like	nonsynonymot SNV	p.Lys183Glu	55.84%	85.45%	43 77	47 55	0	0	0	.	8.00e-04	10.25	N	NA	NA
NFKBIZ	NFKB inhibitor zeta	nonsynonymot SNV	p.Leu545Pro	40%	77.78%	12 30	14 18	0	0	0	.	9.00e-04	27.2	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+	23.3	D	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	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	12.94	D	NA	NA
ZNF705E	zinc finger protein 705E	nonsynonymot SNV		43.15%	76.8%	63 14	96 12	0	0	0	.	NA	NA	NA	NA	NA
ALKBH8	alkB homolog 8, tRNA methyltransferase	nonsynonymot SNV	p.Ser149Cys	54.35%	88.46%	25 46	46 52	0	0	0	.	1.80e-05	24.5	N	NA	NA
ANKK1	ankyrin repeat and kinase domain containing 1	nonsynonymot SNV	p.Arg295Cys	44.3%	78.26%	35 81	36 46	0	0	0	.	8.96e-06	14.80	N	NA	NA

ISG20	interferon stimulated exonuclease gene 20	nonsynonymous SNV		52.03%	81.97%	64 12	50 61	0	0	0	.		NA	NA	NA	NA	NA
ZNF521	zinc finger protein 521	nonsynonymous SNV	p.Glu484Lys	47.55%	85.12%	68 14	103 11	0	0	0	.		1.80e-05	21.9	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	23.4	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	25.3	N	NA	NA
C9orf147	chromosome 9 open reading frame 147	frameshift deletion		66.67%	100%	6 9	16 16	0	0	0	.		NA	NA	NA	NA	NA

### 3.6 Funktionelle Analysen

#### GO

Tabelle 6: Ergebnisse GO Analyse, top 20

Term	Count	Size	p-value	adj.P.Val
response to peptide hormone	3	401	2.94e-02	1e+00
response to peptide	3	448	3.88e-02	1e+00
response to abiotic stimulus	5	1153	4.06e-02	1e+00
negative regulation of intracellular signal transduction	3	468	4.12e-02	1e+00
cellular homeostasis	4	822	4.55e-02	1e+00
neutrophil activation involved in immune response	3	485	4.66e-02	1e+00
neutrophil degranulation	3	485	4.66e-02	1e+00
neutrophil activation	3	490	4.78e-02	1e+00
homeostatic process	6	1621	4.84e-02	1e+00
granulocyte activation	3	495	4.90e-02	1e+00
neutrophil mediated immunity	3	498	4.98e-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
Immune System	7	2002	4.34e-02	1e+00
Neutrophil degranulation	3	476	4.49e-02	1e+00

## 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: 127"
```

### 4.2 CNV Plots

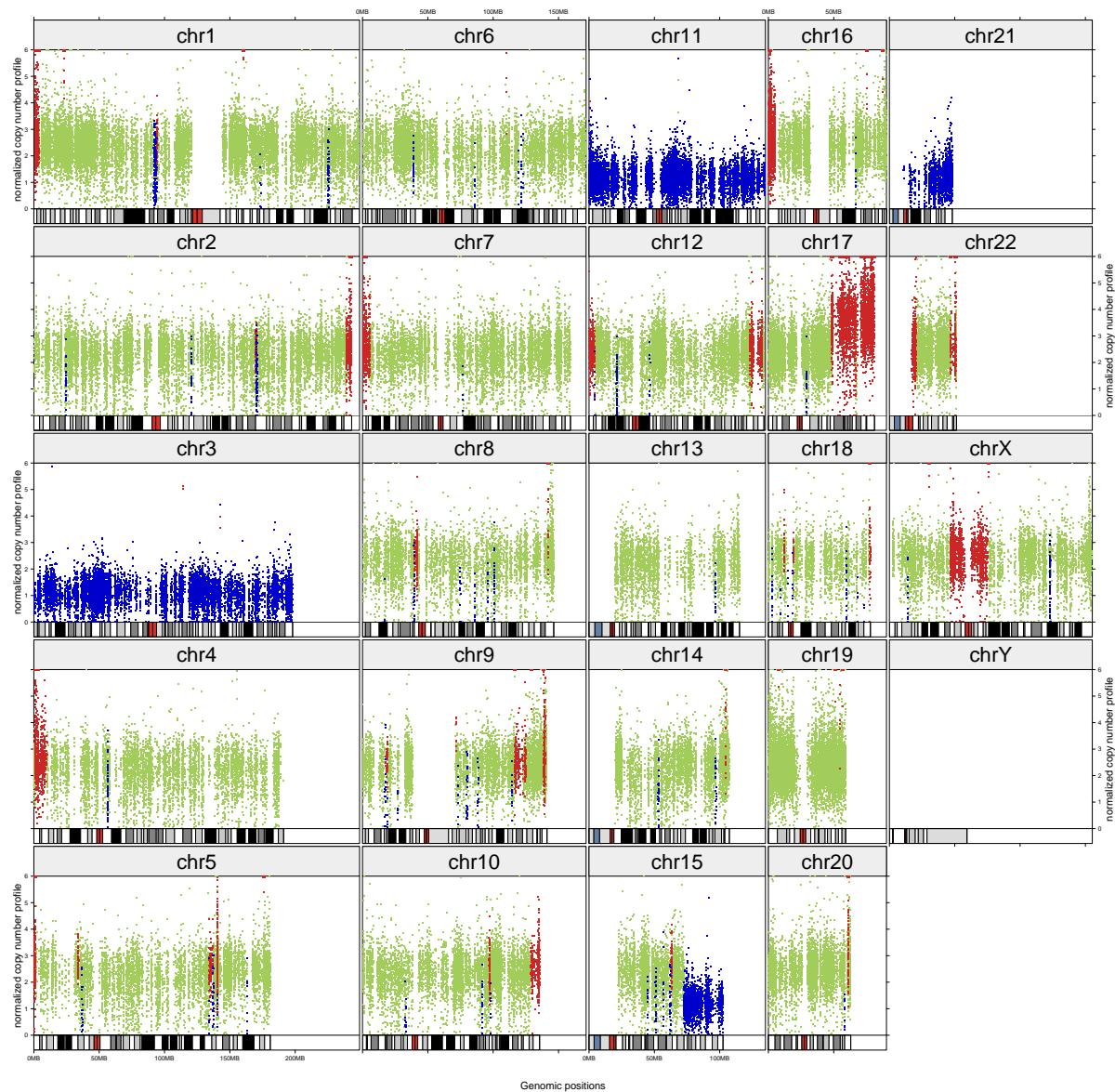


Abbildung 3: Copy Number Variation

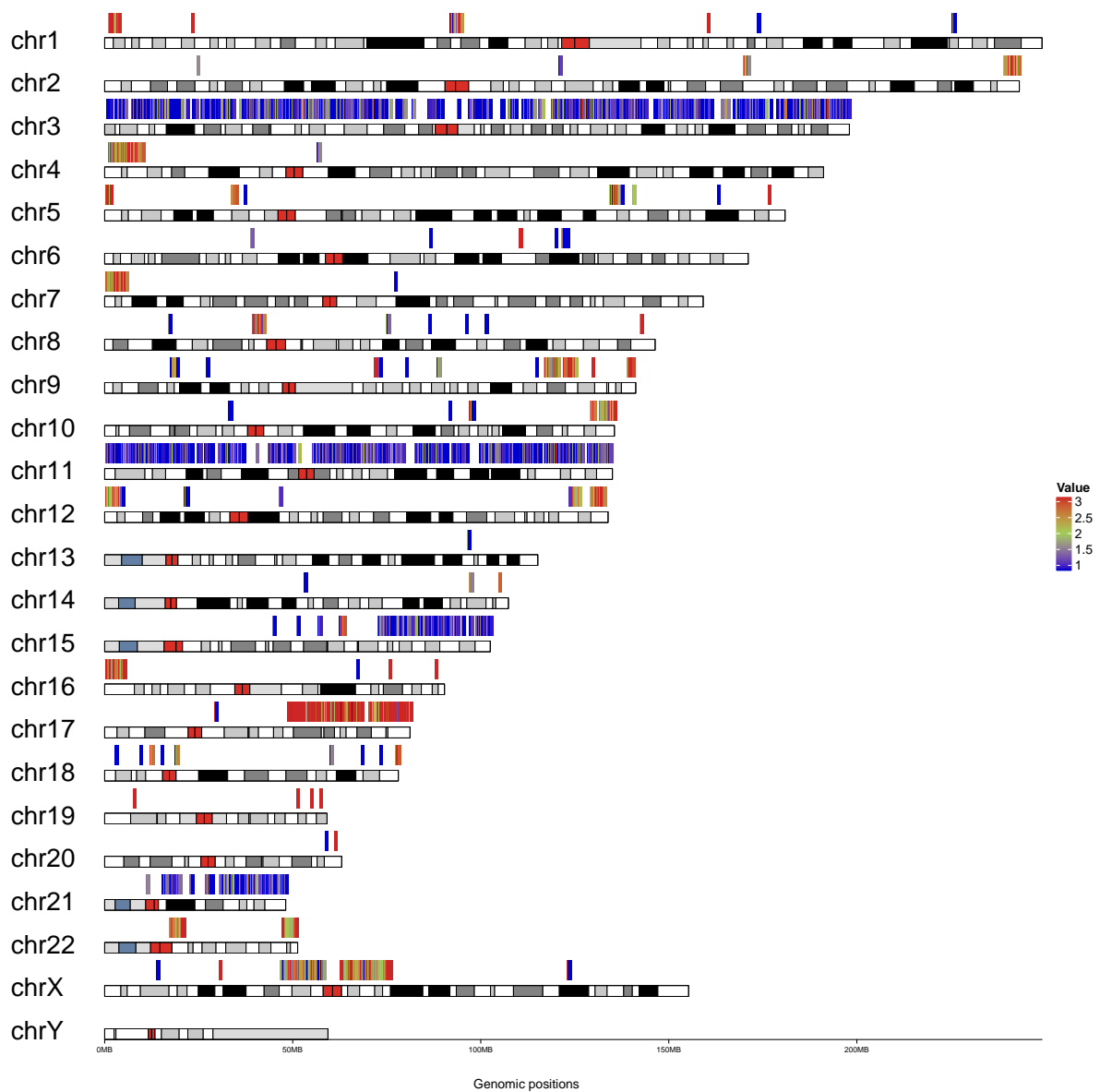


Abbildung 4: Copy Number Variation - Ideogram

### 4.3 Tumorsuppressoren

Tabelle 10: Tumorsuppressoren

chr	copy.number	status	TumorSuppressor
3	1	loss	MLH1,TGFBR2,VHL,BAP1,RYBP,SETD2,SHQ1,PBRM1
3	1	loss	ATR
5	3	gain	SDHA
11	1	loss	MEN1
11	1	loss	ATM,CBL,CHEK1,KMT2A,SDHD
15	1	loss	B2M
15	1	loss	BLM
16	3	gain	TSC2,AXIN1
16	3	gain	CREBBP
17	4	gain	RAD51C,AXIN2,SPOP,RNF43
21	1	loss	RUNX1
X	3	gain	RBM10,KDM5C,AMER1

#### 4.4 Onkogene

Tabelle 11: Onkogene

chr	copy.number	status	Oncogene
3	1	loss	RHOA,CTNNB1,MYD88,RAF1
3	1	loss	PIK3CB
3	1	loss	BCL6,PIK3CA,PRKCI
4	3	gain	FGFR3
5	3	gain	TERT
11	1	loss	HRAS
11	1	loss	IGF2
11	1	loss	RRAS2
11	1	loss	CCND1,FGF3,FGF4,FGF19,YAP1
12	3	gain	CCND2
15	1	loss	IDH2,IGF1R,NTRK3
17	4	gain	PPM1D
17	4	gain	RPTOR
21	1	loss	ERG
21	0	loss	ERG
21	1	loss	ERG,TMPRSS2,U2AF1
X	3	gain	AR,ARAF,MED12

## 4.5 Funktionelle Analyse der CNVs

### GAIN

Tabelle 12: Ergebnisse GO Analyse - GAIN, top 20

Term	Count	Size	p-value	adj.P.Val
embryonic skeletal system development	11	122	5.44e-04	1e+00
negative regulation of mast cell activation	3	12	3.76e-03	1e+00
exploration behavior	4	24	3.86e-03	1e+00
skeletal system morphogenesis	13	209	4.49e-03	1e+00
response to stimulus involved in regulation of muscle adaptation	3	16	7.32e-03	1e+00
JAK-STAT cascade involved in growth hormone signaling pathway	3	15	7.32e-03	1e+00
endocardial cushion morphogenesis	4	29	7.74e-03	1e+00
embryonic skeletal system morphogenesis	7	93	1.41e-02	1e+00
positive regulation of branching involved in ureteric bud morphogenesis	3	19	1.44e-02	1e+00
regulation of AMPA receptor activity	3	19	1.44e-02	1e+00
response to growth hormone	4	35	1.50e-02	1e+00
regulation of mast cell activation	4	38	1.81e-02	1e+00
motile cilium assembly	3	23	1.89e-02	1e+00
hydrogen peroxide catabolic process	3	22	2.15e-02	1e+00
growth hormone receptor signaling pathway	3	22	2.15e-02	1e+00
positive regulation of mesonephros development	3	22	2.15e-02	1e+00
endocardial cushion development	4	39	2.16e-02	1e+00
regulation of long-term neuronal synaptic plasticity	3	23	2.42e-02	1e+00
cartilage development involved in endochondral bone morphogenesis	3	23	2.42e-02	1e+00
cellular response to growth hormone stimulus	3	23	2.42e-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	174	426	1.29e-23	2.00e-19
sensory perception of smell	182	453	2.96e-23	2.29e-19
detection of chemical stimulus involved in sensory perception	179	470	2.09e-19	1.08e-15
detection of stimulus involved in sensory perception	189	520	2.90e-17	1.12e-13
detection of chemical stimulus	184	505	4.93e-17	1.53e-13
sensory perception of chemical stimulus	189	528	1.06e-16	2.74e-13
detection of stimulus	215	678	6.07e-11	1.34e-07
sensory perception	263	953	3.15e-06	6.10e-03
sodium-independent organic anion transport	15	25	4.40e-05	7.57e-02
urate transport	8	10	5.99e-05	9.28e-02
adenylate cyclase-inhibiting dopamine receptor signaling pathway	8	11	6.94e-04	9.78e-01
positive regulation of triglyceride catabolic process	6	8	2.81e-03	1.00e+00
behavioral response to cocaine	10	19	5.07e-03	1.00e+00
G-protein coupled purinergic nucleotide receptor signaling pathway	8	14	6.39e-03	1.00e+00

G-protein coupled purinergic receptor signaling pathway	11	23	8.35e-03	1.00e+00
axon choice point recognition	5	7	9.21e-03	1.00e+00
regulation of triglyceride catabolic process	7	12	9.32e-03	1.00e+00
negative regulation of cyclase activity	13	30	1.16e-02	1.00e+00
axon midline choice point recognition	4	5	1.18e-02	1.00e+00
regulation of basement membrane assembly involved in embryonic body morphogenesis	4	5	1.18e-02	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	3.41
AC3	defect DNA DSB repair hom. recomb.	21.09
AC4	tobacco mutagens, benzo(a)pyrene	13.63
AC6	defect DNA MMR, found in MSI tumors	3.65
AC12	unknown	4.55
AC13	APOBEC	1.27
AC15	defect DNA MMR	4.55
AC20	associated w. small indels at repeats	16.92
AC21	unknown	7.11
AC22	aristocholic acid	1.31
AC23	unknown	4.92
AC30	unknown	17.59

## 6 Versionsinfo

### 6.1 Genome

- UCSC hg19

### 6.2 Programmversionen

- FastQC: 0.11.5
- Trimmomatic: 0.38
- BWA: 0.7.17
- bam-readcount: 0.8.0
- samtools 1.9
- GATK: 3.8.1.0
- picard-tools: 2.18.15
- VarScan: 2.4.3
- annovar 2018-04-16
- bedtools: 2.27.1
- Control-FREEC: 11.0
- Java: 1.8.0\_152
- R: 3.4.1

### 6.3 Annovar Datenbanken

- refGene GRCh37
- esp6500siv2\_ea (ESP3500, European)
- avsnip150 (dbSNP)
- EU.sites.2015\_08 (1000Genome, European)
- cosmic86
- exac03 (ExAC)
- gnomad\_exome
- clinvar\_20180603
- intervar\_20180118



- dbnsfp35a
- cadd13