Amsterdam UMC
University Medical Centers

R2 Introduction Workshop Advanced

26-March-2024

Lieke Hoyng , on behalf of the R2 Team

Dept. CEMM | Location AMC

Amsterdam University Medical Centers (AUMC)

University of Amsterdam, the Netherlands

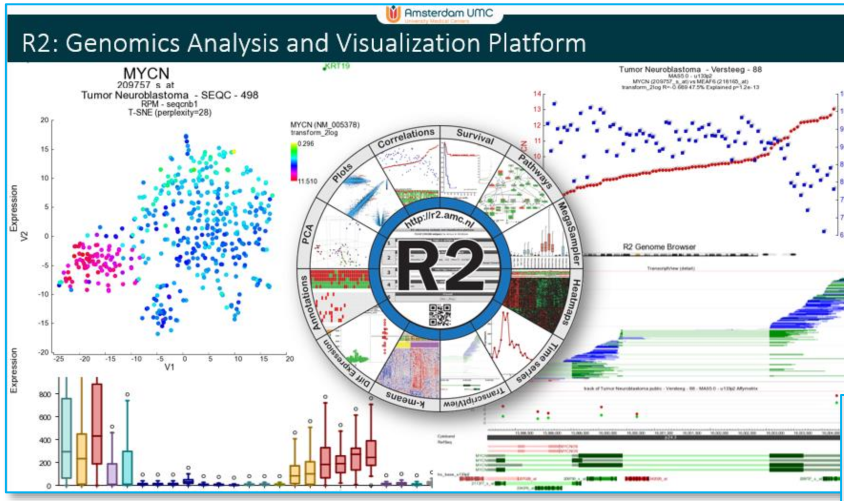
R2 Support: **r2-support@amsterdamumc.nl**

Jan Koster: **jankoster@amsterdamumc.nl**

r2platform.com

R2-Platform

Schedule (+/-)



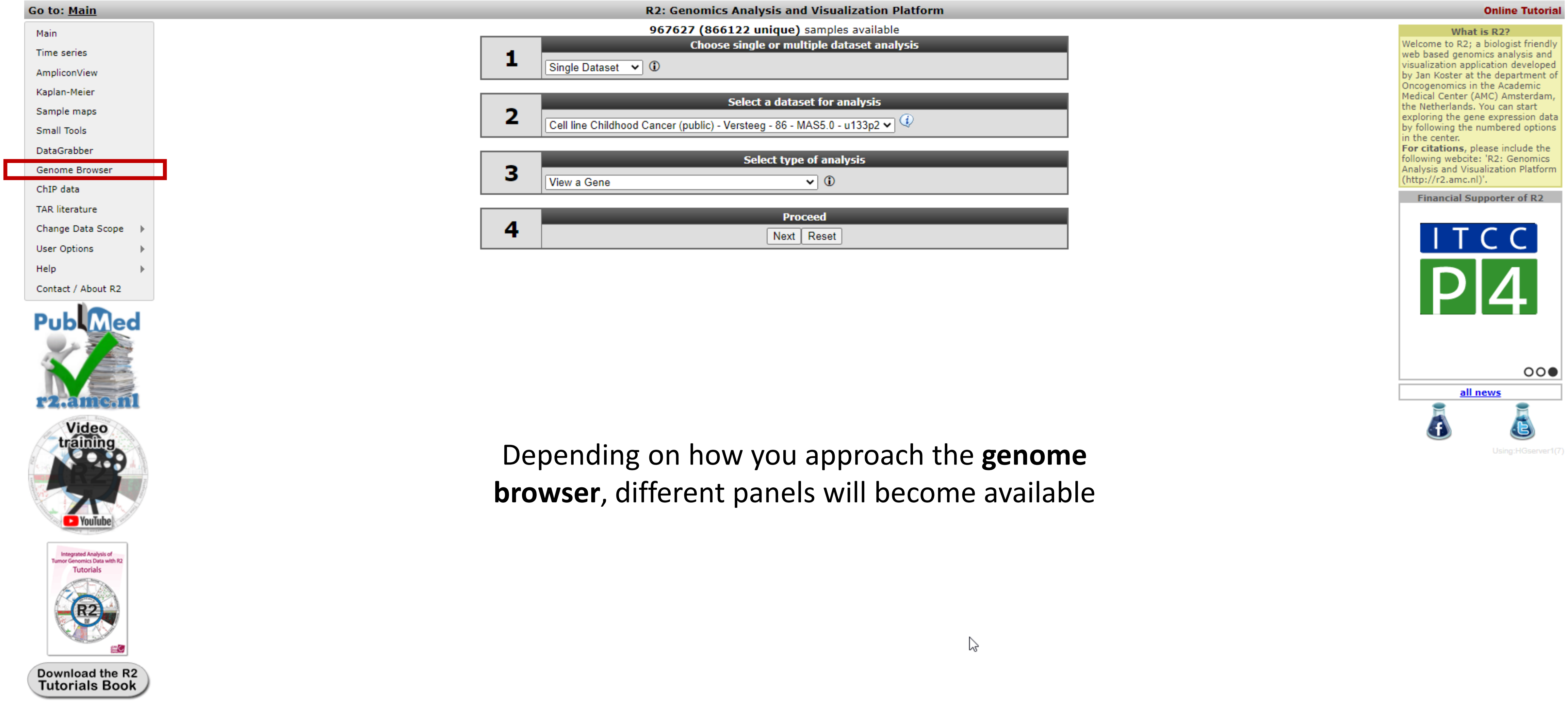
R2: Genomics Analysis and Visualization Platform

This morning

9:30 - 11:00 Presentation Data / Advanced
11:00 - 11:15 Tea / coffee
11:15 - 13:00 R2 play time | Jan visit

Genome Browser

Genome Browser



967627 (866122 unique) samples available

1 Choose single or multiple dataset analysis: Single Dataset

2 Select a dataset for analysis: Cell line Childhood Cancer (public) - Versteeg - 86 - MAS5.0 - u133p2

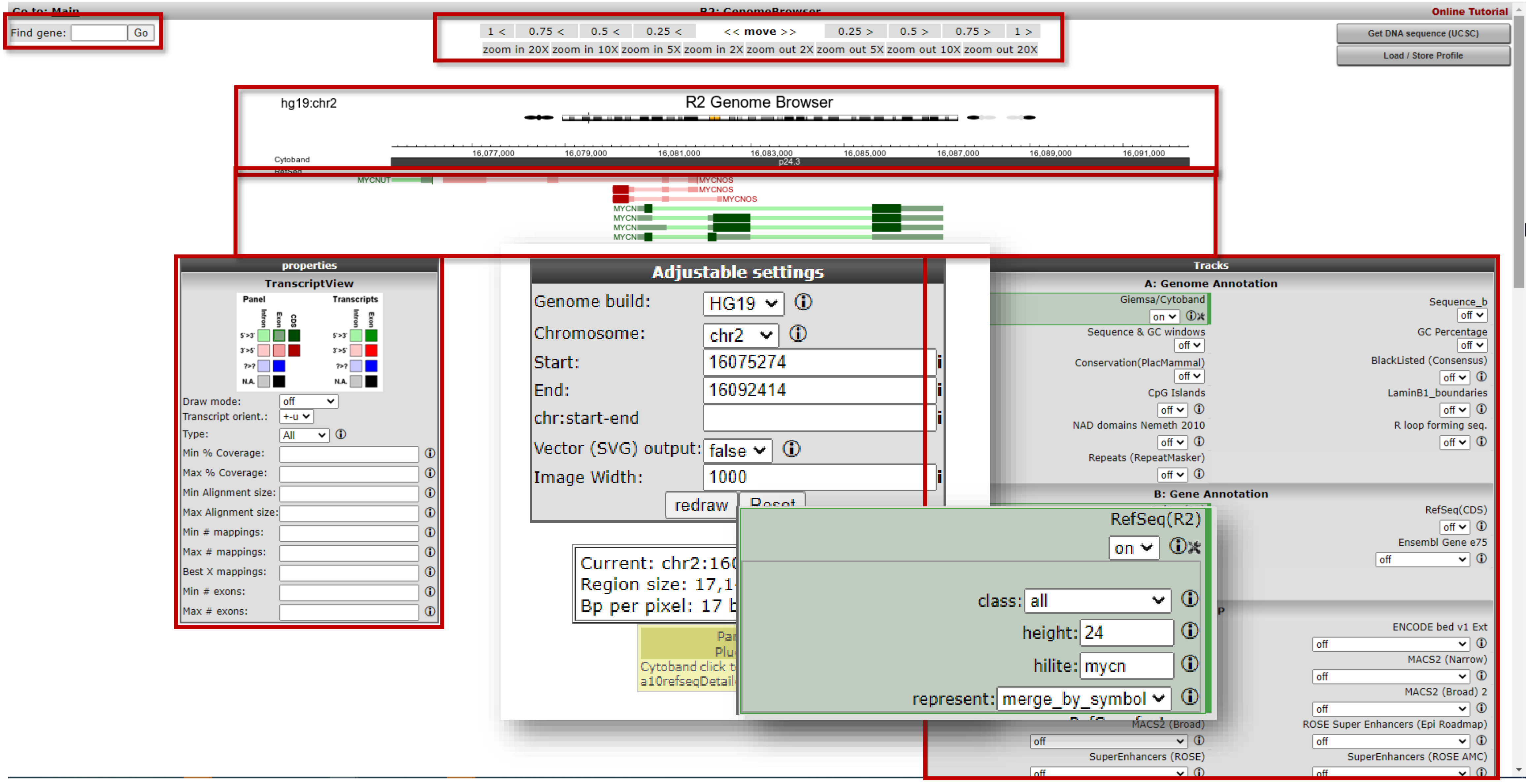
3 Select type of analysis: View a Gene

4 Proceed

What is R2?
Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam, the Netherlands. You can start exploring the gene expression data by following the numbered options in the center.
For citations, please include the following webcite: 'R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl)'.

Depending on how you approach the **genome browser**, different panels will become available

Genome Browser



Find gene:

Draw mode: off
Transcript orient.: +-u
Type: All
Min % Coverage:
Max % Coverage:
Min Alignment size:
Max Alignment size:
Min # mappings:
Max # mappings:
Best X mappings:
Min # exons:
Max # exons:

Genome build: HG19
Chromosome: chr2
Start: 16075274
End: 16092414
chr:start-end
Vector (SVG) output: false
Image Width: 1000

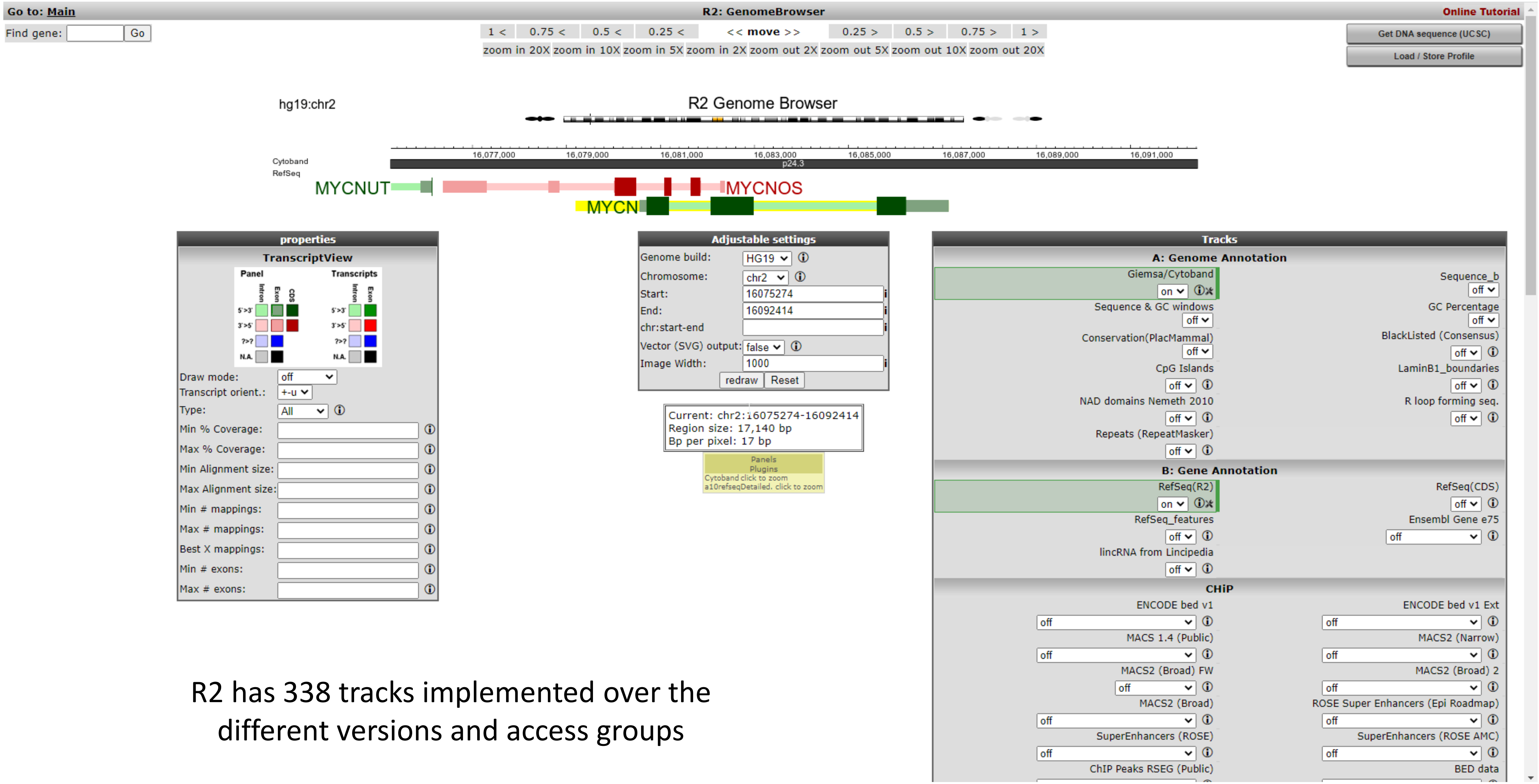
Current: chr2:160
Region size: 17,1
Bp per pixel: 17 b

Giemsa/Cytoband: on
Sequence_b: off
Sequence & GC windows: off
GC Percentage: off
Conservation(PlacMammal): off
BlackListed (Consensus): off
CpG Islands: off
LaminB1_boundaries: off
NAD domains Nemeth 2010: off
R loop forming seq.: off
Repeats (RepeatMasker): off

RefSeq(R2): on
class: all
height: 24
hilite: mycn
represent: merge_by_symbol

RefSeq(CDS): off
Ensembl Gene e75: off
ENCODE bed v1 Ext: off
MACS2 (Narrow): off
MACS2 (Broad) 2: off
MACS2 (Broad): off
ROSE Super Enhancers (Epi Roadmap): off
SuperEnhancers (ROSE): off
SuperEnhancers (ROSE AMC): off

Genome Browser



properties

TranscriptView

Draw mode: off
Transcript orient.: +-u
Type: All
Min % Coverage:
Max % Coverage:
Min Alignment size:
Max Alignment size:
Min # mappings:
Max # mappings:
Best X mappings:
Min # exons:
Max # exons:

Adjustable settings

Genome build: HG19
Chromosome: chr2
Start: 16075274
End: 16092414
chr:start-end
Vector (SVG) output: false
Image Width: 1000

Current: chr2:16075274-16092414
Region size: 17,140 bp
Bp per pixel: 17 bp

Tracks

A: Genome Annotation

Giemsa/Cytoband: on
Sequence_b: off
Sequence & GC windows: off
GC Percentage: off
Conservation(PlacMammal): off
BlackListed (Consensus): off
CpG Islands: off
LaminB1_boundaries: off
NAD domains Nemeth 2010: off
R loop forming seq.: off
Repeats (RepeatMasker): off

B: Gene Annotation

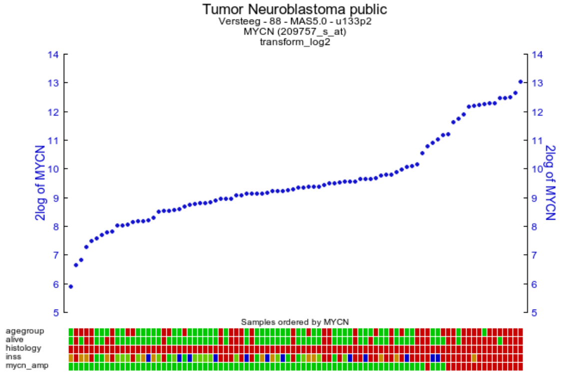
RefSeq(R2): on
RefSeq(CDS): off
RefSeq_features: off
Ensembl Gene e75: off
lincRNA from Lincipedia: off

ChIP

ENCODE bed v1: off
ENCODE bed v1 Ext: off
MACS 1.4 (Public): off
MACS2 (Narrow): off
MACS2 (Broad) FW: off
MACS2 (Broad) 2: off
MACS2 (Broad): off
ROSE Super Enhancers (Epi Roadmap): off
SuperEnhancers (ROSE): off
SuperEnhancers (ROSE AMC): off
ChIP Peaks RSEG (Public)
BED data

R2 has 338 tracks implemented over the different versions and access groups

Genome Browser from basic gene expression view

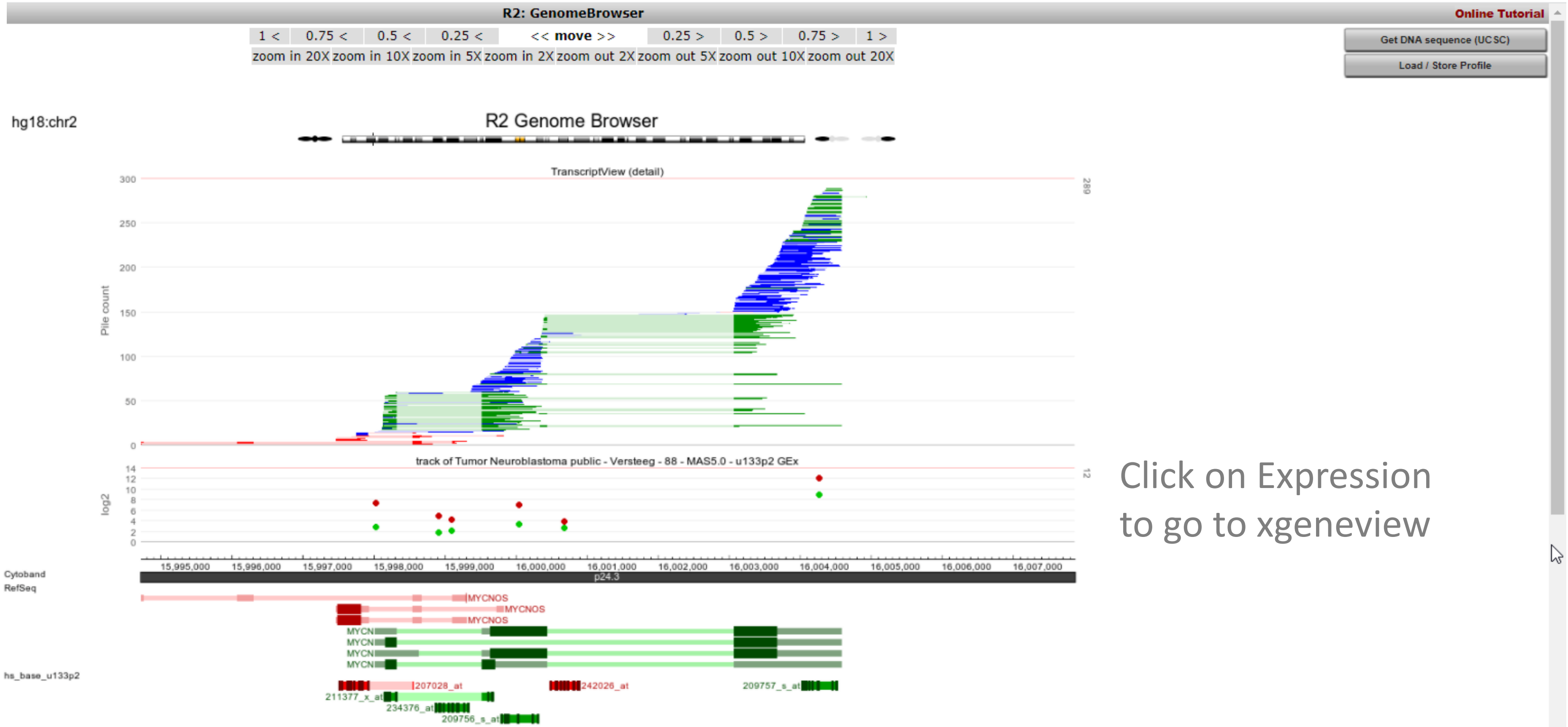


▼ **View additional details**

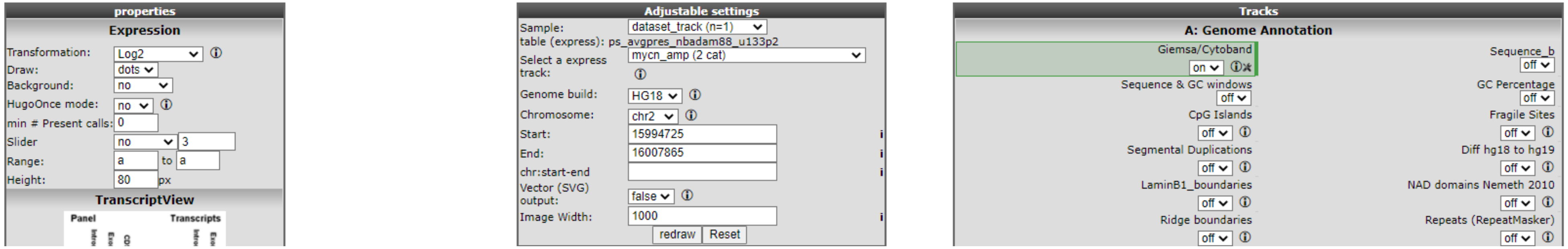
Alternative Reporters		
Symbol	**Number**	**Reporter**
MYCN view all	5	**209757_s_at** (avg 1369.7 in 88 samples) 209756_s_at (avg 235.6 in 14 samples) 211377_x_at (avg 158.8 in 5 samples) 234376_at (avg 71.7 in 3 samples) 242026_at (avg 22.8 in 5 samples)

ProbesetVerification (hg18)					
symbol	**probeset**	**rank**	**gene overlap**	**exon overlap**	**probes found**
MYCN	**209757_s_at**	GS	YES	YES	YES
MYCN	242026_at	WS	NO	NO	NO
MYCN	209756_s_at	3 GS	YES	YES	YES
MYCN	211377_x_at	4 GS	YES	YES	YES
MYCN	234376_at	5 GS	YES	YES	NO

Probeset Genome Location (hg18):					
reporter	**chrom**	**start**	**end**	**strand**	**link**
209757_s_at	chr2	16,004,019	16,004,525	1	TView



Click on Expression to go to xgeneview



properties

Expression

Transformation: Log2
Draw: dots
Background: no
HugoOnce mode: no
min # Present calls: 0
Slider: no 3
Range: a to a
Height: 80 px

TranscriptView

Adjustable settings

Sample: dataset_track (n=1)
table (express): ps_avgpres_nbadam88_u133p2
Select a express track: mycn_amp (2 cat)
Genome build: HG18
Chromosome: chr2
Start: 15994725
End: 16007865
chr:start-end:
Vector (SVG) output: false
Image Width: 1000

Tracks

A: Genome Annotation

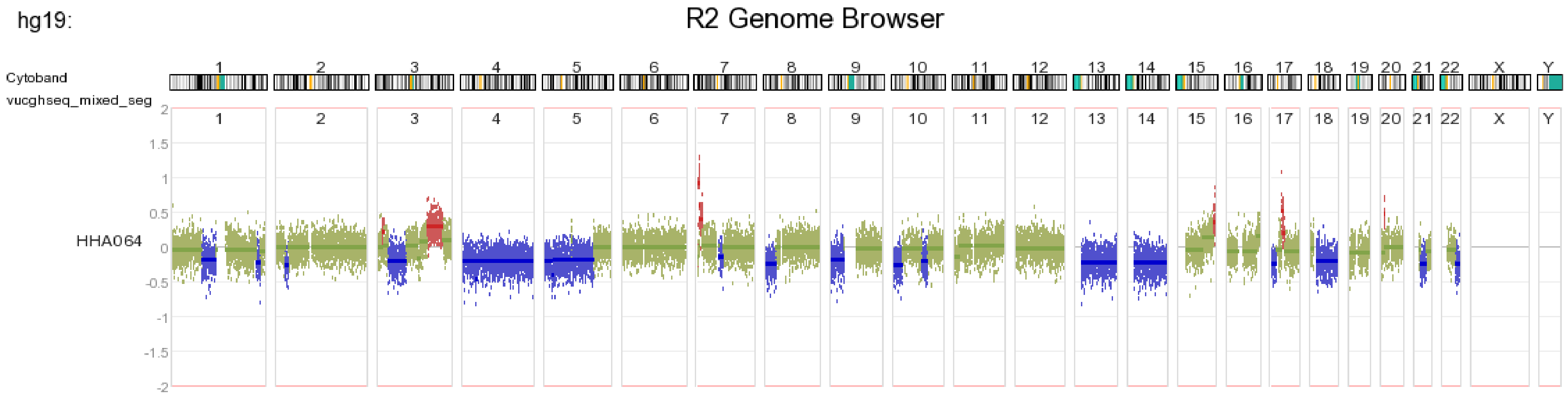
Giemsa/Cytoband: on
Sequence_b: off
Sequence & GC windows: off
GC Percentage: off
CpG Islands: off
Fragile Sites: off
Segmental Duplications: off
Diff hg18 to hg19: off
LaminB1_boundaries: off
NAD domains Nemeth 2010: off
Ridge boundaries: off
Repeats (RepeatMasker): off

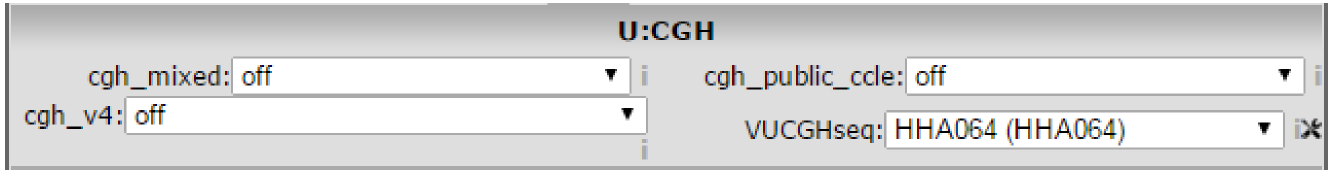
Other data types than mRNA

- Thus far mostly looked at mRNA
    - Similar functionalities for the other datatypes
        - aCGH / SNP / miRNA / methylation / drug response / mutation
        - Some with specific extentions/views

aCGH / aCGH-like

- Visualization of aCGH(-like) data in the embedded genome browser of R2
    - aCGH, NGS coverage based (Whole Genome or QDNAseq)




U:CGH

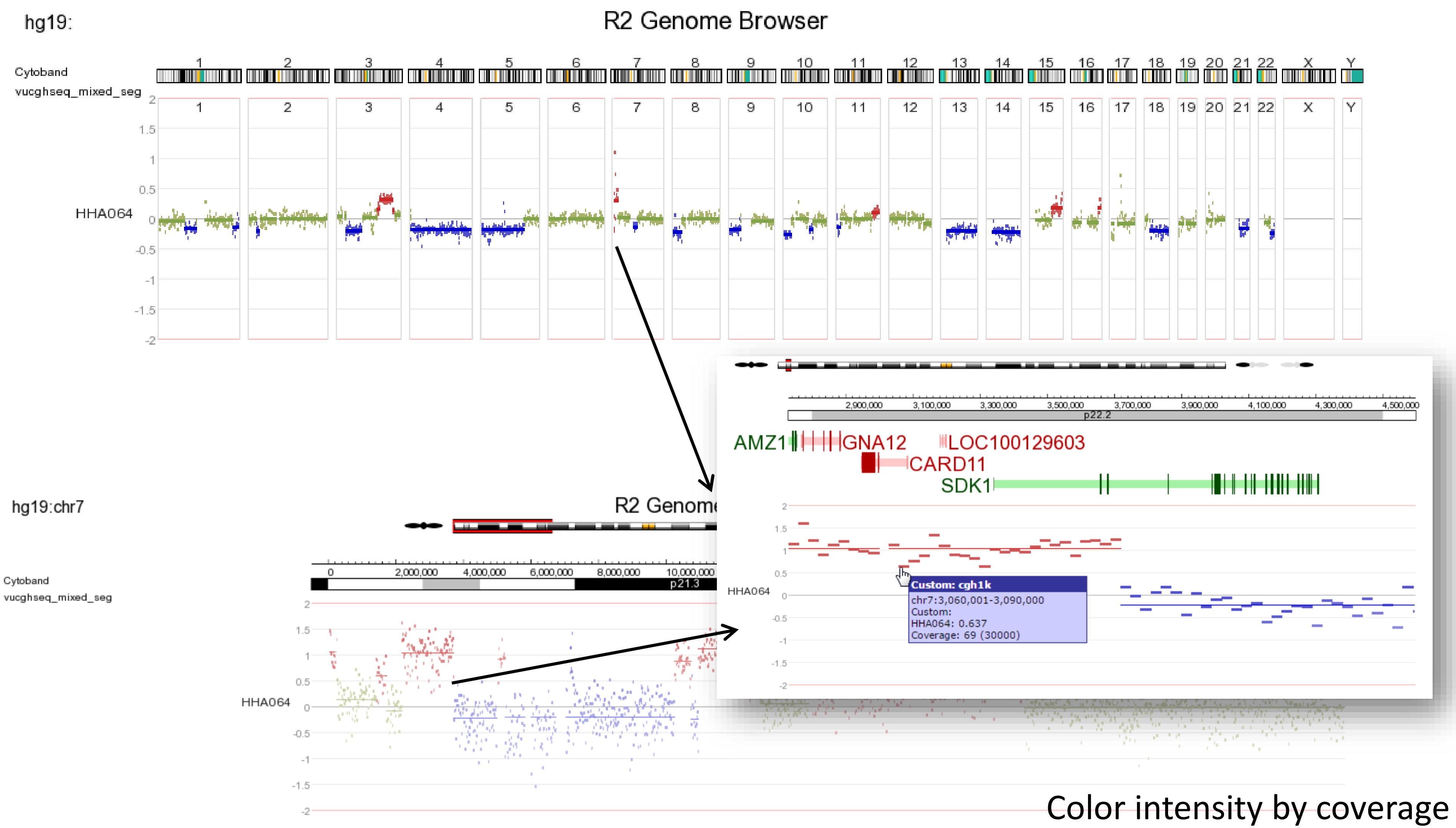
cgh_mixed: off

cgh_public_ccle: off

cgh_v4: off

VUCGHseq: HHA064 (HHA064)

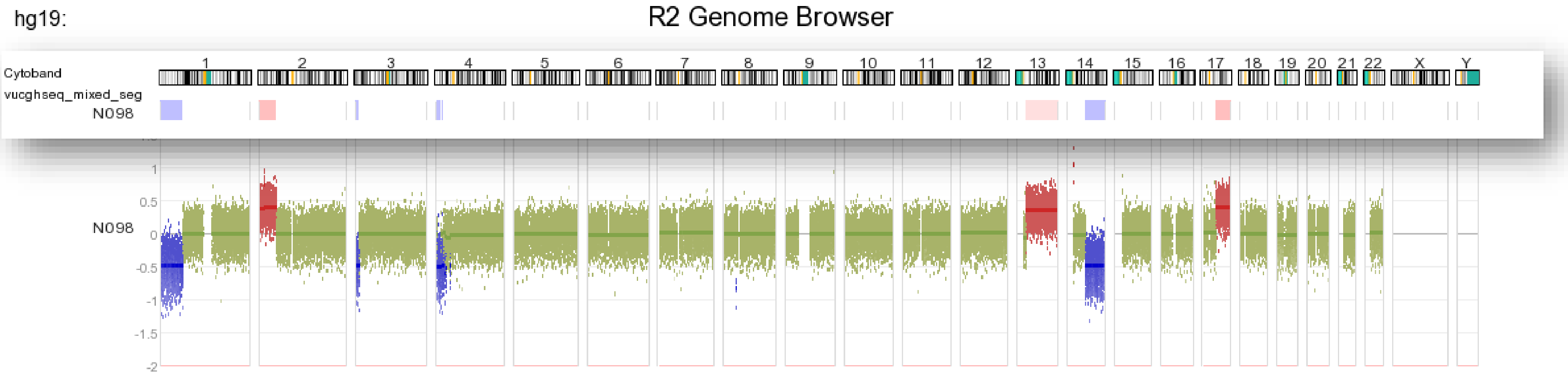
aCGH / aCGH-like

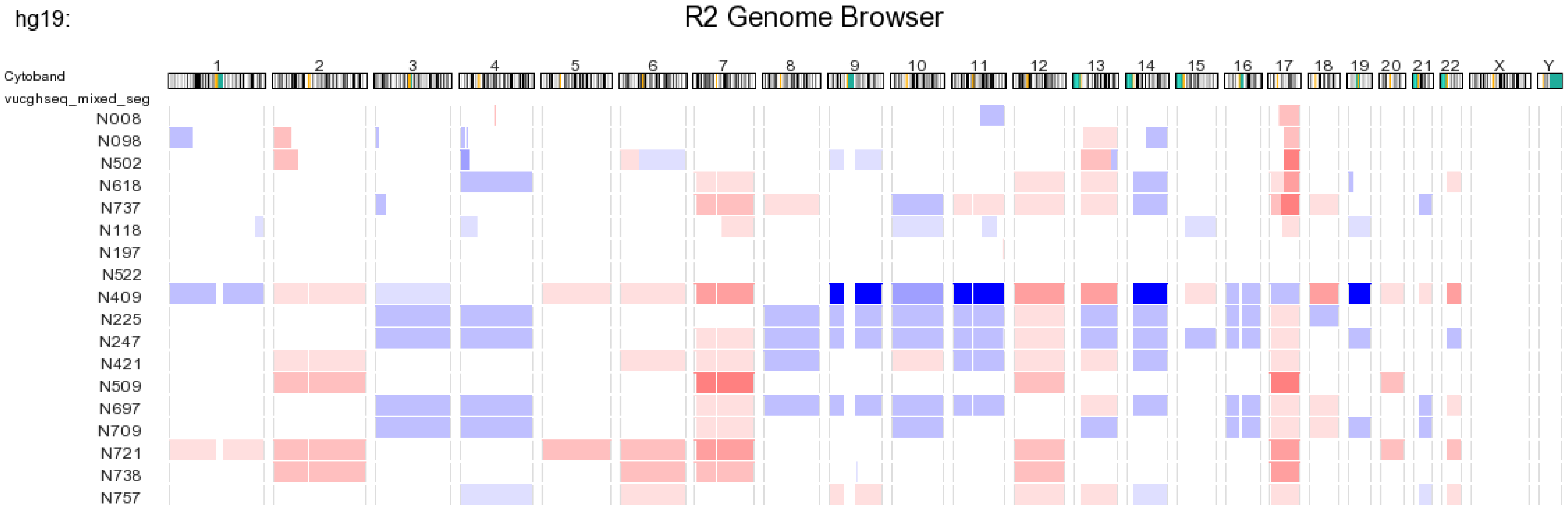


Custom: cgh1k
chr7:3,060,001-3,090,000
Custom:
HHA064: 0.637
Coverage: 69 (30000)

Color intensity by coverage

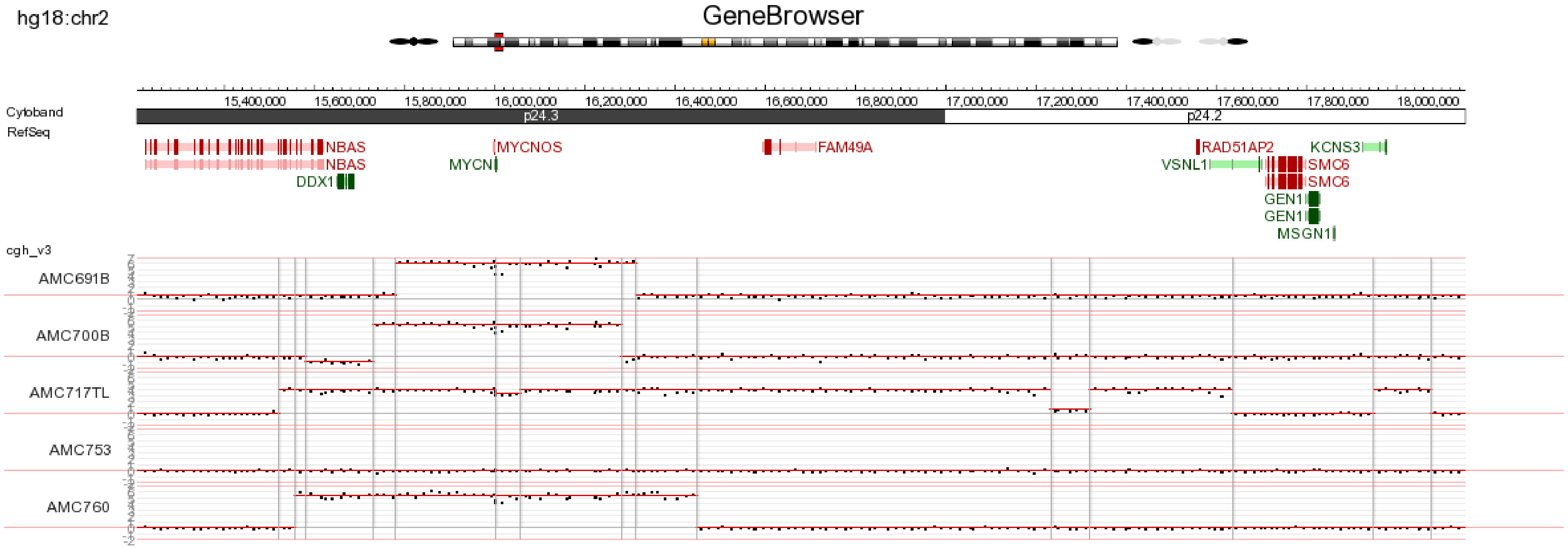
aCGH / aCGH-like cohort





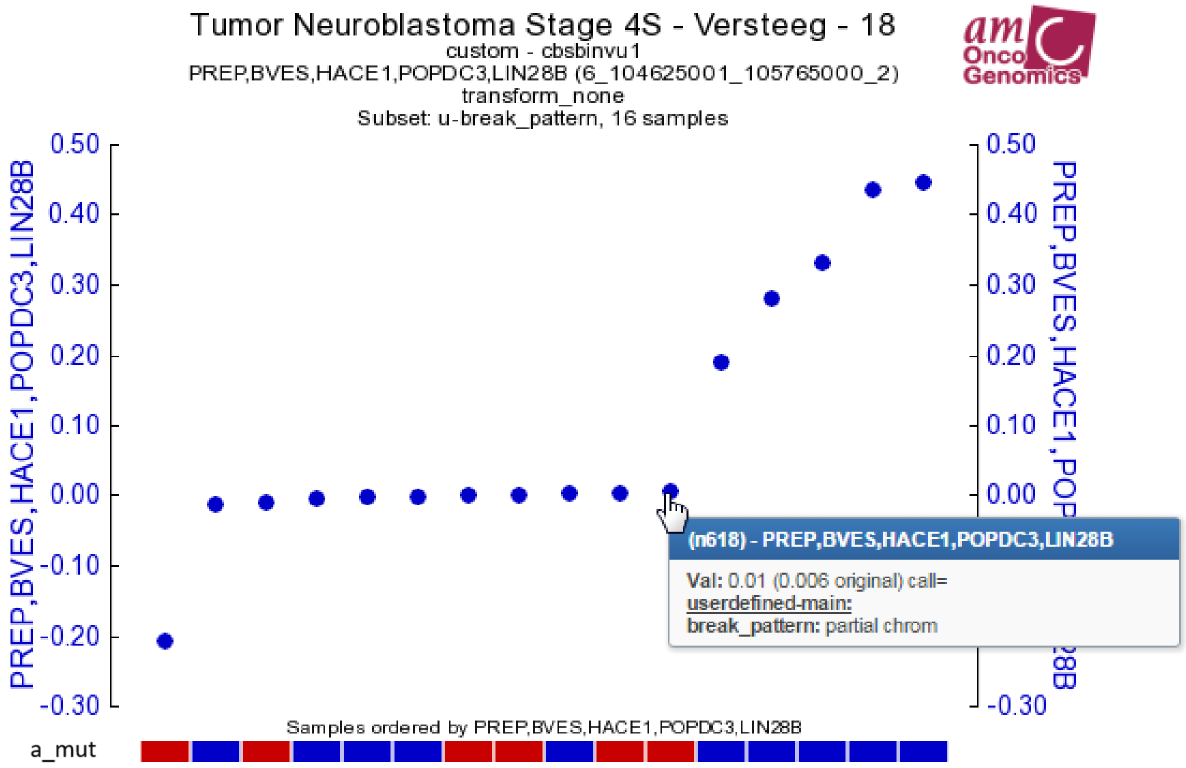
aCGH / aCGH-like cohort dataset

- Efficient CBSbin datasets
    - Circular Binary Segmentation on raw reporter values
    - Extend segments to meet halfway
    - Superimpose (SI) all segments within a cohort
    - Annotate SI segments by overlap with gene bodies



CGH patterns as dataset

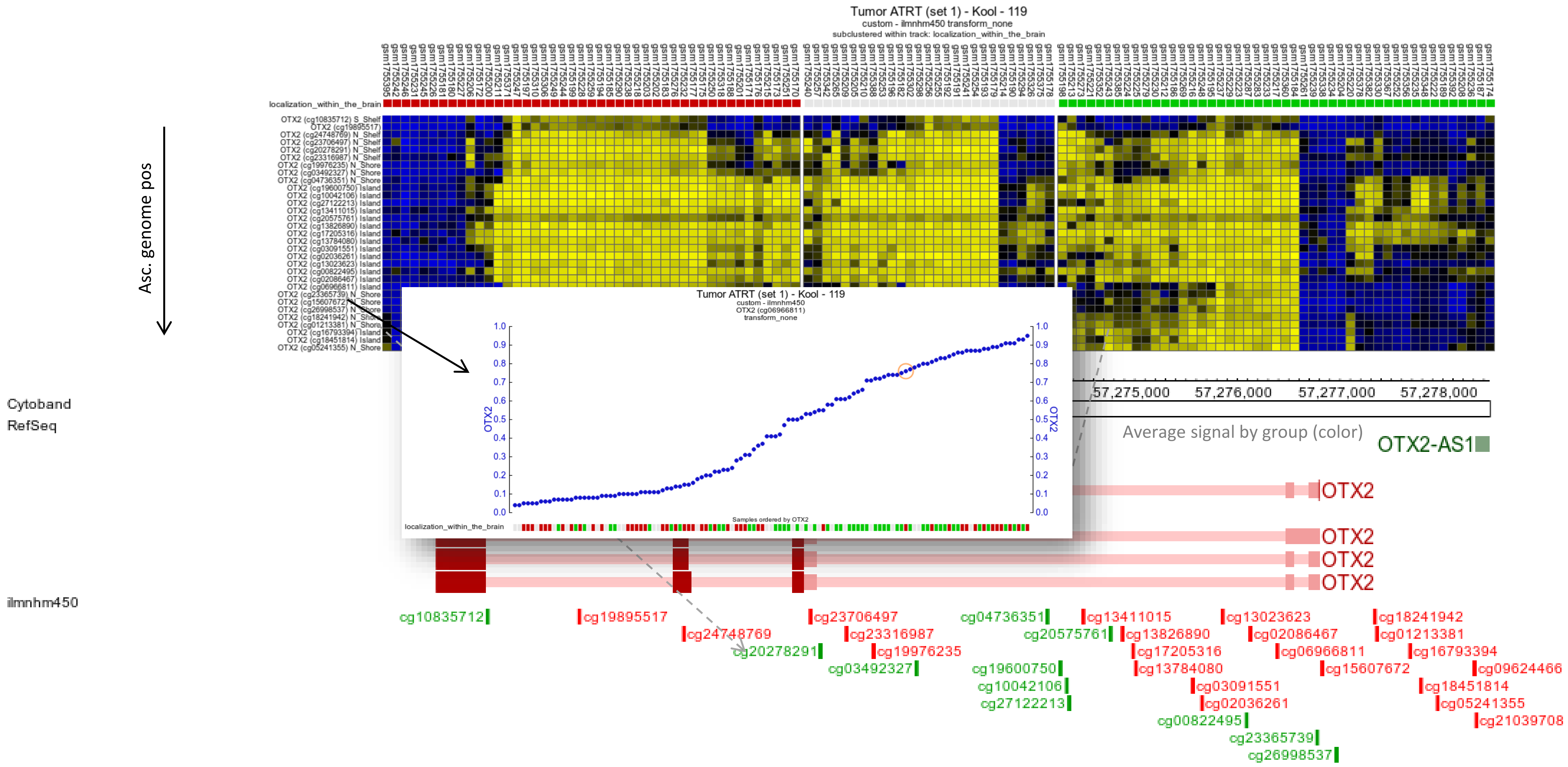
- 30k profiles



(n618) - PREP,BVES,HACE1,POPDC3,LIN28B

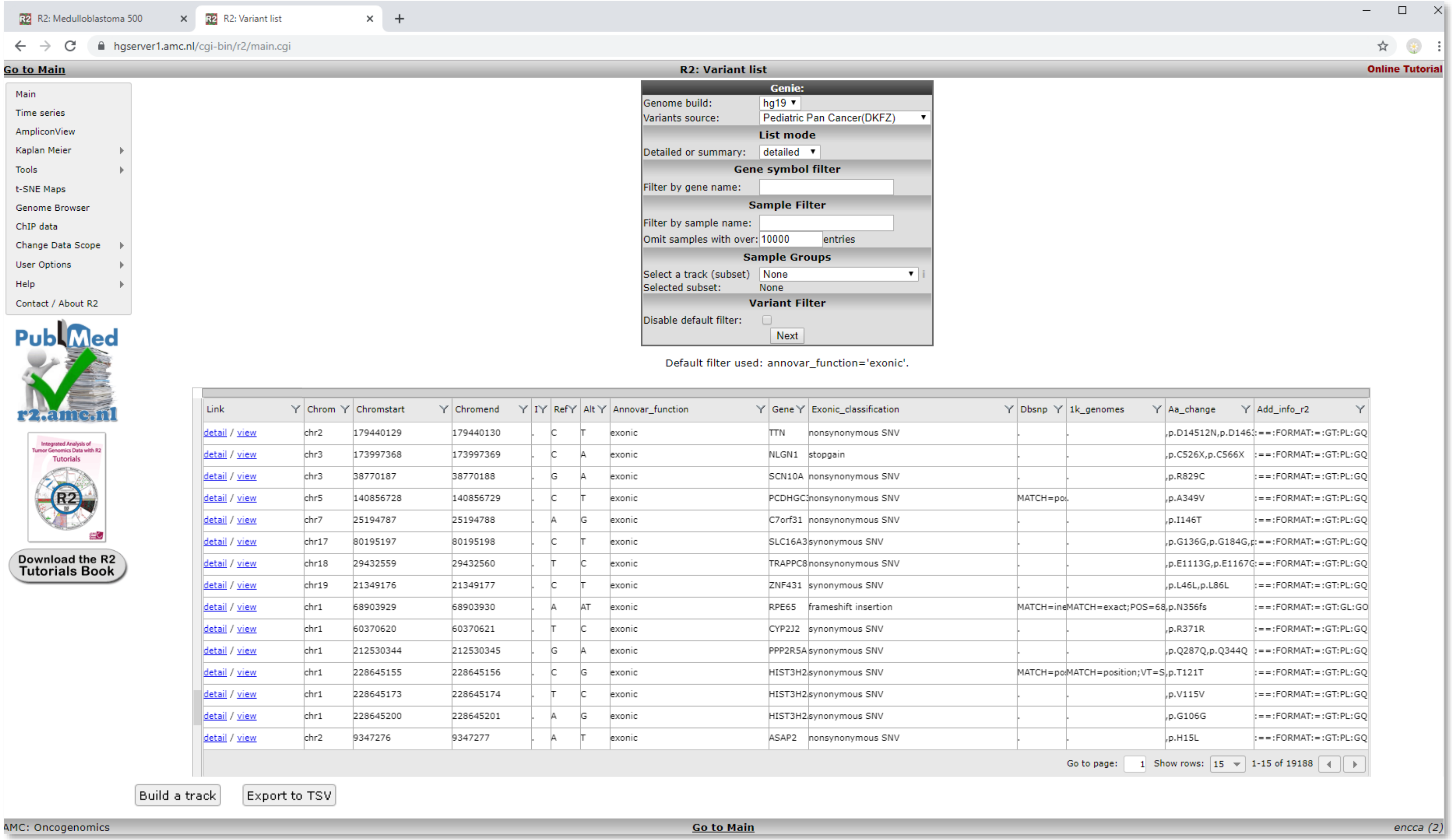
Val: 0.01 (0.006 original) call=
userdefined-main:
break_pattern: partial chrom

Methylation data


Asc. genome pos

Average signal by group (color)

Somatic mutation data



R2: Variant list

Genie:

Genome build: hg19
Variants source: Pediatric Pan Cancer(DKFZ)

List mode

Detailed or summary: detailed

Gene symbol filter

Filter by gene name:

Sample Filter

Filter by sample name:
Omit samples with over: 10000 entries

Sample Groups

Select a track (subset) None
Selected subset: None

Variant Filter

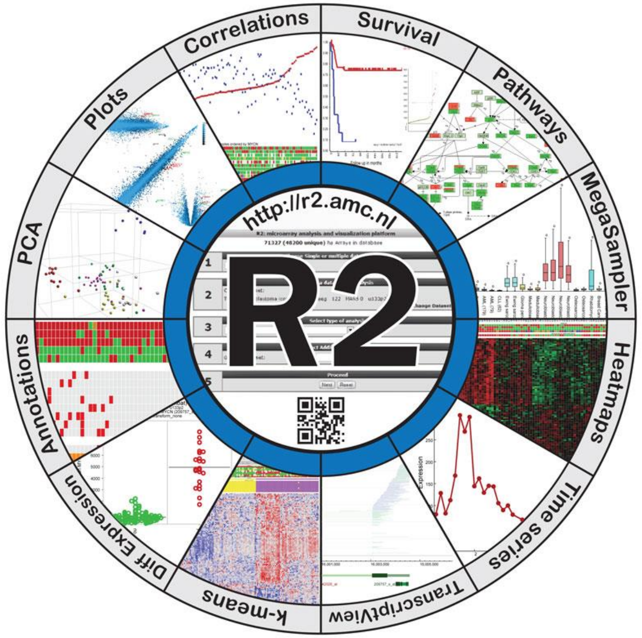
Disable default filter: ☐

Default filter used: annovar_function='exonic'.

Link	Chrom	Chromstart	Chromend	I	Ref	Alt	Annovar_function	Gene	Exonic_classification	Dbsnp	1k_genomes	Aa_change	Add_info_r2
detail / view	chr2	179440129	179440130	.	C	T	exonic	TTN	nonsynonymous SNV	.	.	,p.D14512N,p.D146	:==:FORMAT:=:GT:PL:GQ
detail / view	chr3	173997368	173997369	.	C	A	exonic	NLGN1	stopgain	.	.	,p.C526X,p.C566X	:==:FORMAT:=:GT:PL:GQ
detail / view	chr3	38770187	38770188	.	G	A	exonic	SCN10A	nonsynonymous SNV	.	.	,p.R829C	:==:FORMAT:=:GT:PL:GQ
detail / view	chr5	140856728	140856729	.	C	T	exonic	PCDHGC	nonsynonymous SNV	MATCH=po	.	,p.A349V	:==:FORMAT:=:GT:PL:GQ
detail / view	chr7	25194787	25194788	.	A	G	exonic	C7orf31	nonsynonymous SNV	.	.	,p.I146T	:==:FORMAT:=:GT:PL:GQ
detail / view	chr17	80195197	80195198	.	C	T	exonic	SLC16A3	synonymous SNV	.	.	,p.G136G,p.G184G,p	:==:FORMAT:=:GT:PL:GQ
detail / view	chr18	29432559	29432560	.	T	C	exonic	TRAPPC8	nonsynonymous SNV	.	.	,p.E1113G,p.E1167G	:==:FORMAT:=:GT:PL:GQ
detail / view	chr19	21349176	21349177	.	C	T	exonic	ZNF431	synonymous SNV	.	.	,p.L46L,p.L86L	:==:FORMAT:=:GT:PL:GQ
detail / view	chr1	68903929	68903930	.	A	AT	exonic	RPE65	frameshift insertion	MATCH=ine	MATCH=exact;POS=68	,p.N356fs	:==:FORMAT:=:GT:GL:GO
detail / view	chr1	60370620	60370621	.	T	C	exonic	CYP2J2	synonymous SNV	.	.	,p.R371R	:==:FORMAT:=:GT:PL:GQ
detail / view	chr1	212530344	212530345	.	G	A	exonic	PPP2R5A	synonymous SNV	.	.	,p.Q287Q,p.Q344Q	:==:FORMAT:=:GT:PL:GQ
detail / view	chr1	228645155	228645156	.	C	G	exonic	HIST3H2	synonymous SNV	MATCH=po	MATCH=position;VT=S	,p.T121T	:==:FORMAT:=:GT:PL:GQ
detail / view	chr1	228645173	228645174	.	T	C	exonic	HIST3H2	synonymous SNV	.	.	,p.V115V	:==:FORMAT:=:GT:PL:GQ
detail / view	chr1	228645200	228645201	.	A	G	exonic	HIST3H2	synonymous SNV	.	.	,p.G106G	:==:FORMAT:=:GT:PL:GQ
detail / view	chr2	9347276	9347277	.	A	T	exonic	ASAP2	nonsynonymous SNV	.	.	,p.H15L	:==:FORMAT:=:GT:PL:GQ

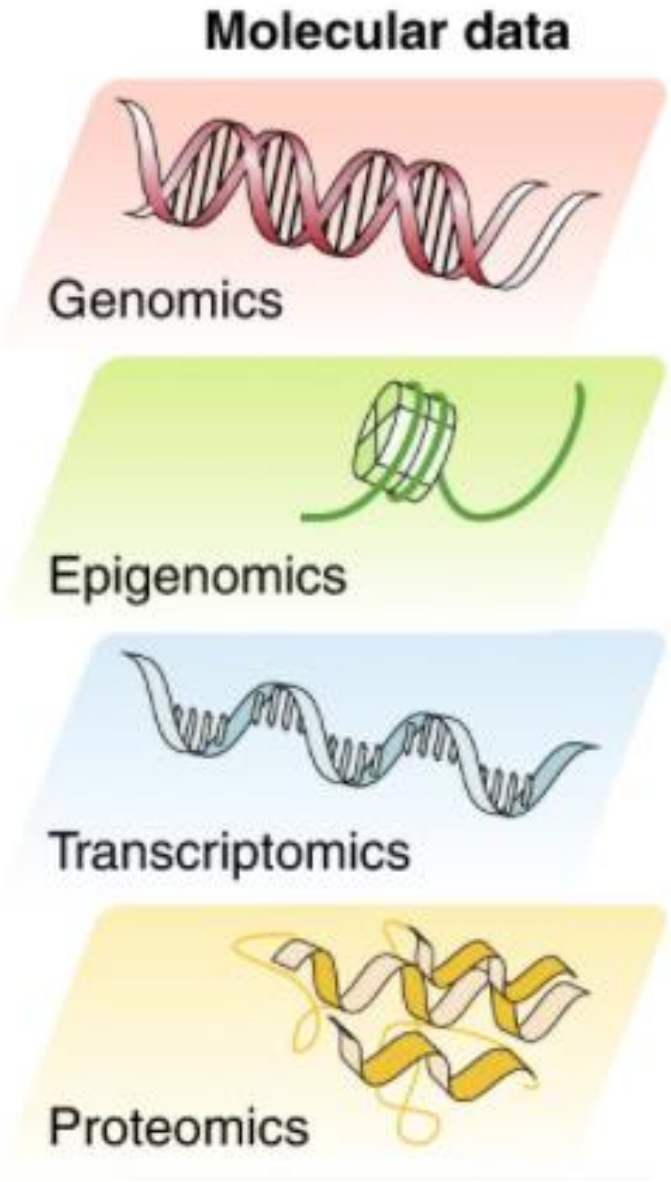
Go to page: 1 Show rows: 15 1-15 of 19188

Integrative Analyses

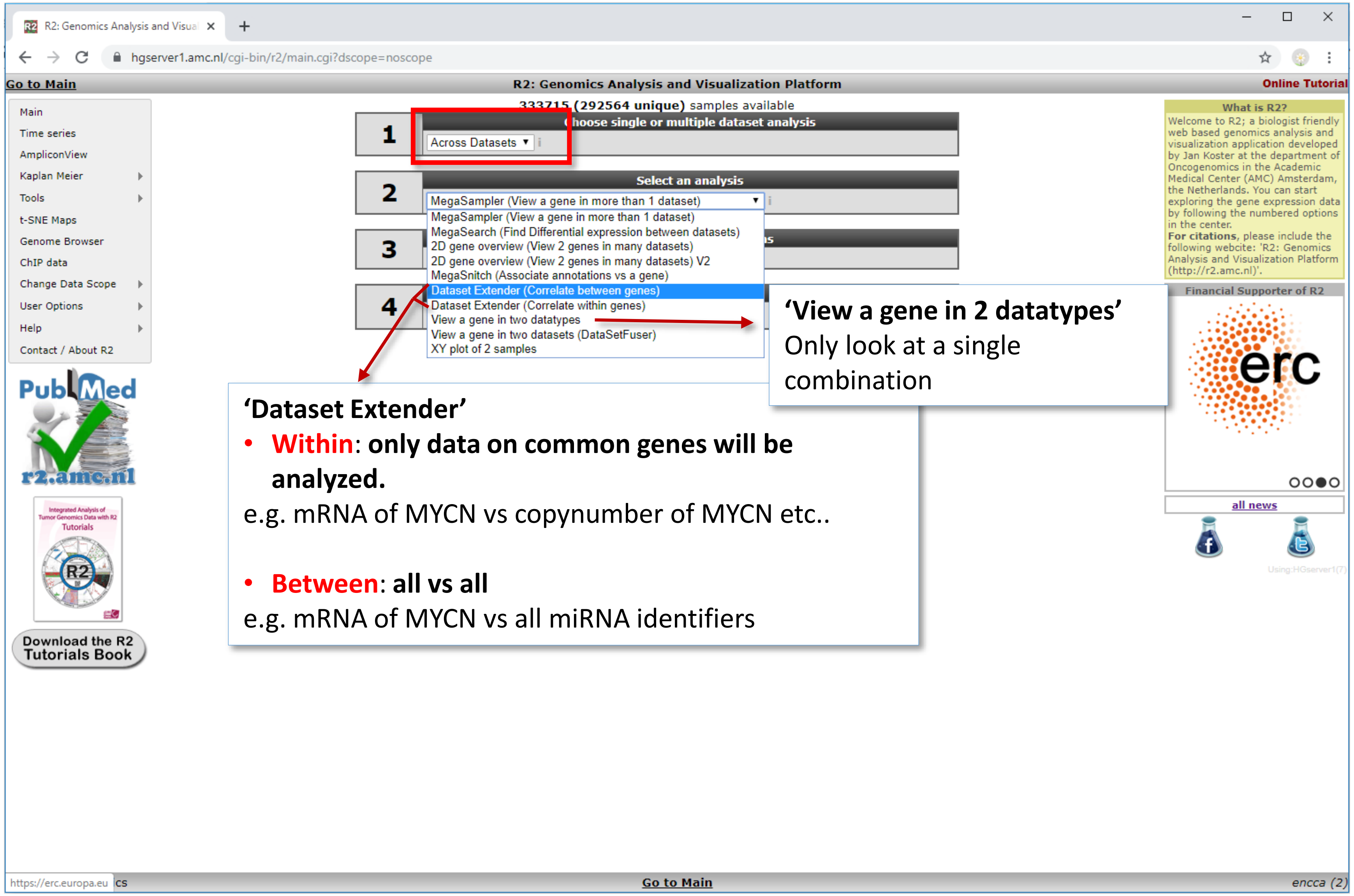


Integrative analyses

- Multiple types of measurement on the same samples
- R2 can perform analyses on the basis of overlapping sample names in 2 different data types
  - E.g. mRNA vs miRNA
- 'Across datasets' option from R2 perspective
- R2 will automatically determine the intersection of overlapping samples



Dataset Extender (2 types)



R2: Genomics Analysis and Visualization Platform

333715 (292564 unique) samples available

1 Choose single or multiple dataset analysis: Across Datasets

2 Select an analysis: MegaSampler (View a gene in more than 1 dataset)

- MegaSampler (View a gene in more than 1 dataset)
- MegaSearch (Find Differential expression between datasets)
- 2D gene overview (View 2 genes in many datasets)
- 2D gene overview (View 2 genes in many datasets) V2
- MegaSnitch (Associate annotations vs a gene)
- Dataset Extender (Correlate between genes)
- Dataset Extender (Correlate within genes)
- View a gene in two datatypes
- View a gene in two datasets (DataSetFuser)
- XY plot of 2 samples

What is R2?

Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam, the Netherlands. You can start exploring the gene expression data by following the numbered options in the center.
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'View a gene in 2 datatypes'
Only look at a single combination

'Dataset Extender'

- **Within: only data on common genes will be analyzed.**

e.g. mRNA of MYCN vs copynumber of MYCN etc..

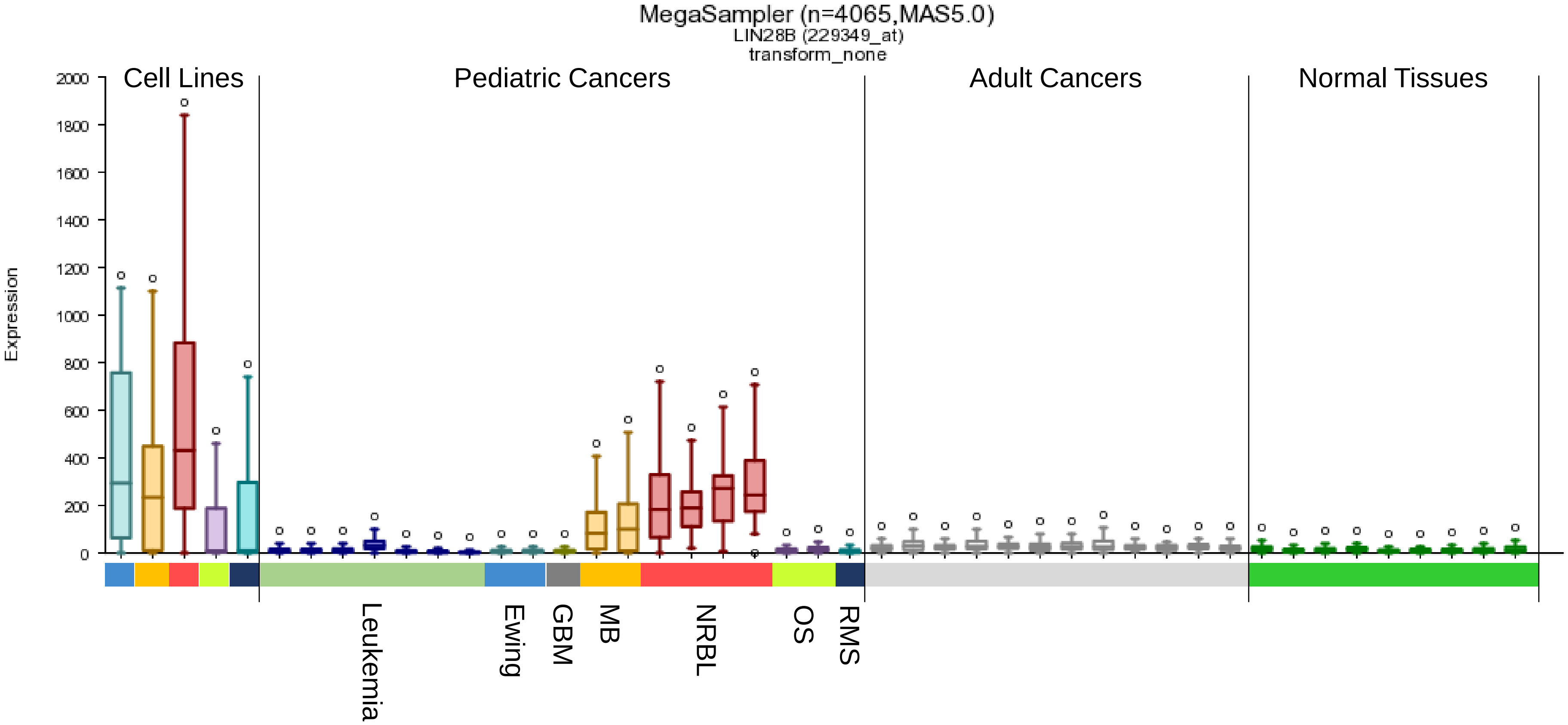
- **Between: all vs all**

e.g. mRNA of MYCN vs all miRNA identifiers

R2-support@amsterdamumc.nl

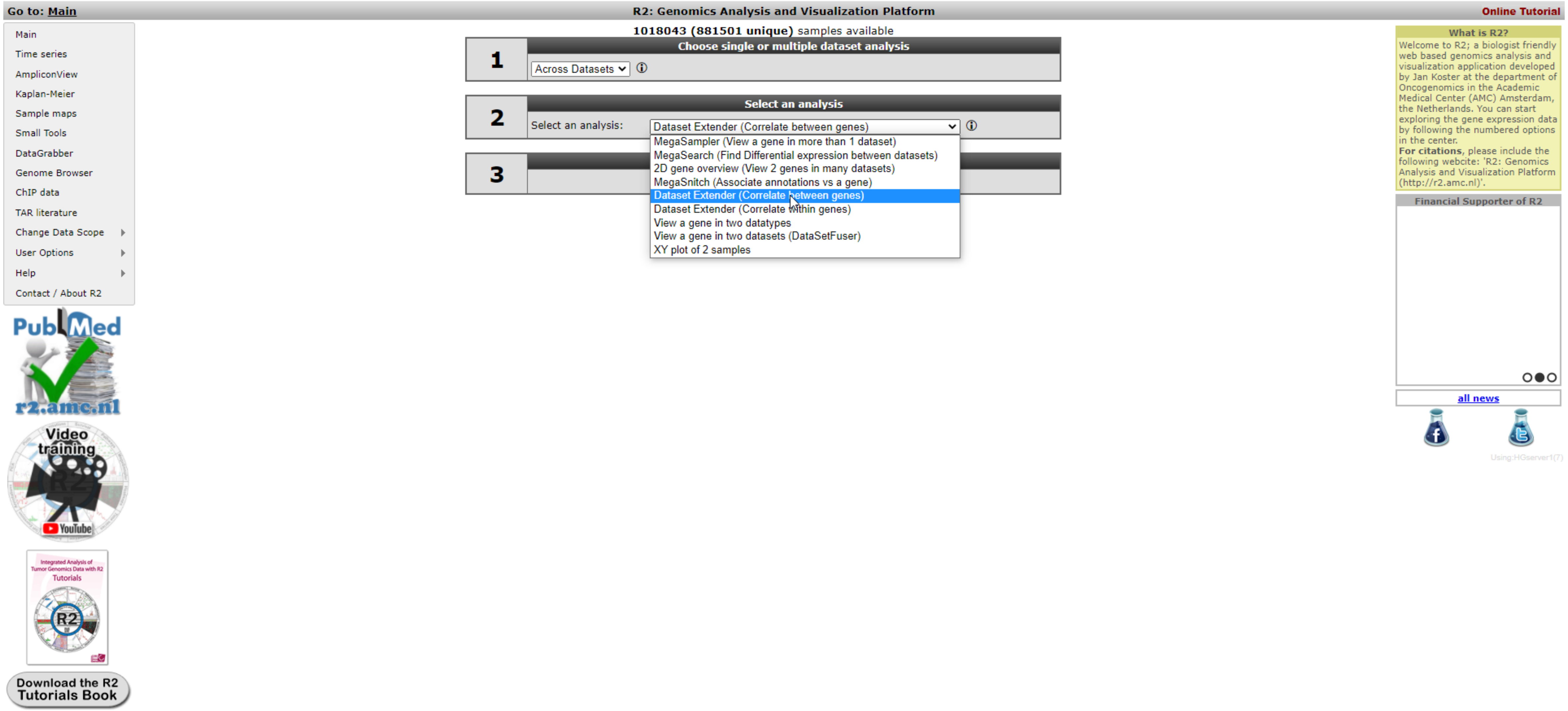
mRNA vs miRNA

- Assess, which miRNAs are correlated with LIN28B mRNA expression



Molenaar et al, Nat Genet, 2012

mRNA vs miRNA



Go to: Main

R2: Genomics Analysis and Visualization Platform

Online Tutorial

- Main
- Time series
- AmpliconView
- Kaplan-Meier
- Sample maps
- Small Tools
- DataGrabber
- Genome Browser
- ChIP data
- TAR literature
- Change Data Scope
- User Options
- Help
- Contact / About R2

1018043 (881501 unique) samples available

1 Choose single or multiple dataset analysis

Across Datasets

2 Select an analysis

Select an analysis: Dataset Extender (Correlate between genes)

- MegaSampler (View a gene in more than 1 dataset)
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3

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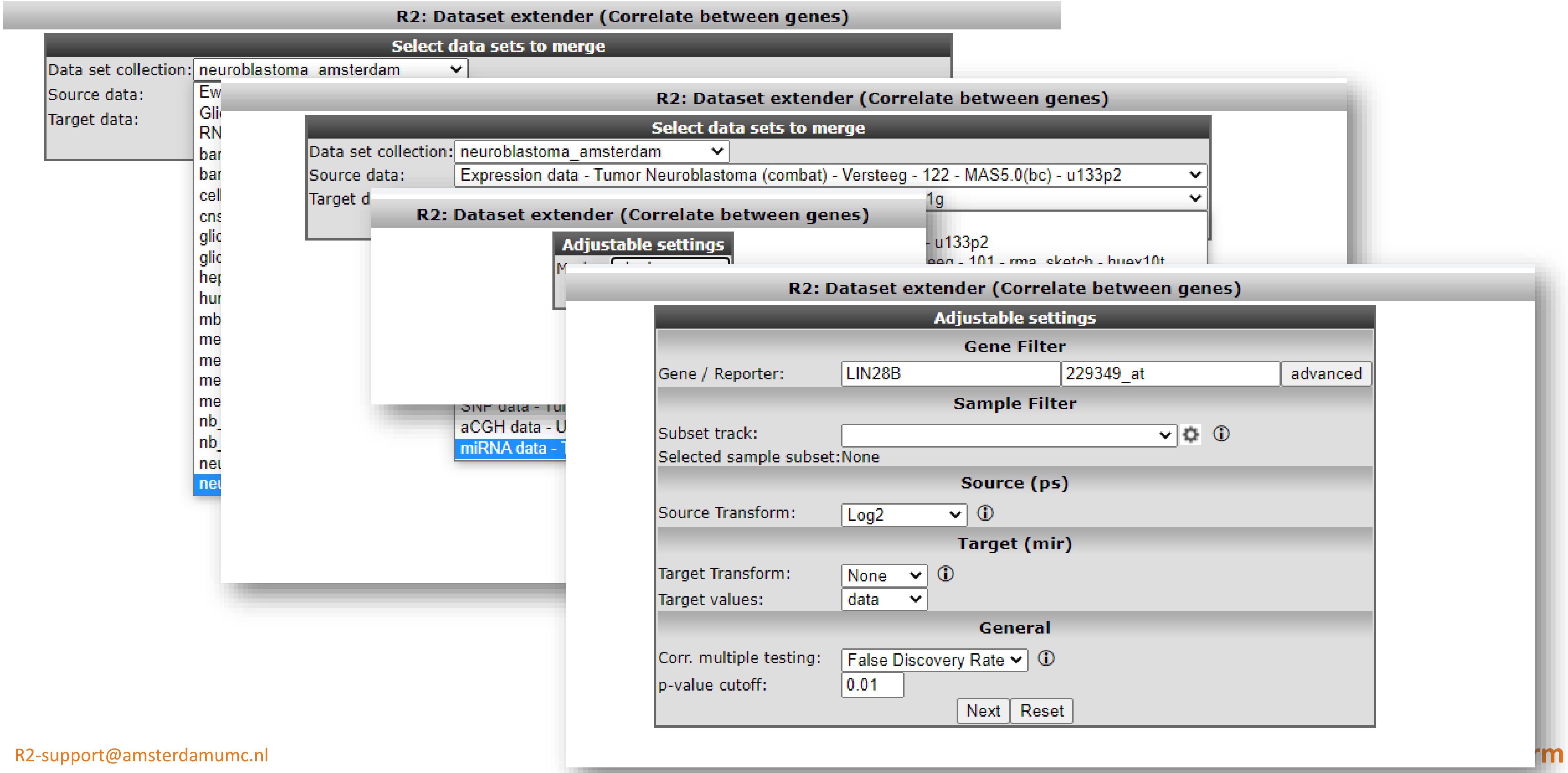
Financial Supporter of R2

all news

mRNA vs miRNA



R2: Dataset extender (Correlate between genes)

Select data sets to merge

Data set collection: neuroblastoma_amsterdam

Source data: Expression data - Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2

Target data:

R2: Dataset extender (Correlate between genes)

Adjustable settings

Gene Filter

Gene / Reporter: LIN28B 229349_at

Sample Filter

Subset track:

Selected sample subset: None

Source (ps)

Source Transform: Log2

Target (mir)

Target Transform: None

Target values: data

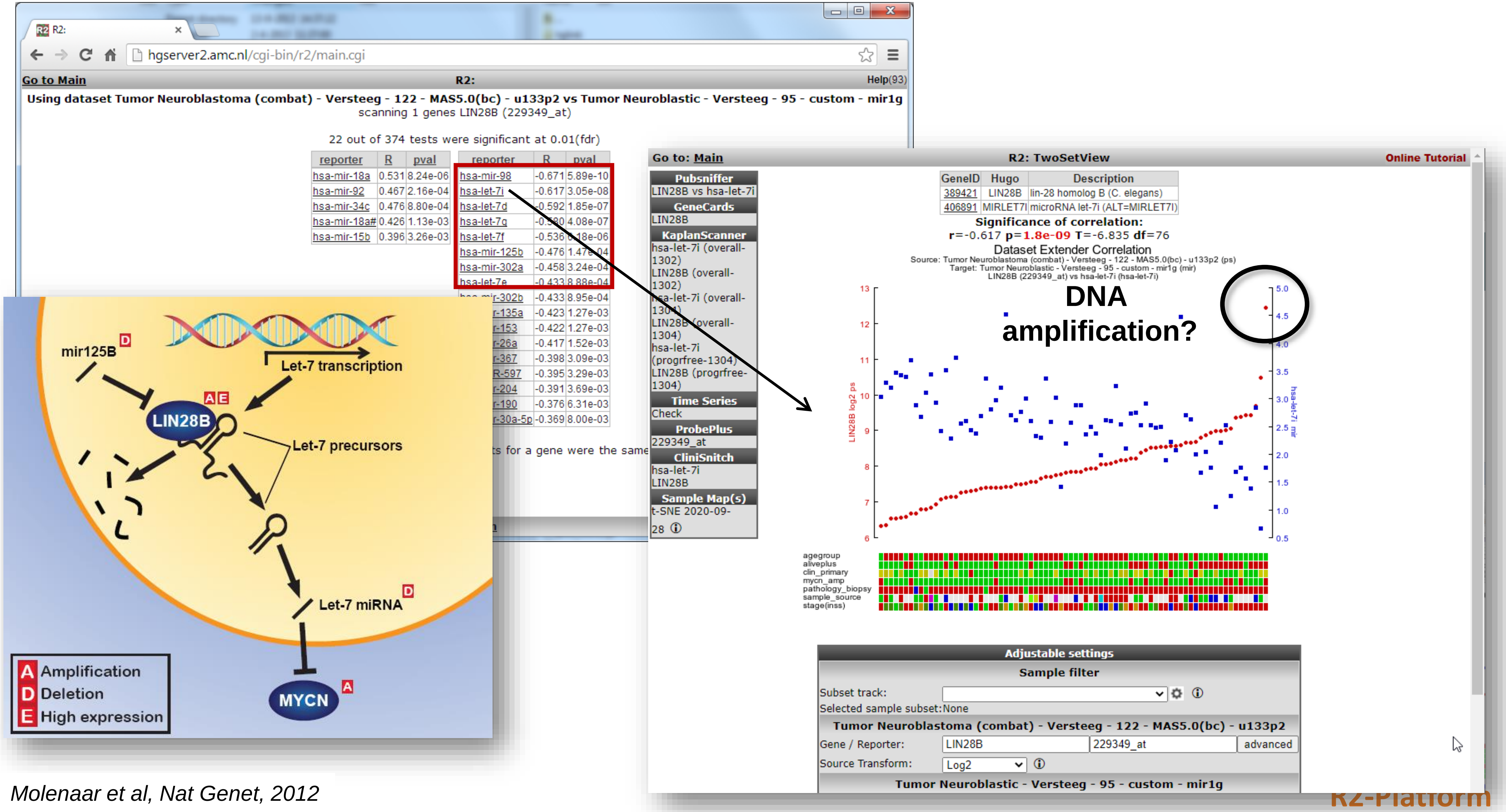
General

Corr. multiple testing: False Discovery Rate

p-value cutoff: 0.01

R2-support@amsterdamumc.nl

mRNA vs miRNA



R2:

hgserver2.amc.nl/cgi-bin/r2/main.cgi

Go to Main R2: Help(93)

Using dataset Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2 vs Tumor Neuroblastic - Versteeg - 95 - custom - mir1g

scanning 1 genes LIN28B (229349_at)

22 out of 374 tests were significant at 0.01(fdr)

reporter	R	pval
hsa-mir-18a	0.531	8.24e-06
hsa-mir-92	0.467	2.16e-04
hsa-mir-34c	0.476	8.80e-04
hsa-mir-18a#	0.426	1.13e-03
hsa-mir-15b	0.396	3.26e-03

reporter	R	pval
hsa-mir-98	-0.671	5.89e-10
hsa-let-7i	-0.617	3.05e-08
hsa-let-7d	-0.592	1.85e-07
hsa-let-7g	-0.580	4.08e-07
hsa-let-7f	-0.536	6.18e-06
hsa-mir-125b	-0.476	1.47e-04
hsa-mir-302a	-0.458	3.24e-04
hsa-let-7e	-0.433	8.88e-04
hsa-mir-302b	-0.433	8.95e-04
r-135a	-0.423	1.27e-03
r-153	-0.422	1.27e-03
r-26a	-0.417	1.52e-03
r-367	-0.398	3.09e-03
R-597	-0.395	3.29e-03
r-204	-0.391	3.69e-03
r-190	-0.376	6.31e-03
r-30a-5p	-0.369	8.00e-03

ts for a gene were the same

Go to: Main R2: TwoSetView Online Tutorial

Pubsniffer
LIN28B vs hsa-let-7i
GeneCards
LIN28B
KaplanScanner
hsa-let-7i (overall-1302)
LIN28B (overall-1302)
hsa-let-7i (overall-1304)
LIN28B (overall-1304)
hsa-let-7i (progrfree-1304)
LIN28B (progrfree-1304)
Time Series
Check
ProbePlus
229349_at
CliniSnitch
hsa-let-7i
LIN28B
Sample Map(s)
t-SNE 2020-09-28

GeneID	Hugo	Description
389421	LIN28B	lin-28 homolog B (C. elegans)
406891	MIRLET7I	microRNA let-7i (ALT=MIRLET7I)

Significance of correlation:
r=-0.617 **p**=1.8e-09 **T**=-6.835 **df**=76

Dataset Extender Correlation
Source: Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2 (ps)
Target: Tumor Neuroblastic - Versteeg - 95 - custom - mir1g (mir)
LIN28B (229349_at) vs hsa-let-7i (hsa-let-7i)

DNA amplification?

Adjustable settings

Sample filter

Subset track:
Selected sample subset: None

Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2

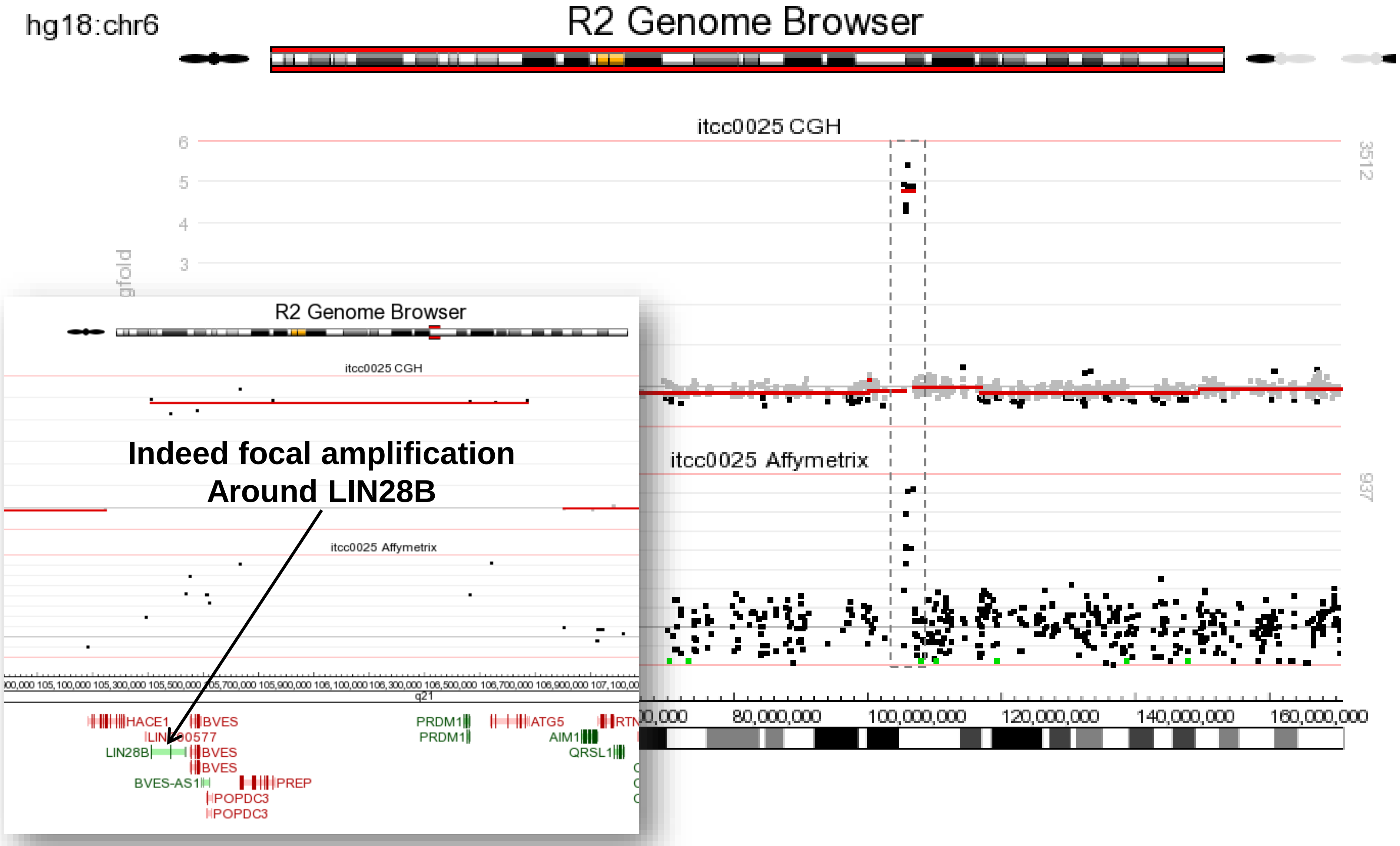
Gene / Reporter: LIN28B 229349_at advanced

Source Transform: Log2

Tumor Neuroblastic - Versteeg - 95 - custom - mir1g

Molenaar et al, Nat Genet, 2012

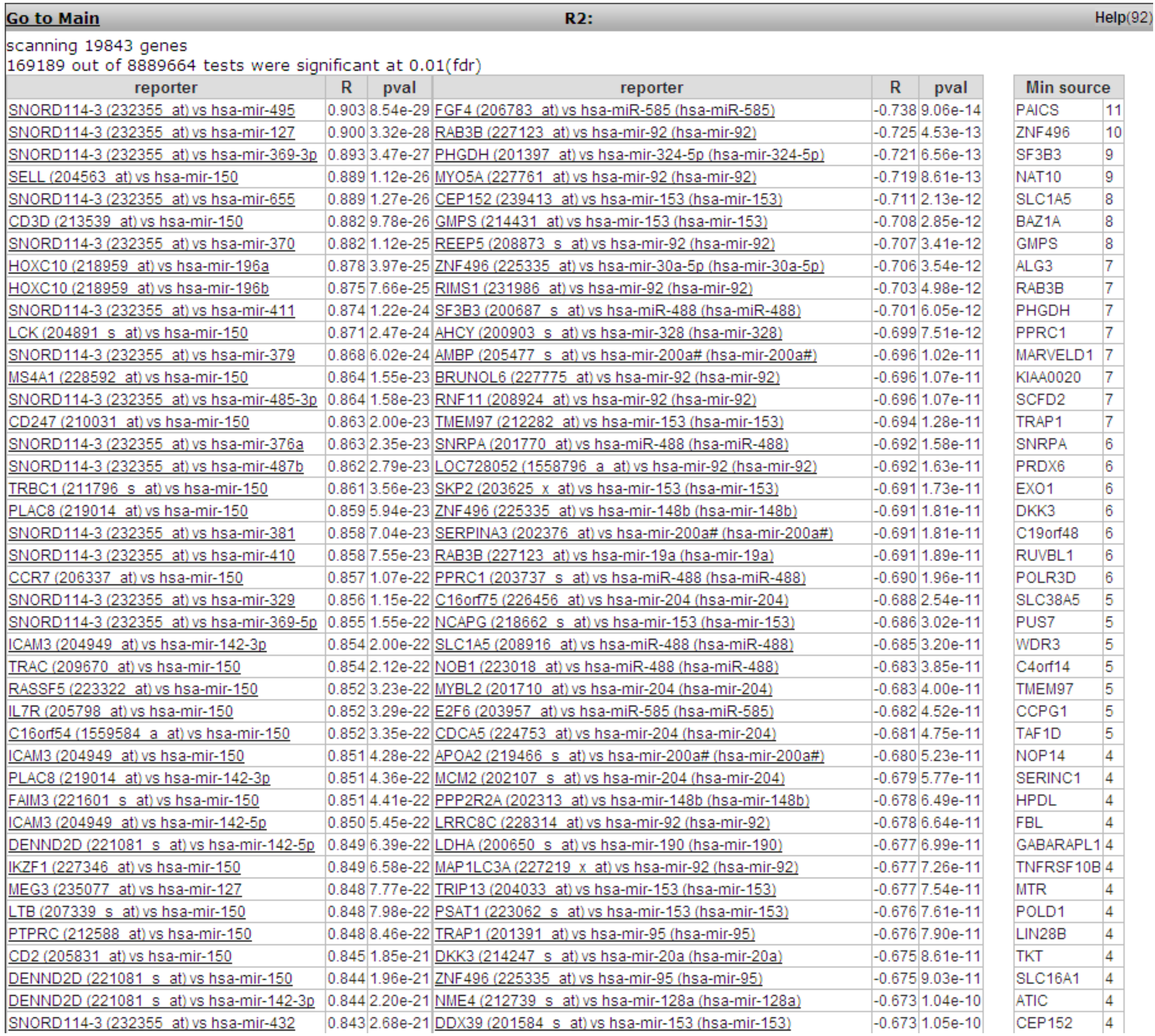
mRNA vs aCGH



Indeed focal amplification Around LIN28B

Molenaar et al, Nat Genet, 2012

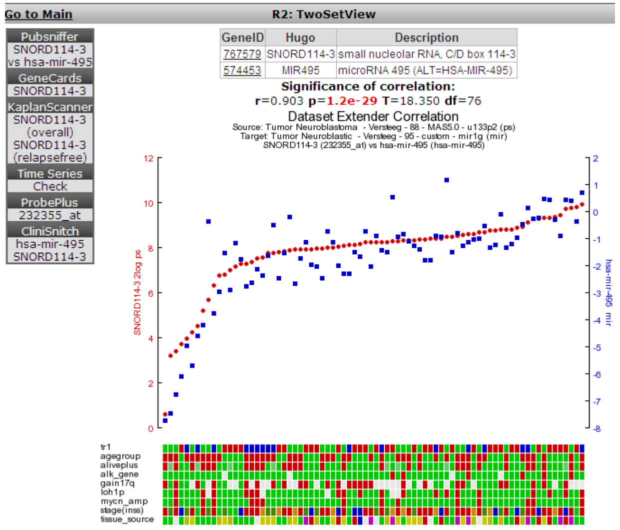
Best correlating pairs miRNA vs gene express



Go to Main R2: Help(92)

scanning 19843 genes
169189 out of 8889664 tests were significant at 0.01(fdr)

reporter	R	pval	reporter	R	pval	Min source	
SNORD114-3 (232355_at) vs hsa-mir-495	0.903	8.54e-29	FGF4 (206783_at) vs hsa-miR-585 (hsa-miR-585)	-0.738	9.06e-14	PAICS	11
SNORD114-3 (232355_at) vs hsa-mir-127	0.900	3.32e-28	RAB3B (227123_at) vs hsa-mir-92 (hsa-mir-92)	-0.725	4.53e-13	ZNF496	10
SNORD114-3 (232355_at) vs hsa-mir-369-3p	0.893	3.47e-27	PHGDH (201397_at) vs hsa-mir-324-5p (hsa-mir-324-5p)	-0.721	6.56e-13	SF3B3	9
SELL (204563_at) vs hsa-mir-150	0.889	1.12e-26	MYO5A (227761_at) vs hsa-mir-92 (hsa-mir-92)	-0.719	8.61e-13	NAT10	9
SNORD114-3 (232355_at) vs hsa-mir-655	0.889	1.27e-26	CEP152 (239413_at) vs hsa-mir-153 (hsa-mir-153)	-0.711	2.13e-12	SLC1A5	8
CD3D (213539_at) vs hsa-mir-150	0.882	9.78e-26	GMPS (214431_at) vs hsa-mir-153 (hsa-mir-153)	-0.708	2.85e-12	BAZ1A	8
SNORD114-3 (232355_at) vs hsa-mir-370	0.882	1.12e-25	REEP5 (208873_s_at) vs hsa-mir-92 (hsa-mir-92)	-0.707	3.41e-12	GMPS	8
HOXC10 (218959_at) vs hsa-mir-196a	0.878	3.97e-25	ZNF496 (225335_at) vs hsa-mir-30a-5p (hsa-mir-30a-5p)	-0.706	3.54e-12	ALG3	7
HOXC10 (218959_at) vs hsa-mir-196b	0.875	7.66e-25	RIMS1 (231986_at) vs hsa-mir-92 (hsa-mir-92)	-0.703	4.98e-12	RAB3B	7
SNORD114-3 (232355_at) vs hsa-mir-411	0.874	1.22e-24	SF3B3 (200687_s_at) vs hsa-miR-488 (hsa-miR-488)	-0.701	6.05e-12	PHGDH	7
LCK (204891_s_at) vs hsa-mir-150	0.871	2.47e-24	AHCY (200903_s_at) vs hsa-mir-328 (hsa-mir-328)	-0.699	7.51e-12	PPRC1	7
SNORD114-3 (232355_at) vs hsa-mir-379	0.868	6.02e-24	AMBP (205477_s_at) vs hsa-mir-200a# (hsa-mir-200a#)	-0.696	1.02e-11	MARVELD1	7
MS4A1 (228592_at) vs hsa-mir-150	0.864	1.55e-23	BRUNOL6 (227775_at) vs hsa-mir-92 (hsa-mir-92)	-0.696	1.07e-11	KIAA0020	7
SNORD114-3 (232355_at) vs hsa-mir-485-3p	0.864	1.58e-23	RNF11 (208924_at) vs hsa-mir-92 (hsa-mir-92)	-0.696	1.07e-11	SCFD2	7
CD247 (210031_at) vs hsa-mir-150	0.863	2.00e-23	TMEM97 (212282_at) vs hsa-mir-153 (hsa-mir-153)	-0.694	1.28e-11	TRAP1	7
SNORD114-3 (232355_at) vs hsa-mir-376a	0.863	2.35e-23	SNRPA (201770_at) vs hsa-miR-488 (hsa-miR-488)	-0.692	1.58e-11	SNRPA	6
SNORD114-3 (232355_at) vs hsa-mir-487b	0.862	2.79e-23	LOC728052 (1558796_a_at) vs hsa-mir-92 (hsa-mir-92)	-0.692	1.63e-11	PRDX6	6
TRBC1 (211796_s_at) vs hsa-mir-150	0.861	3.56e-23	SKP2 (203625_x_at) vs hsa-mir-153 (hsa-mir-153)	-0.691	1.73e-11	EXO1	6
PLAC8 (219014_at) vs hsa-mir-150	0.859	5.94e-23	ZNF496 (225335_at) vs hsa-mir-148b (hsa-mir-148b)	-0.691	1.81e-11	DKK3	6
SNORD114-3 (232355_at) vs hsa-mir-381	0.858	7.04e-23	SERPINA3 (202376_at) vs hsa-mir-200a# (hsa-mir-200a#)	-0.691	1.81e-11	C19orf48	6
SNORD114-3 (232355_at) vs hsa-mir-410	0.858	7.55e-23	RAB3B (227123_at) vs hsa-mir-19a (hsa-mir-19a)	-0.691	1.89e-11	RUVBL1	6
CCR7 (206337_at) vs hsa-mir-150	0.857	1.07e-22	PPRC1 (203737_s_at) vs hsa-miR-488 (hsa-miR-488)	-0.690	1.96e-11	POLR3D	6
SNORD114-3 (232355_at) vs hsa-mir-329	0.856	1.15e-22	C16orf75 (226456_at) vs hsa-mir-204 (hsa-mir-204)	-0.688	2.54e-11	SLC38A5	5
SNORD114-3 (232355_at) vs hsa-mir-369-5p	0.855	1.55e-22	NCAPG (218662_s_at) vs hsa-mir-153 (hsa-mir-153)	-0.686	3.02e-11	PUS7	5
ICAM3 (204949_at) vs hsa-mir-142-3p	0.854	2.00e-22	SLC1A5 (208916_at) vs hsa-miR-488 (hsa-miR-488)	-0.685	3.20e-11	WDR3	5
TRAC (209670_at) vs hsa-mir-150	0.854	2.12e-22	NOB1 (223018_at) vs hsa-miR-488 (hsa-miR-488)	-0.683	3.85e-11	C4orf14	5
RASSF5 (223322_at) vs hsa-mir-150	0.852	3.23e-22	MYBL2 (201710_at) vs hsa-mir-204 (hsa-mir-204)	-0.683	4.00e-11	TMEM97	5
IL7R (205798_at) vs hsa-mir-150	0.852	3.29e-22	E2F6 (203957_at) vs hsa-miR-585 (hsa-miR-585)	-0.682	4.52e-11	CCPG1	5
C16orf54 (1559584_a_at) vs hsa-mir-150	0.852	3.35e-22	CDCA5 (224753_at) vs hsa-mir-204 (hsa-mir-204)	-0.681	4.75e-11	TAF1D	5
ICAM3 (204949_at) vs hsa-mir-150	0.851	4.28e-22	APOA2 (219466_s_at) vs hsa-mir-200a# (hsa-mir-200a#)	-0.680	5.23e-11	NOP14	4
PLAC8 (219014_at) vs hsa-mir-142-3p	0.851	4.36e-22	MCM2 (202107_s_at) vs hsa-mir-204 (hsa-mir-204)	-0.679	5.77e-11	SERINC1	4
FAIM3 (221601_s_at) vs hsa-mir-150	0.851	4.41e-22	PPP2R2A (202313_at) vs hsa-mir-148b (hsa-mir-148b)	-0.678	6.49e-11	HPDL	4
ICAM3 (204949_at) vs hsa-mir-142-5p	0.850	5.45e-22	LRRC8C (228314_at) vs hsa-mir-92 (hsa-mir-92)	-0.678	6.64e-11	FBL	4
DENND2D (221081_s_at) vs hsa-mir-142-5p	0.849	6.39e-22	LDHA (200650_s_at) vs hsa-mir-190 (hsa-mir-190)	-0.677	6.99e-11	GABARAPL1	4
IKZF1 (227346_at) vs hsa-mir-150	0.849	6.58e-22	MAP1LC3A (227219_x_at) vs hsa-mir-92 (hsa-mir-92)	-0.677	7.26e-11	TNFRSF10B	4
MEG3 (235077_at) vs hsa-mir-127	0.848	7.77e-22	TRIP13 (204033_at) vs hsa-mir-153 (hsa-mir-153)	-0.677	7.54e-11	MTR	4
LTB (207339_s_at) vs hsa-mir-150	0.848	7.98e-22	PSAT1 (223062_s_at) vs hsa-mir-153 (hsa-mir-153)	-0.676	7.61e-11	POLD1	4
PTPRC (212588_at) vs hsa-mir-150	0.848	8.46e-22	TRAP1 (201391_at) vs hsa-mir-95 (hsa-mir-95)	-0.676	7.90e-11	LIN28B	4
CD2 (205831_at) vs hsa-mir-150	0.845	1.85e-21	DKK3 (214247_s_at) vs hsa-mir-20a (hsa-mir-20a)	-0.675	8.61e-11	TKT	4
DENND2D (221081_s_at) vs hsa-mir-150	0.844	1.96e-21	ZNF496 (225335_at) vs hsa-mir-95 (hsa-mir-95)	-0.675	9.03e-11	SLC16A1	4
DENND2D (221081_s_at) vs hsa-mir-142-3p	0.844	2.20e-21	NME4 (212739_s_at) vs hsa-mir-128a (hsa-mir-128a)	-0.673	1.04e-10	ATIC	4
SNORD114-3 (232355_at) vs hsa-mir-432	0.843	2.68e-21	DDX39 (201584_s_at) vs hsa-mir-153 (hsa-mir-153)	-0.673	1.05e-10	CEP152	4

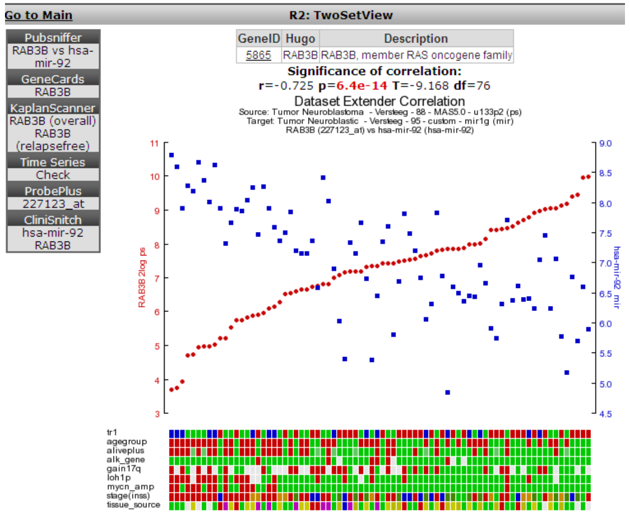


Go to Main R2: TwoSetView

GeneID	Hugo	Description
767579	SNORD114-3	small nucleolar RNA, C/D box 114-3
574453	MIR495	microRNA 495 (ALT=HSA-MIR-495)

Significance of correlation:
r=0.903 **p**=1.2e-29 **T**=18.350 **df**=76

Dataset Extender Correlation
Source: Tumor Neuroblastoma - Versteeg - 88 - MAS5.0 - u133p2 (ps)
Target: Tumor Neuroblastic - Versteeg - 95 - custom - mir1g (mir)
SNORD114-3 (232355_at) vs hsa-mir-495 (hsa-mir-495)



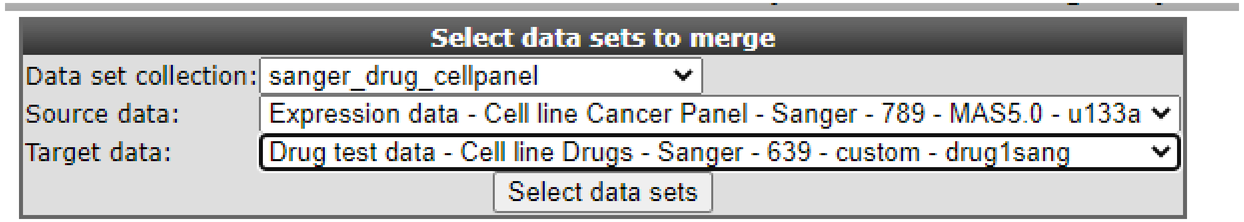
Go to Main R2: TwoSetView

GeneID	Hugo	Description
5865	RAB3B	RAB3B, member RAS oncogene family

Significance of correlation:
r=-0.725 **p**=6.4e-14 **T**=-9.168 **df**=76

Dataset Extender Correlation
Source: Tumor Neuroblastoma - Versteeg - 88 - MAS5.0 - u133p2 (ps)
Target: Tumor Neuroblastic - Versteeg - 95 - custom - mir1g (mir)
RAB3B (227123_at) vs hsa-mir-92 (hsa-mir-92)

Relate Gene Expression to drug sensitivity

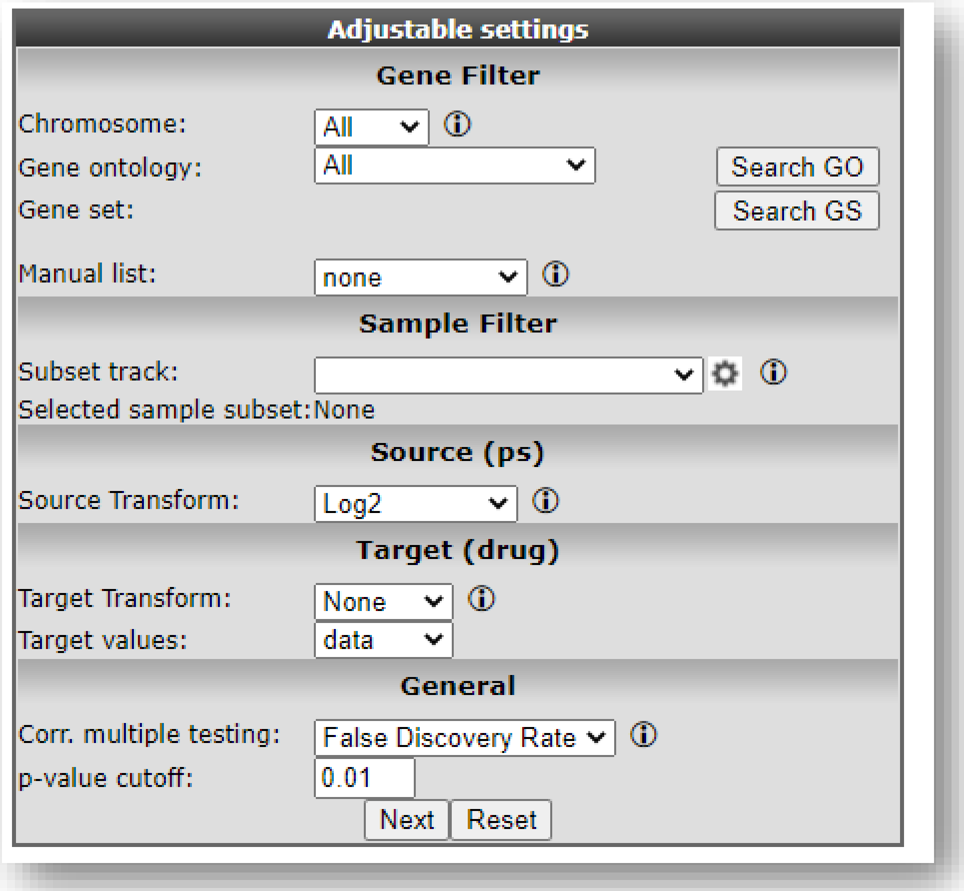


Select data sets to merge

Data set collection: sanger_drug_cellpanel

Source data: Expression data - Cell line Cancer Panel - Sanger - 789 - MAS5.0 - u133a

Target data: Drug test data - Cell line Drugs - Sanger - 639 - custom - drug1sang



Adjustable settings

Gene Filter

Chromosome: All

Gene ontology: All

Gene set:

Manual list: none

Sample Filter

Subset track:

Selected sample subset: None

Source (ps)

Source Transform: Log2

Target (drug)

Target Transform: None

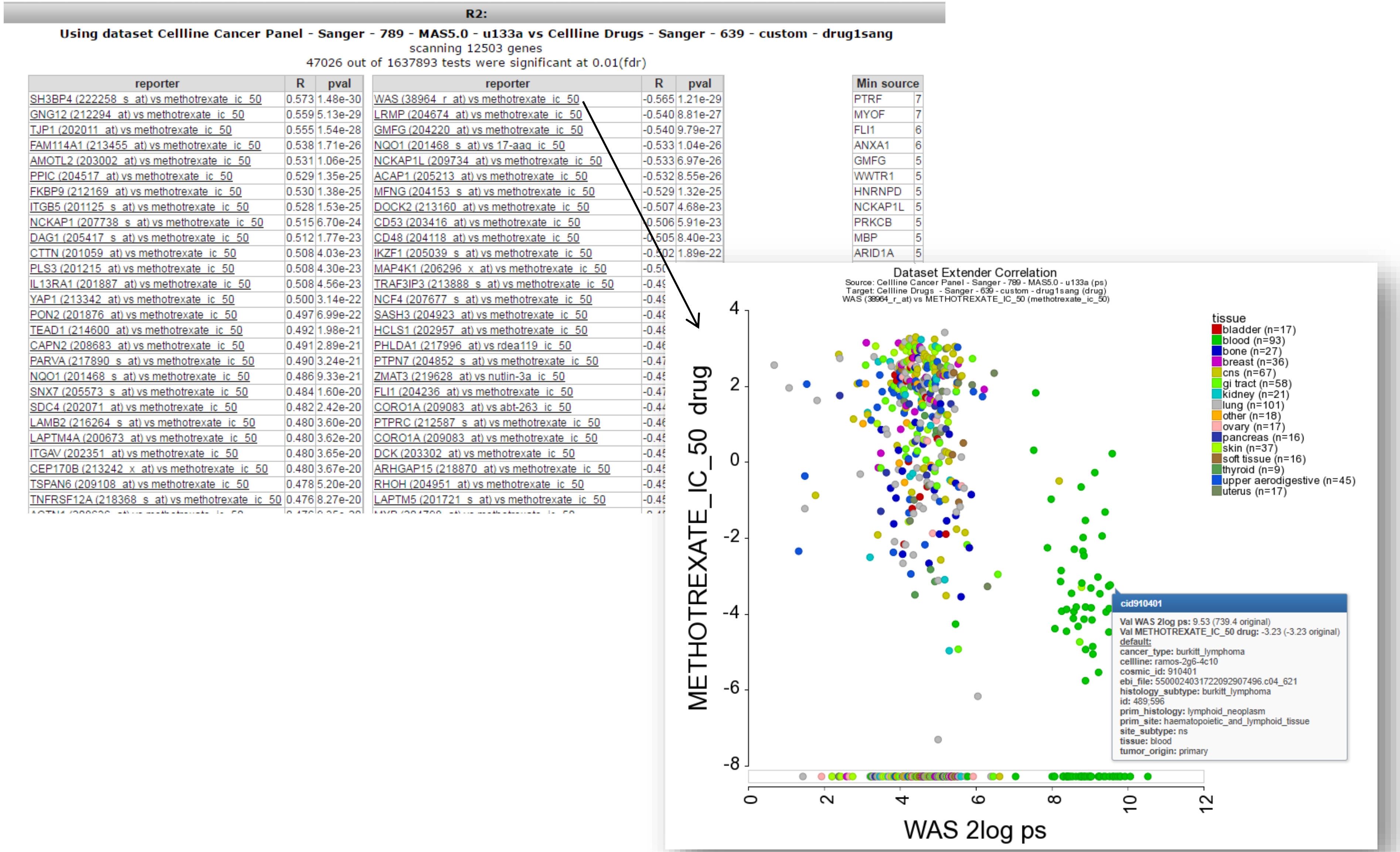
Target values: data

General

Corr. multiple testing: False Discovery Rate

p-value cutoff: 0.01

Drug (IC50) data



R2:

Using dataset Cellline Cancer Panel - Sanger - 789 - MAS5.0 - u133a vs Cellline Drugs - Sanger - 639 - custom - drug1sang
scanning 12503 genes
47026 out of 1637893 tests were significant at 0.01(fdr)

reporter	R	pval
SH3BP4 (222258 s at) vs methotrexate ic 50	0.573	1.48e-30
GNG12 (212294 at) vs methotrexate ic 50	0.559	5.13e-29
TJP1 (202011 at) vs methotrexate ic 50	0.555	1.54e-28
FAM114A1 (213455 at) vs methotrexate ic 50	0.538	1.71e-26
AMOTL2 (203002 at) vs methotrexate ic 50	0.531	1.06e-25
PPIC (204517 at) vs methotrexate ic 50	0.529	1.35e-25
FKBP9 (212169 at) vs methotrexate ic 50	0.530	1.38e-25
ITGB5 (201125 s at) vs methotrexate ic 50	0.528	1.53e-25
NCKAP1 (207738 s at) vs methotrexate ic 50	0.515	6.70e-24
DAG1 (205417 s at) vs methotrexate ic 50	0.512	1.77e-23
CTTN (201059 at) vs methotrexate ic 50	0.508	4.03e-23
PLS3 (201215 at) vs methotrexate ic 50	0.508	4.30e-23
IL13RA1 (201887 at) vs methotrexate ic 50	0.508	4.56e-23
YAP1 (213342 at) vs methotrexate ic 50	0.500	3.14e-22
PON2 (201876 at) vs methotrexate ic 50	0.497	6.99e-22
TEAD1 (214600 at) vs methotrexate ic 50	0.492	1.98e-21
CAPN2 (208683 at) vs methotrexate ic 50	0.491	2.89e-21
PARVA (217890 s at) vs methotrexate ic 50	0.490	3.24e-21
NQO1 (201468 s at) vs methotrexate ic 50	0.486	9.33e-21
SNX7 (205573 s at) vs methotrexate ic 50	0.484	1.60e-20
SDC4 (202071 at) vs methotrexate ic 50	0.482	2.42e-20
LAMB2 (216264 s at) vs methotrexate ic 50	0.480	3.60e-20
LAPTM4A (200673 at) vs methotrexate ic 50	0.480	3.62e-20
ITGAV (202351 at) vs methotrexate ic 50	0.480	3.65e-20
CEP170B (213242 x at) vs methotrexate ic 50	0.480	3.67e-20
TSPAN6 (209108 at) vs methotrexate ic 50	0.478	5.20e-20
TNFRSF12A (218368 s at) vs methotrexate ic 50	0.476	8.27e-20

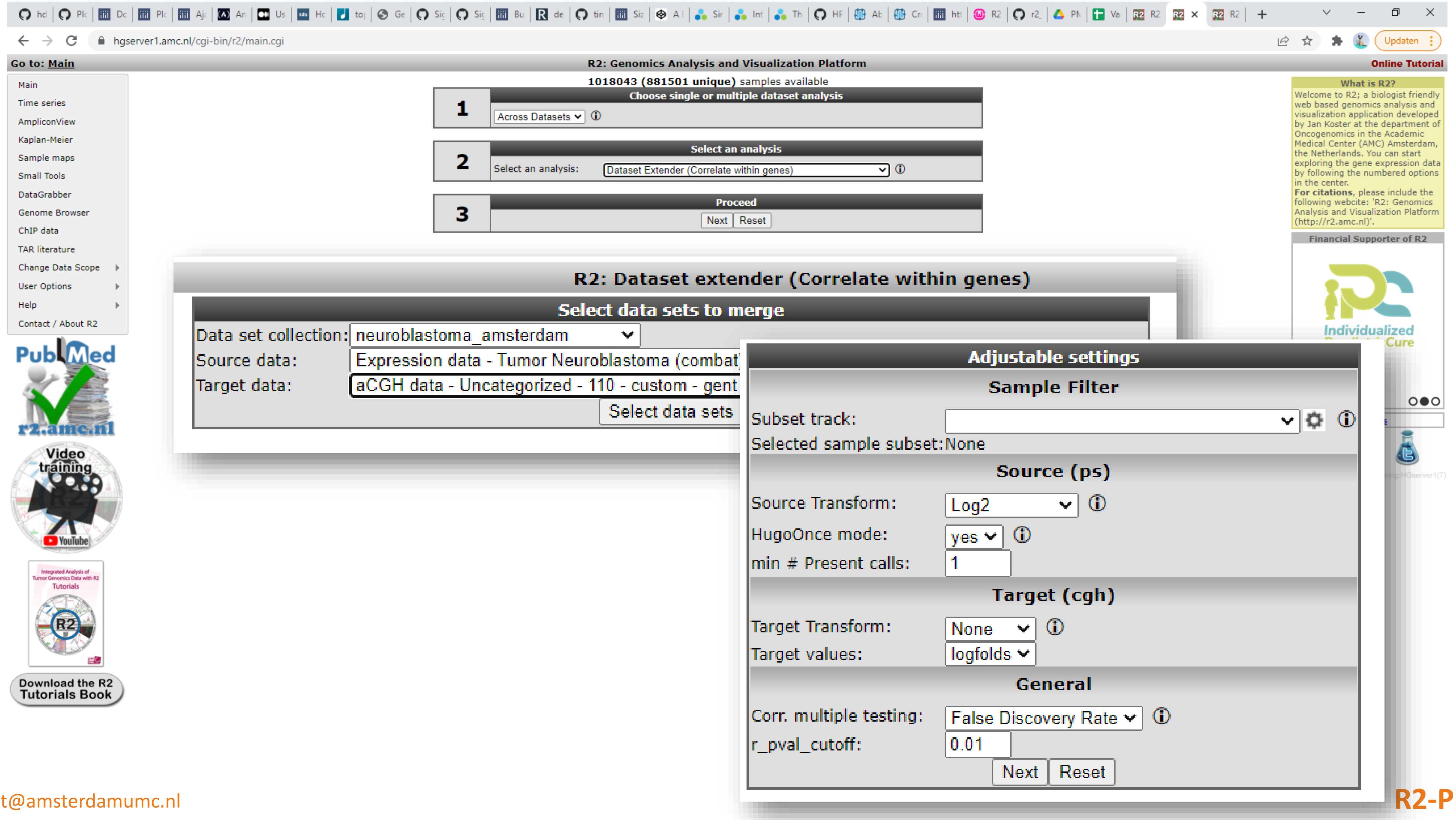
reporter	R	pval
WAS (38964 r at) vs methotrexate ic 50	-0.565	1.21e-29
LRMP (204674 at) vs methotrexate ic 50	-0.540	8.81e-27
GMFG (204220 at) vs methotrexate ic 50	-0.540	9.79e-27
NQO1 (201468 s at) vs 17-aag ic 50	-0.533	1.04e-26
NCKAP1L (209734 at) vs methotrexate ic 50	-0.533	6.97e-26
ACAP1 (205213 at) vs methotrexate ic 50	-0.532	8.55e-26
MFNG (204153 s at) vs methotrexate ic 50	-0.529	1.32e-25
DOCK2 (213160 at) vs methotrexate ic 50	-0.507	4.68e-23
CD53 (203416 at) vs methotrexate ic 50	-0.506	5.91e-23
CD48 (204118 at) vs methotrexate ic 50	-0.505	8.40e-23
IKZF1 (205039 s at) vs methotrexate ic 50	-0.502	1.89e-22
MAP4K1 (206296 x at) vs methotrexate ic 50	-0.50	
TRAF3IP3 (213888 s at) vs methotrexate ic 50	-0.49	
NCF4 (207677 s at) vs methotrexate ic 50	-0.49	
SASH3 (204923 at) vs methotrexate ic 50	-0.48	
HCLS1 (202957 at) vs methotrexate ic 50	-0.48	
PHLDA1 (217996 at) vs rdea119 ic 50	-0.46	
PTPN7 (204852 s at) vs methotrexate ic 50	-0.47	
ZMAT3 (219628 at) vs nutlin-3a ic 50	-0.45	
FLI1 (204236 at) vs methotrexate ic 50	-0.47	
CORO1A (209083 at) vs abt-263 ic 50	-0.44	
PTPRC (212587 s at) vs methotrexate ic 50	-0.46	
CORO1A (209083 at) vs methotrexate ic 50	-0.45	
DCK (203302 at) vs methotrexate ic 50	-0.45	
ARHGAP15 (218870 at) vs methotrexate ic 50	-0.45	
RHOH (204951 at) vs methotrexate ic 50	-0.45	
LAPTM5 (201721 s at) vs methotrexate ic 50	-0.45	

Min source	
PTRF	7
MYOF	7
FLI1	6
ANXA1	6
GMFG	5
WWTR1	5
HNRNPD	5
NCKAP1L	5
PRKCB	5
MBP	5
ARID1A	5

Dataset Extender Correlation
Source: Cellline Cancer Panel - Sanger - 789 - MAS5.0 - u133a (ps)
Target: Cellline Drugs - Sanger - 639 - custom - drug1sang (drug)
WAS (38964_r_at) vs METHOTREXATE_IC_50 (methotrexate_ic_50)

cid910401
Val WAS 2log ps: 9.53 (739.4 original)
Val METHOTREXATE_IC_50 drug: -3.23 (-3.23 original)
default:
cancer_type: burkitt_lymphoma
cellline: ramos-2g6-4c10
cosmic_id: 910401
ebi_file: 5500024031722092907496.c04_621
histology_subtype: burkitt_lymphoma
id: 489;596
prim_histology: lymphoid_neoplasm
prim_site: haematopoietic_and_lymphoid_tissue
site_subtype: ns
tissue: blood
tumor_origin: primary

Correlate within genes (Gex vs Copynumber)



1018043 (881501 unique) samples available

1 Choose single or multiple dataset analysis: Across Datasets

2 Select an analysis: Dataset Extender (Correlate within genes)

3 Proceed: Next | Reset

What is R2?
Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam, the Netherlands. You can start exploring the gene expression data by following the numbered options in the center.
For citations, please include the following website: 'R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl)'.

R2: Dataset extender (Correlate within genes)

Select data sets to merge

Data set collection: neuroblastoma_amsterdam
Source data: Expression data - Tumor Neuroblastoma (combat
Target data: aCGH data - Uncategorized - 110 - custom - gent
Select data sets

Adjustable settings

Sample Filter

Subset track:
Selected sample subset: None

Source (ps)

Source Transform: Log2
HugoOnce mode: yes
min # Present calls: 1

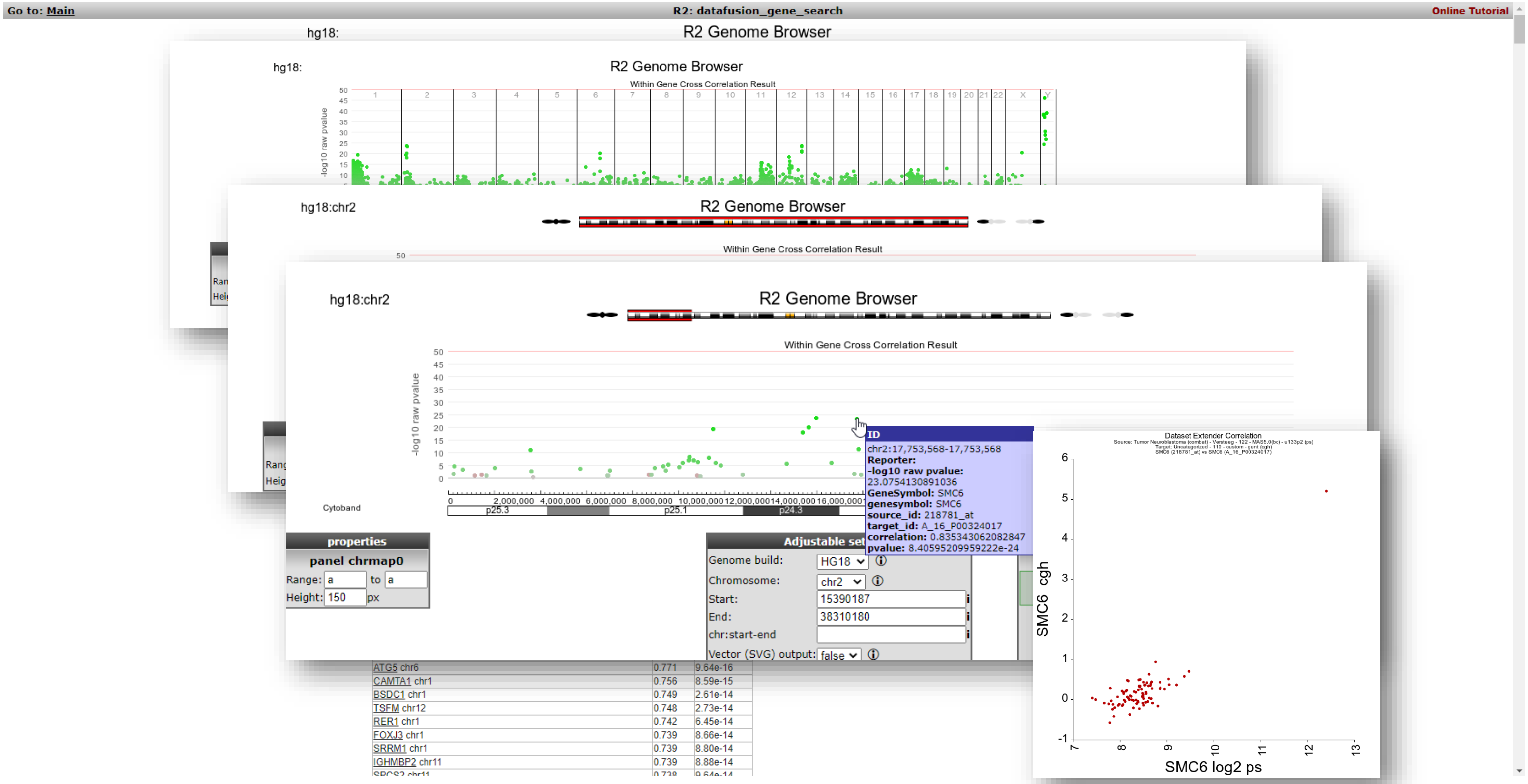
Target (cgh)

Target Transform: None
Target values: logfolds

General

Corr. multiple testing: False Discovery Rate
r_pval_cutoff: 0.01
Next | Reset

Correlate within genes (Gex vs Copynumber)



ID
chr2:17,753,568-17,753,568
Reporter:
-log10 raw pvalue:
23.0754130891036
GeneSymbol: SMC6
genesymbol: SMC6
source_id: 218781_at
target_id: A_16_P00324017
correlation: 0.835343062082847
pvalue: 8.40595209959222e-24

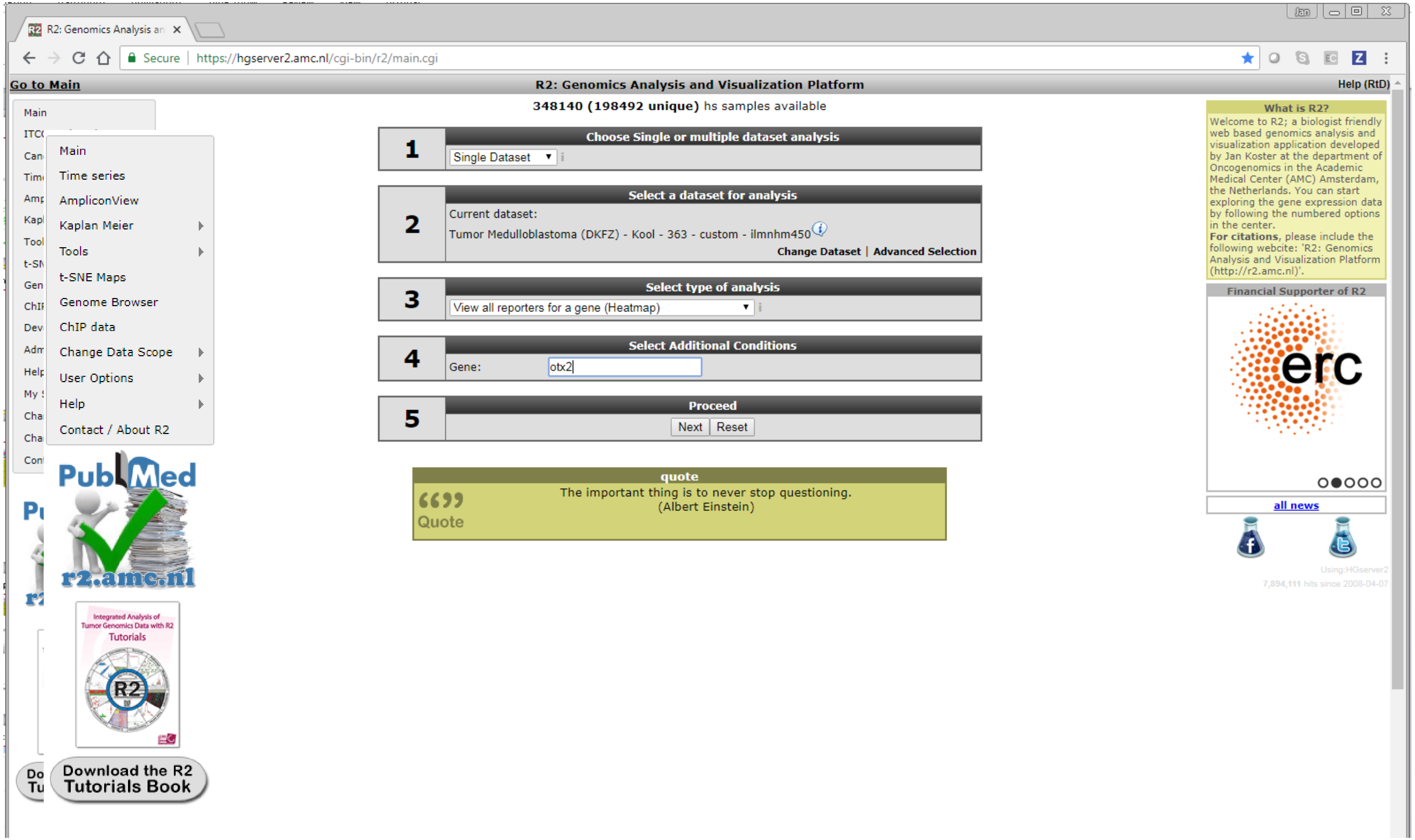
Source: Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2 (ps)
Target: Uncategorized - 110 - custom - gent (cgh)
SMC6 (218781_at) vs SMC6 (A_16_P00324017)

properties
panel chrmap0
Range: a to a
Height: 150 px

Adjustable set
Genome build: HG18
Chromosome: chr2
Start: 15390187
End: 38310180
chr:start-end
Vector (SVG) output: false

ATG5 chr6	0.771	9.64e-16
CAMTA1 chr1	0.756	8.59e-15
BSDC1 chr1	0.749	2.61e-14
TSFM chr12	0.748	2.73e-14
RER1 chr1	0.742	6.45e-14
FOXJ3 chr1	0.739	8.66e-14
SRRM1 chr1	0.739	8.80e-14
IGHMBP2 chr11	0.739	8.88e-14
SPCS2 chr11	0.738	9.64e-14

View all reporters for a gene (module)



R2: Genomics Analysis and Visualization Platform

348140 (198492 unique) hs samples available

1 **Choose Single or multiple dataset analysis**
Single Dataset

2 **Select a dataset for analysis**
Current dataset:
Tumor Medulloblastoma (DKFZ) - Kool - 363 - custom - ilmnhm450
Change Dataset | **Advanced Selection**

3 **Select type of analysis**
View all reporters for a gene (Heatmap)

4 **Select Additional Conditions**
Gene: otx2

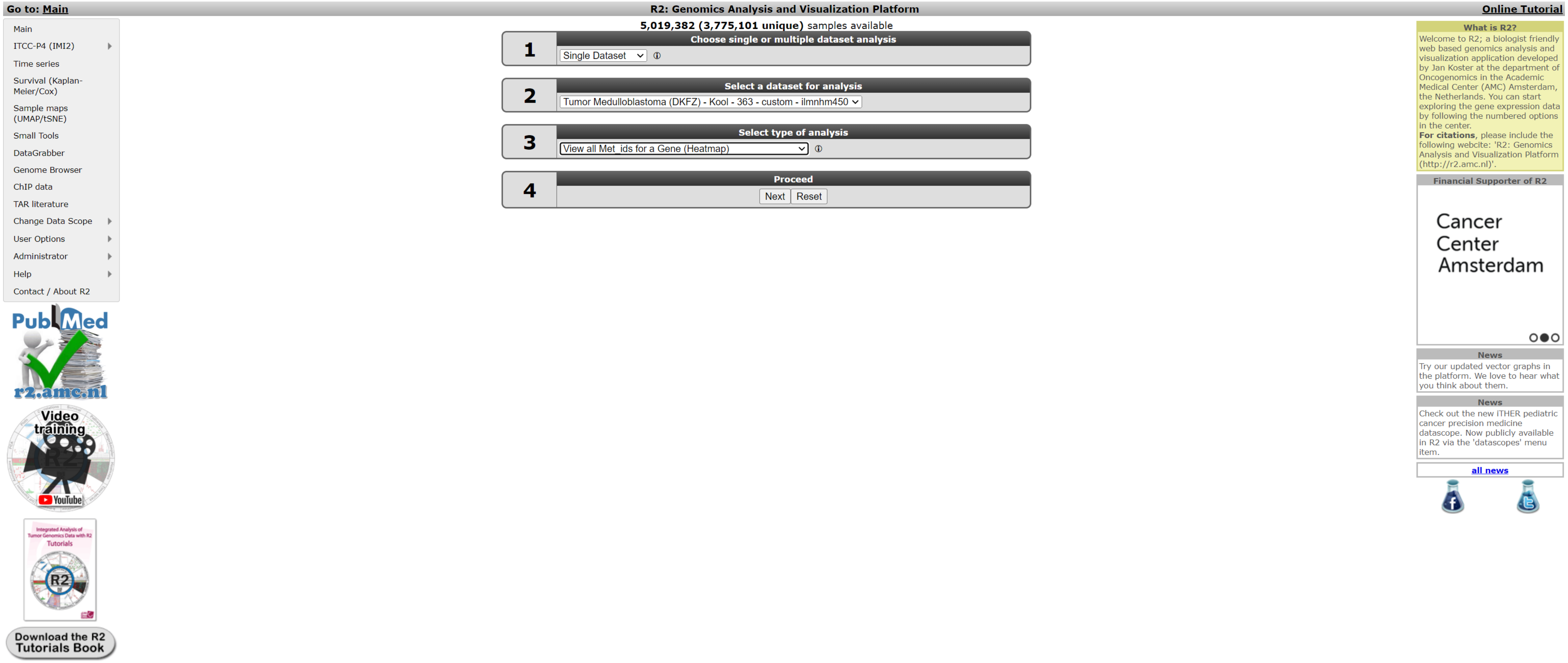
5 **Proceed**
Next Reset

quote
The important thing is to never stop questioning.
(Albert Einstein)

What is R2?
Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam, the Netherlands. You can start exploring the gene expression data by following the numbered options in the center.
For citations, please include the following webcite: 'R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl)'.

Financial Supporter of R2

Using:HGserver2
7,894,111 hits since 2008-04-07



5,019,382 (3,775,101 unique) samples available

1 Choose single or multiple dataset analysis: Single Dataset

2 Select a dataset for analysis: Tumor Medulloblastoma (DKFZ) - Kool - 363 - custom - ilmnhm450

3 Select type of analysis: View all Met_ids for a Gene (Heatmap)

4 Proceed

What is R2?

Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam, the Netherlands. You can start exploring the gene expression data by following the numbered options in the center.
For citations, please include the following webcite: 'R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl)'.

Financial Supporter of R2

Cancer Center Amsterdam

News

Try our updated vector graphs in the platform. We love to hear what you think about them.

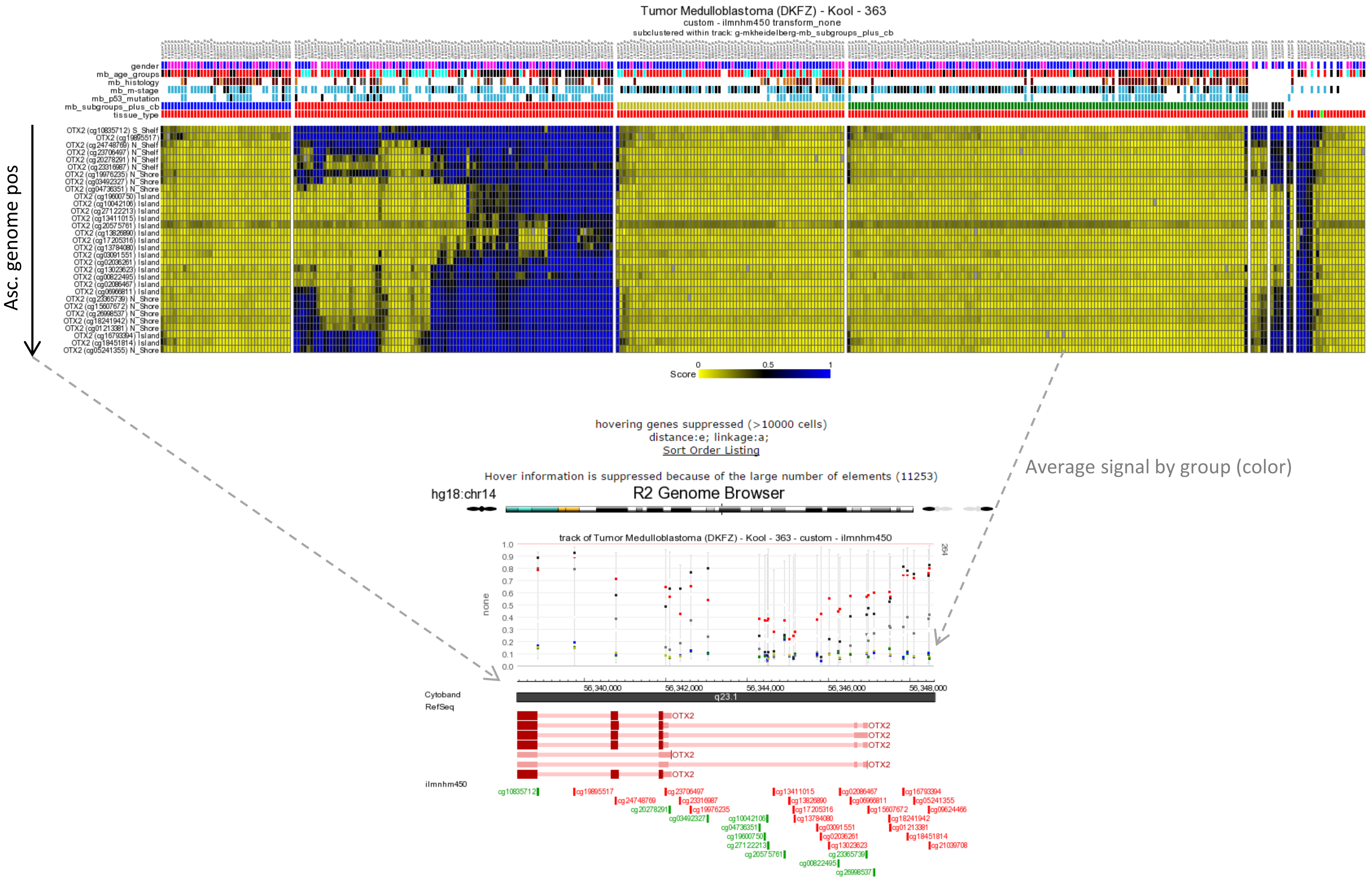
News

Check out the new iTHER pediatric cancer precision medicine datascope. Now publicly available in R2 via the 'datascopes' menu item.

R2-support@amsterdamumc.nl

R2-Platform

Methylation arrays



Tumor Medulloblastoma (DKFZ) - Kool - 363
custom - ilmnhm450 transform_none
subclustered within track: g-mkheidelberg-mb_subgroups_plus_cb

hovering genes suppressed (>10000 cells)
distance:e; linkage:a;
Sort Order Listing

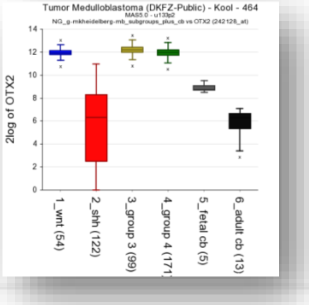
Hover information is suppressed because of the large number of elements (11253)

R2 Genome Browser

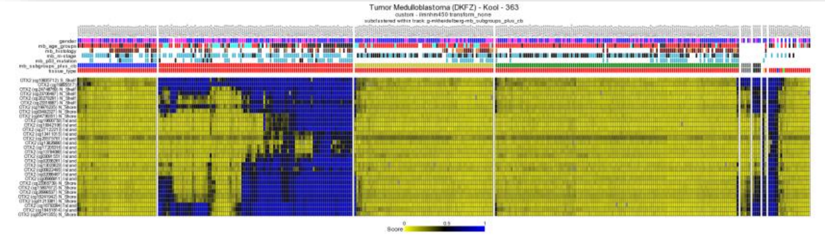
track of Tumor Medulloblastoma (DKFZ) - Kool - 363 - custom - ilmnhm450

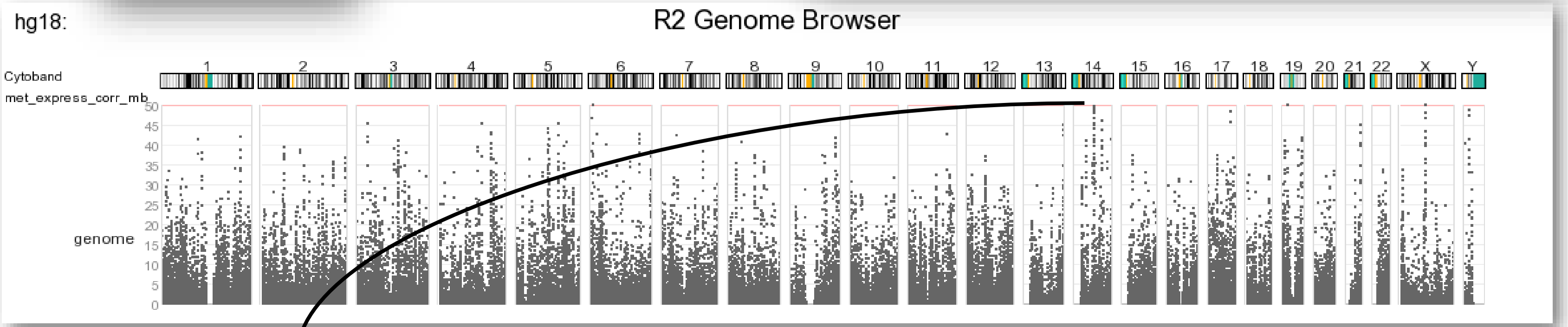
Average signal by group (color)

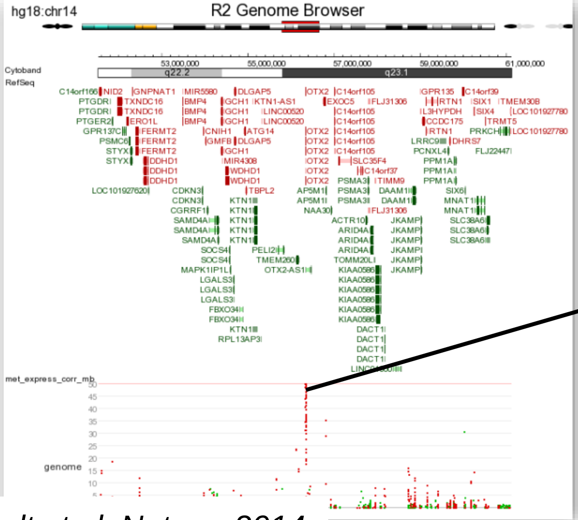
Integration Methylation vs Gene Expression

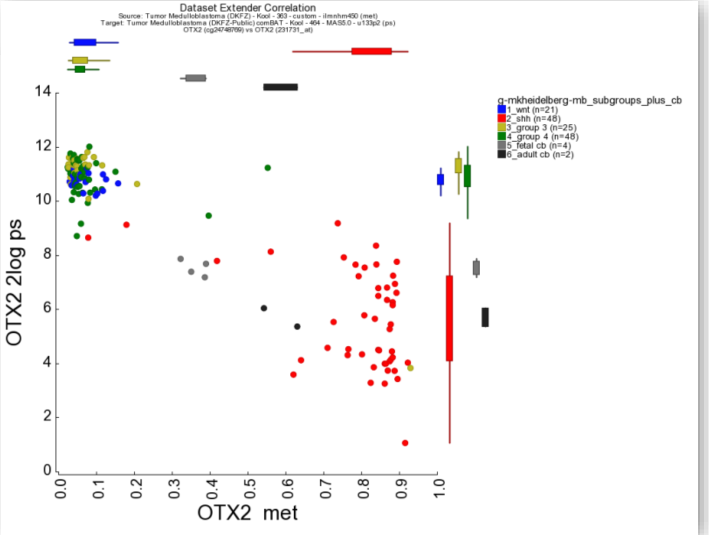


+







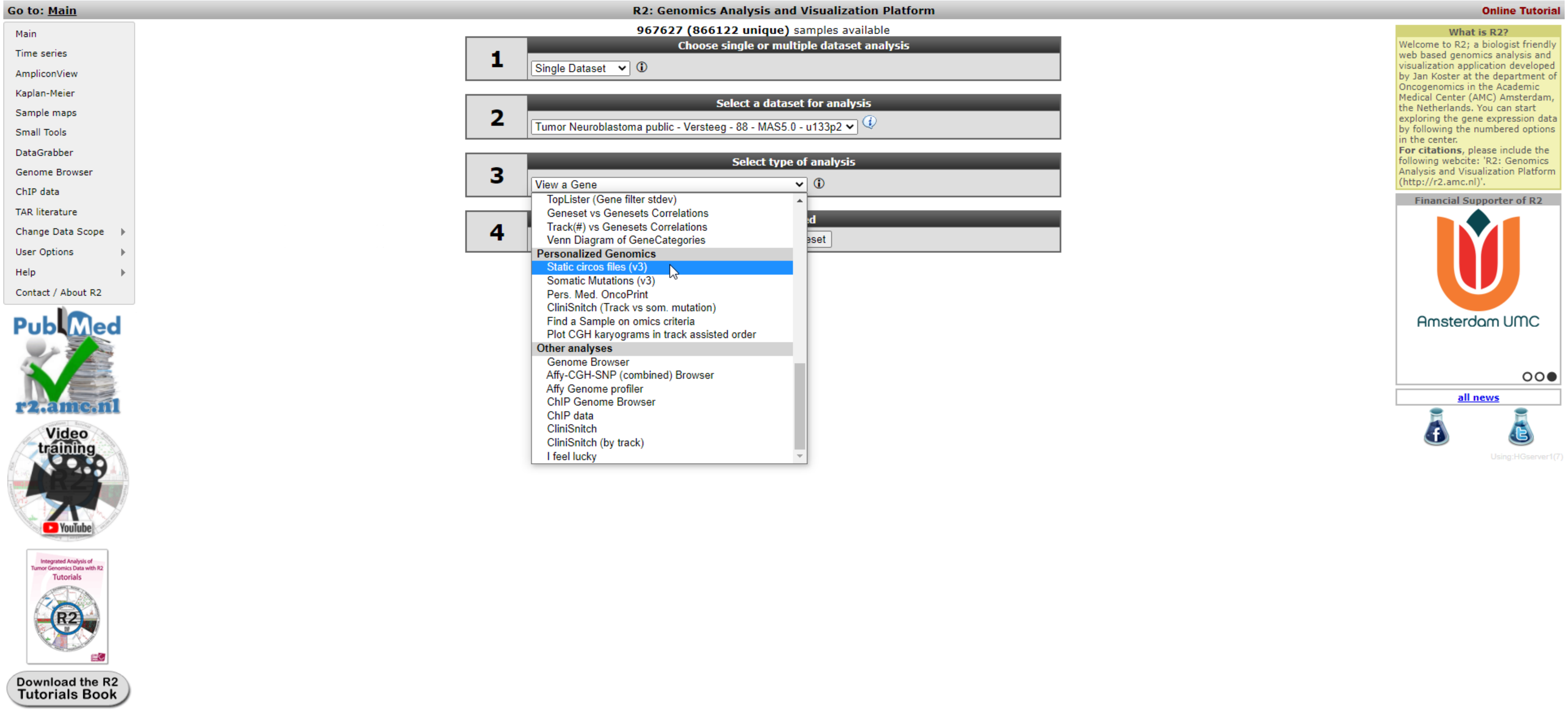


R2-support@amsterda

Hovestadt et al, Nature, 2014

R2-Platform

Whole genome sequencing data in R2



R2: Genomics Analysis and Visualization Platform

967627 (866122 unique) samples available

1 Choose single or multiple dataset analysis: Single Dataset

2 Select a dataset for analysis: Tumor Neuroblastoma public - Versteeg - 88 - MAS5.0 - u133p2

3 Select type of analysis: View a Gene

What is R2?

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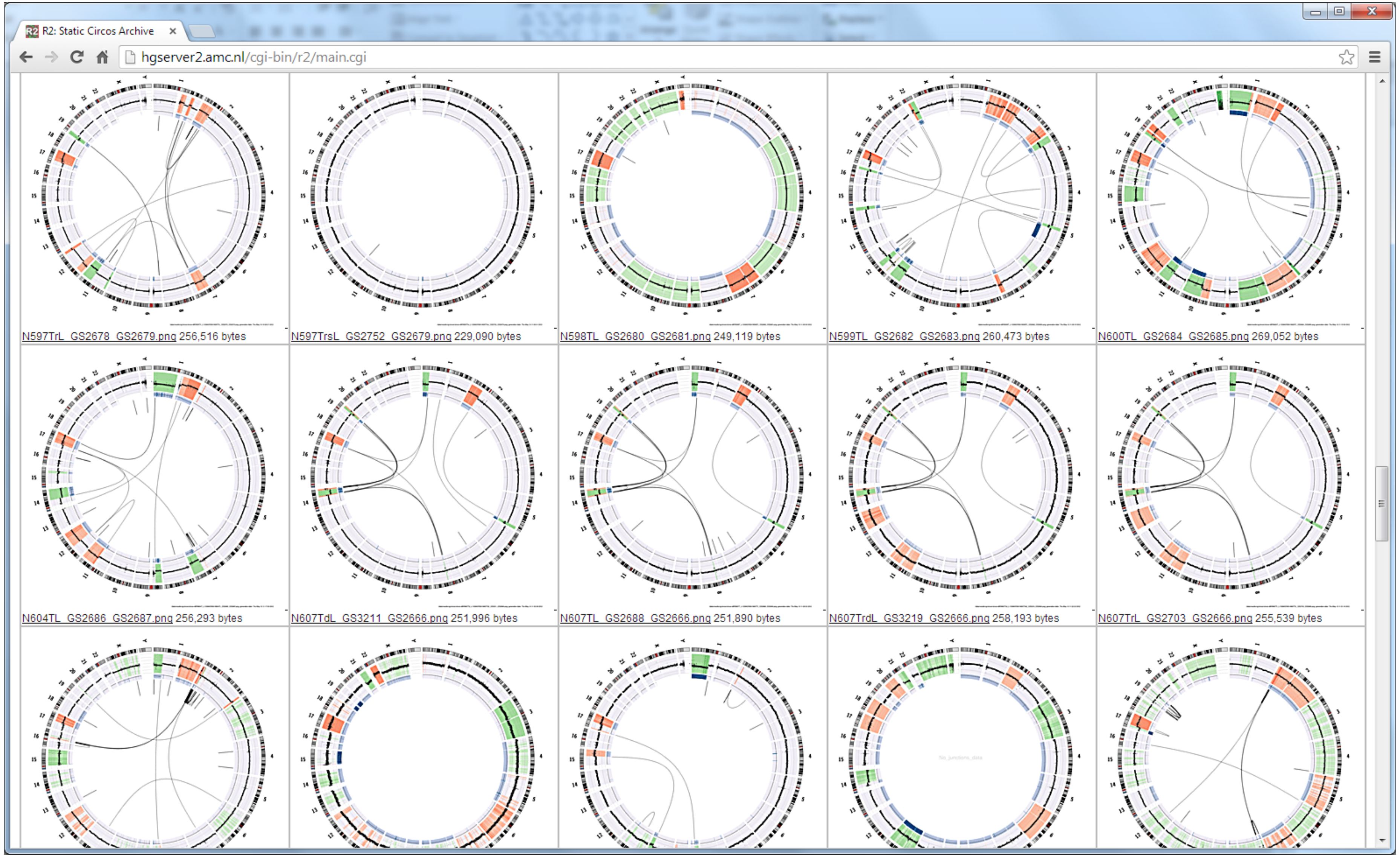
Whole genome sequencing data in R2



R2: Static Circos Archive

hgserver2.amc.nl/cgi-bin/r2/main.cgi

N597TrL_GS2678_GS2679.png 256,516 bytes

N597TrsL_GS2752_GS2679.png 229,090 bytes

N598TL_GS2680_GS2681.png 249,119 bytes

N599TL_GS2682_GS2683.png 260,473 bytes

N600TL_GS2684_GS2685.png 269,052 bytes

N604TL_GS2686_GS2687.png 256,293 bytes

N607TdL_GS3211_GS2666.png 251,996 bytes

N607TL_GS2688_GS2666.png 251,890 bytes

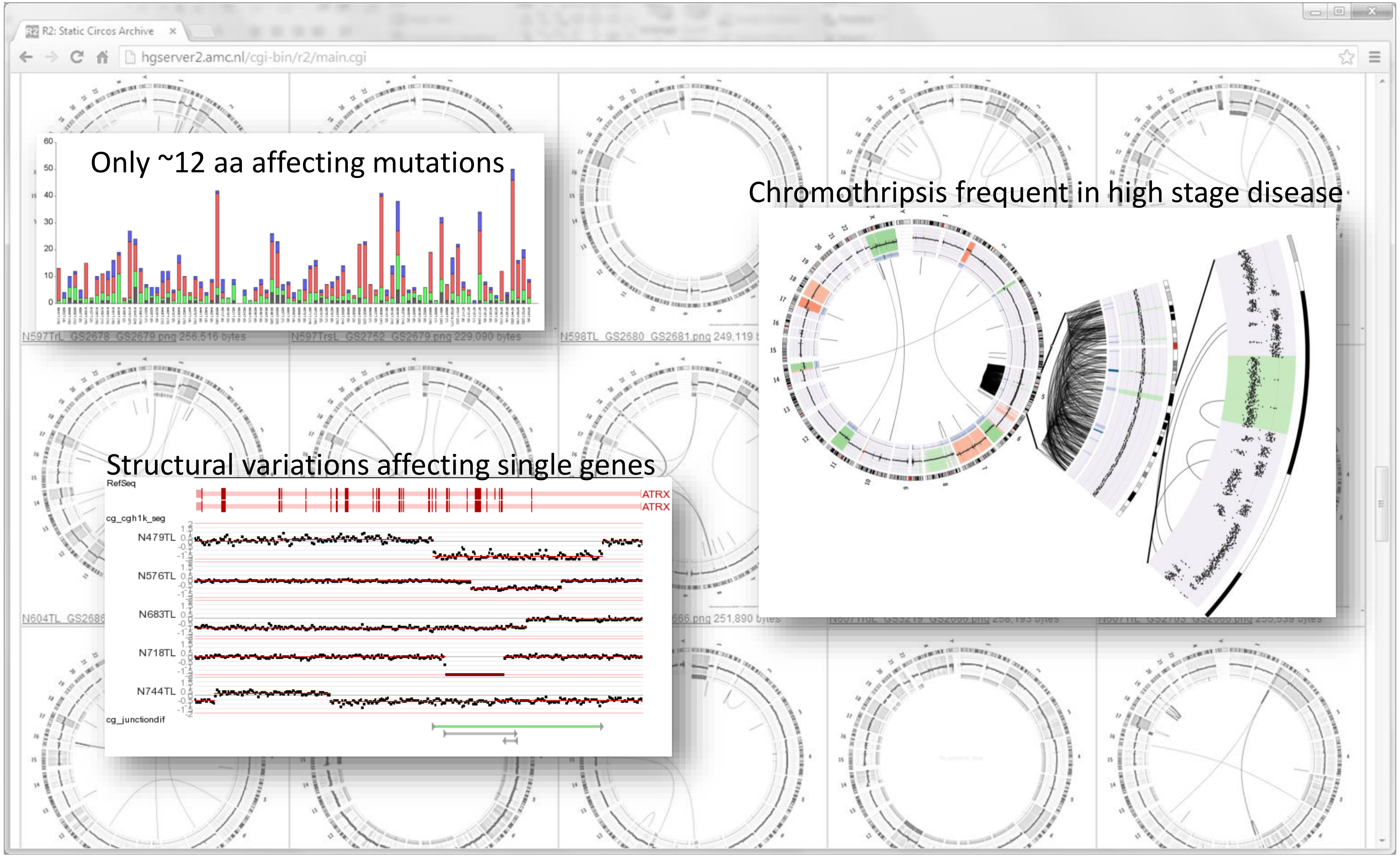
N607TrdL_GS3219_GS2666.png 258,193 bytes

N607TrL_GS2703_GS2666.png 255,539 bytes

R2-support@amsterda

Molenaar & Koster et al, Nature, 2012

Whole genome sequencing data in R2



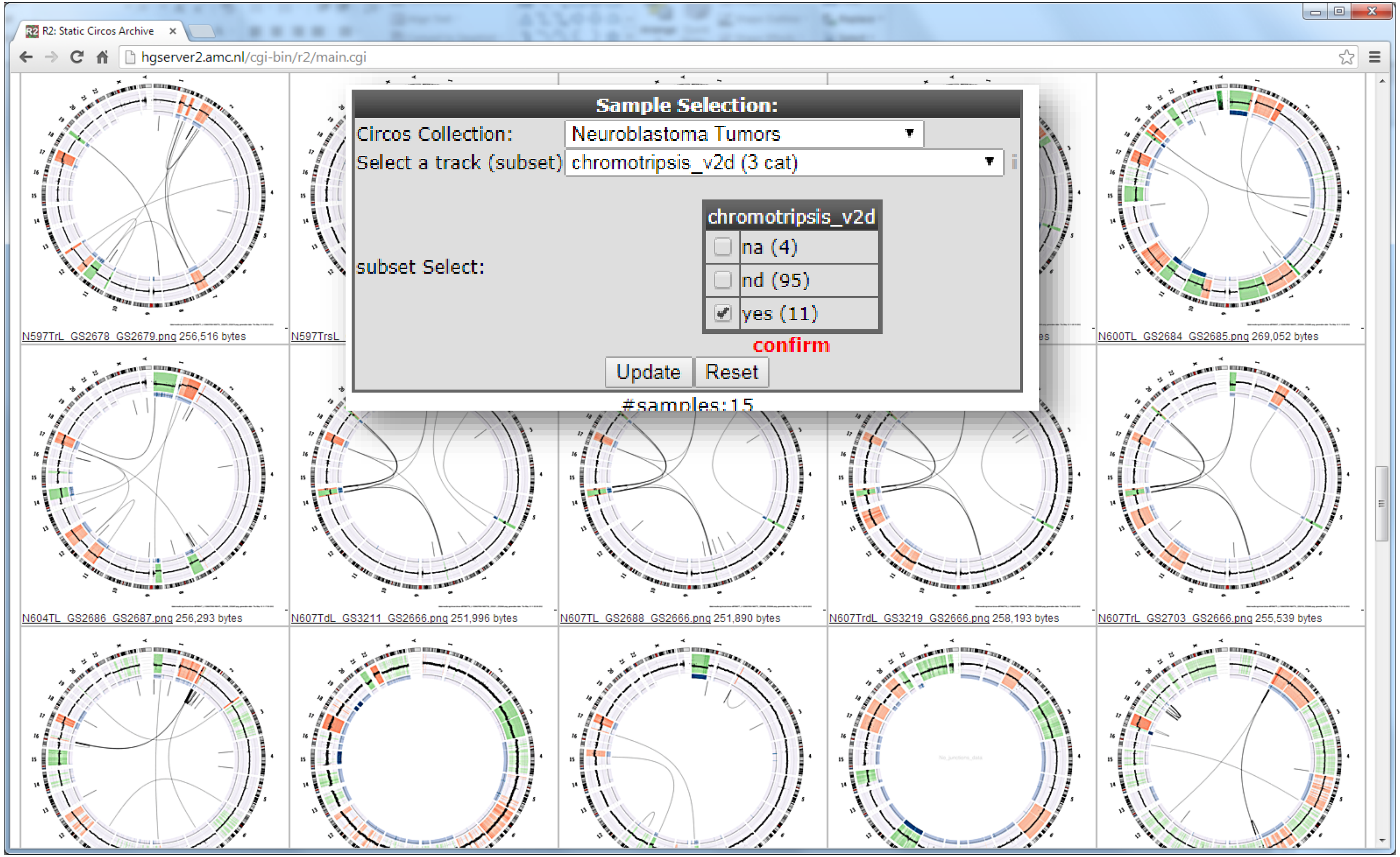
Only ~12 aa affecting mutations

Chromothripsis frequent in high stage disease

Structural variations affecting single genes

Molenaar & Koster et al, Nature, 2012

Whole genome sequencing data in R2



Sample Selection:

Circos Collection: Neuroblastoma Tumors

Select a track (subset) chromotripsis_v2d (3 cat)

subset Select:

chromotripsis_v2d
☐ na (4)
☐ nd (95)
☑ yes (11)

confirm

#samples:15

N597TrL_GS2678_GS2679.png 256,516 bytes

N597TrsL

N600TL_GS2684_GS2685.png 269,052 bytes

N604TL_GS2686_GS2687.png 256,293 bytes

N607TdL_GS3211_GS2666.png 251,996 bytes

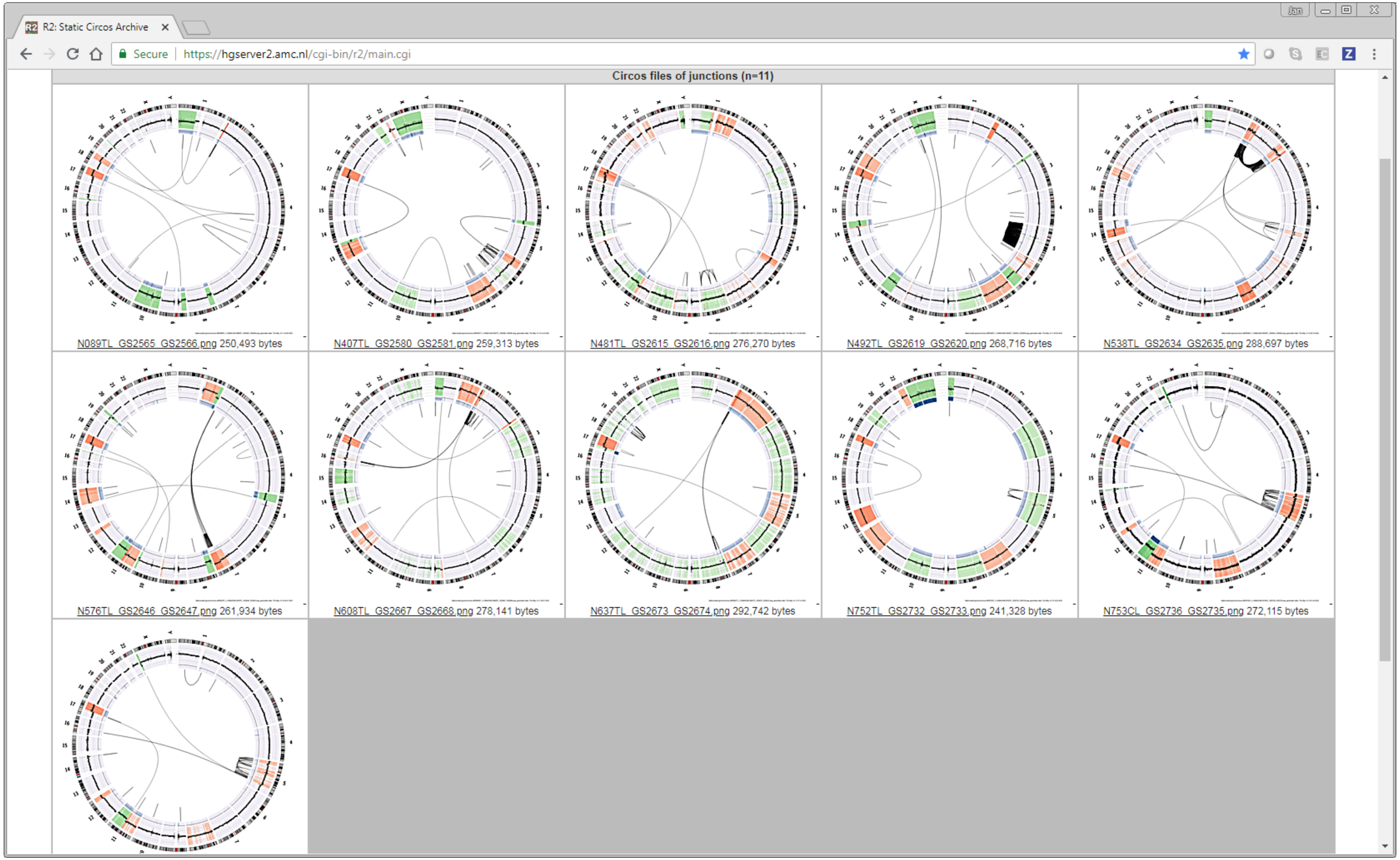
N607TL_GS2688_GS2666.png 251,890 bytes

N607TrdL_GS3219_GS2666.png 258,193 bytes

N607TrL_GS2703_GS2666.png 255,539 bytes

Molenaar & Koster et al, Nature, 2012

Whole genome sequencing data in R2

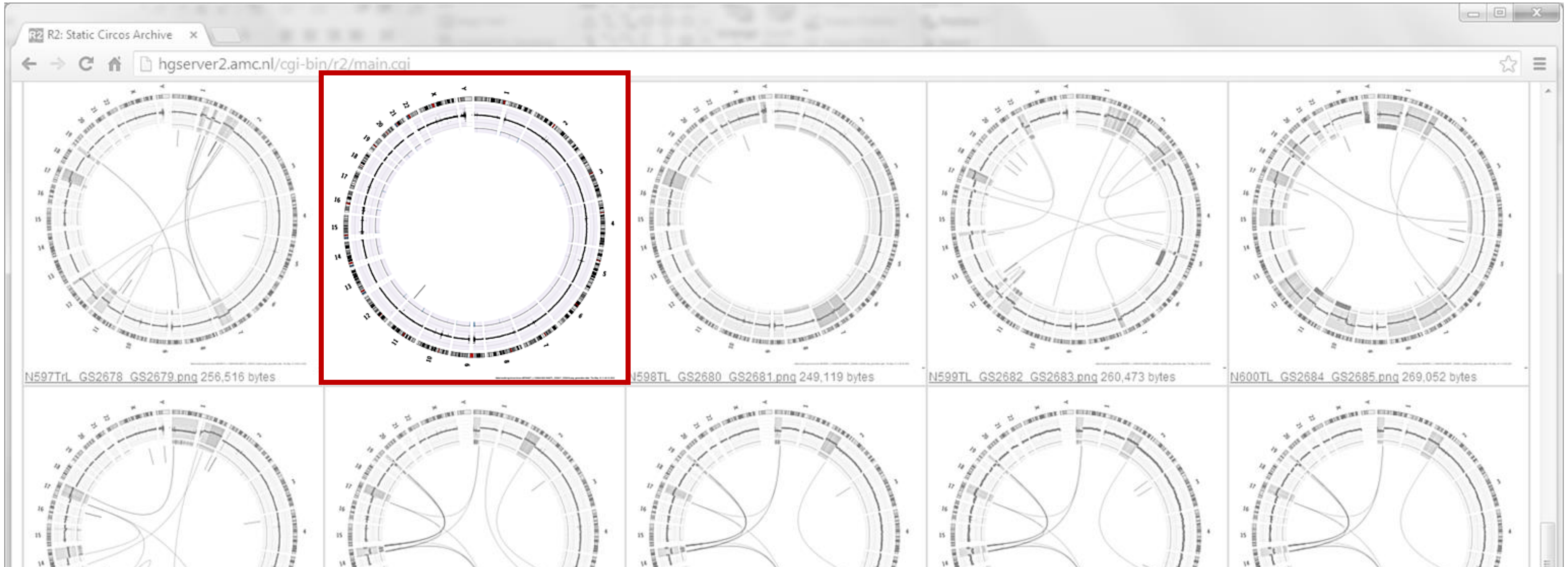


https://hgserver2.amc.nl/cgi-bin/r2/main.cgi

Circos files of junctions (n=11)

N089TL_GS2565_GS2566.png 250,493 bytes
N407TL_GS2580_GS2581.png 259,313 bytes
N481TL_GS2615_GS2616.png 276,270 bytes
N492TL_GS2619_GS2620.png 268,716 bytes
N538TL_GS2634_GS2635.png 288,697 bytes
N576TL_GS2646_GS2647.png 261,934 bytes
N608TL_GS2667_GS2668.png 278,141 bytes
N637TL_GS2673_GS2674.png 292,742 bytes
N752TL_GS2732_GS2733.png 241,328 bytes
N753CL_GS2736_GS2735.png 272,115 bytes

Whole genome sequencing data in R2



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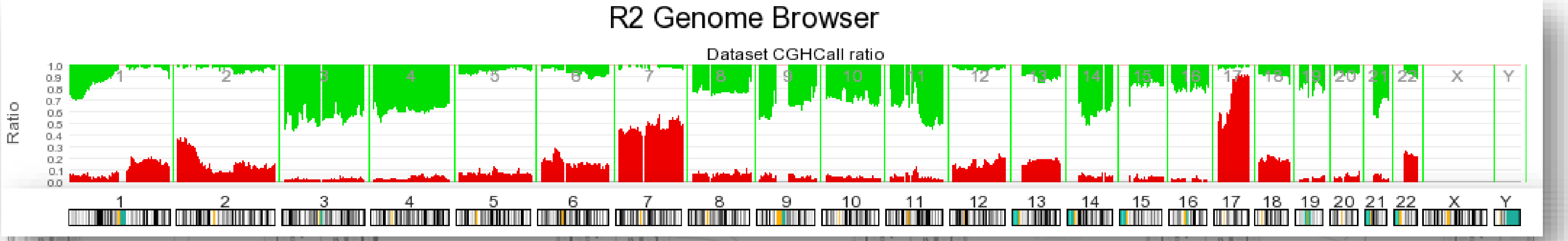
598TL_GS2680_GS2681.png 249,119 bytes

N599TL_GS2682_GS2683.png 260,473 bytes

N600TL_GS2684_GS2685.png 269,052 bytes

Neuroblastoma Tumor DNA Landscape



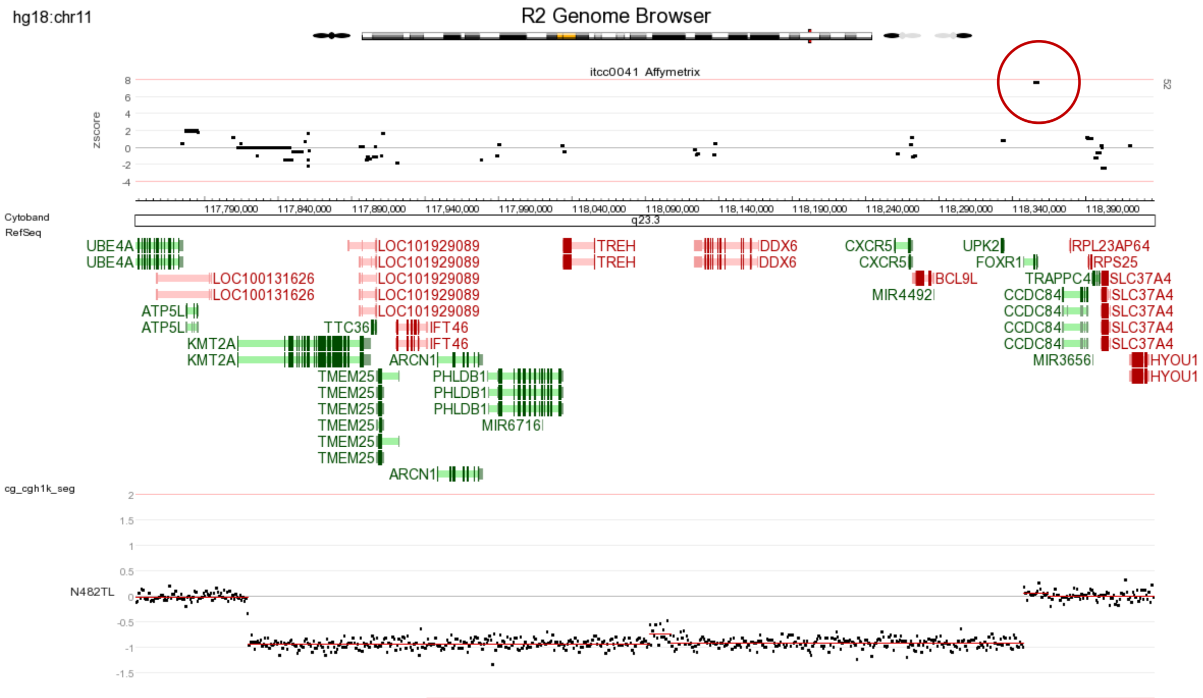
R2 Genome Browser

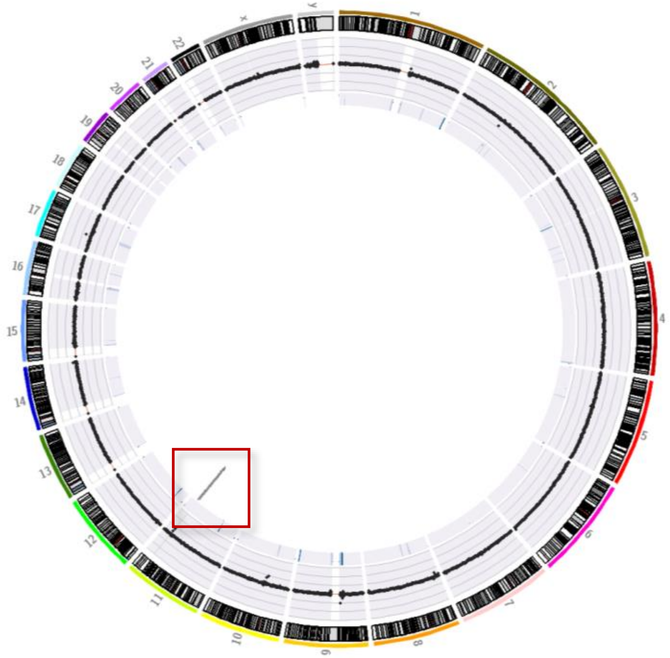
Dataset CGHCall ratio

R2-support@amsterdamumc.nl

R2-Platform

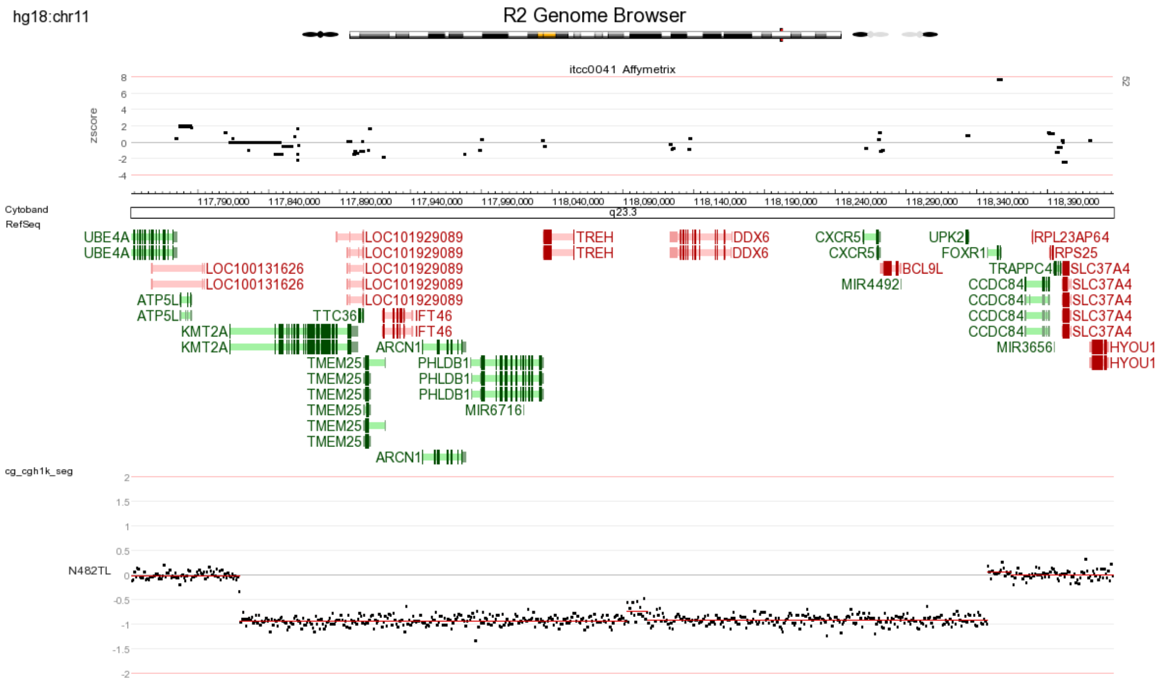
Neuroblastoma patient with single event

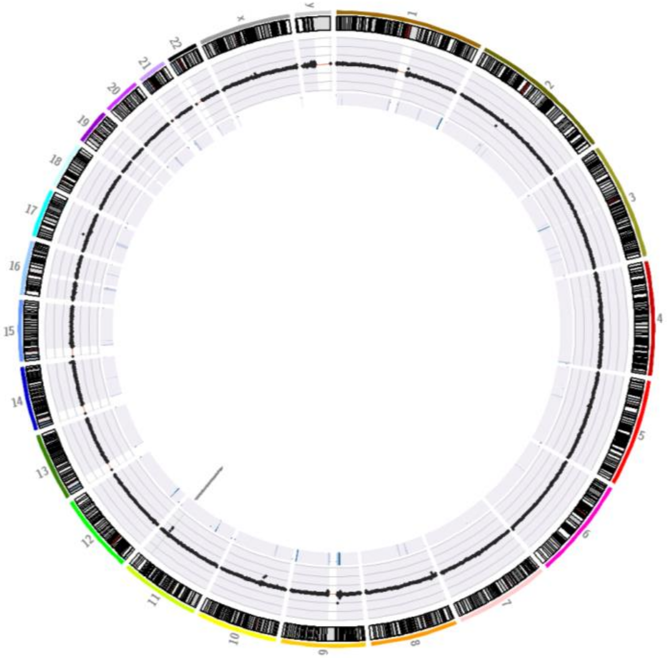


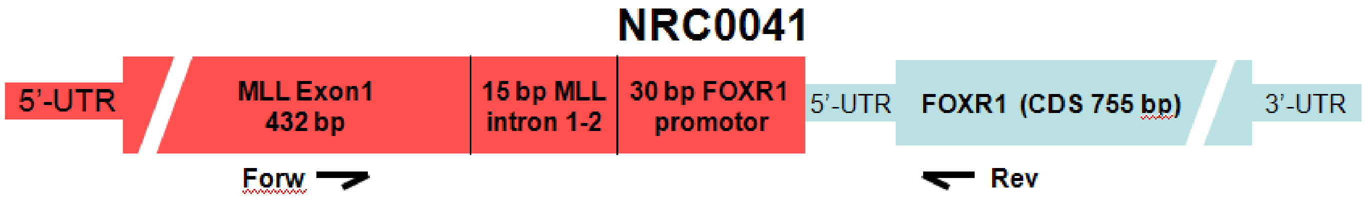


Santo et al, Oncogene, 2012

Neuroblastoma patient with single event





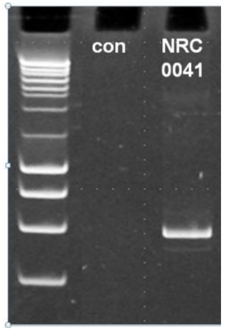


NRC0041

5'-UTR | MLL Exon1 432 bp | 15 bp MLL intron 1-2 | 30 bp FOXR1 promotor | 5'-UTR | FOXR1 (CDS 755 bp) | 3'-UTR

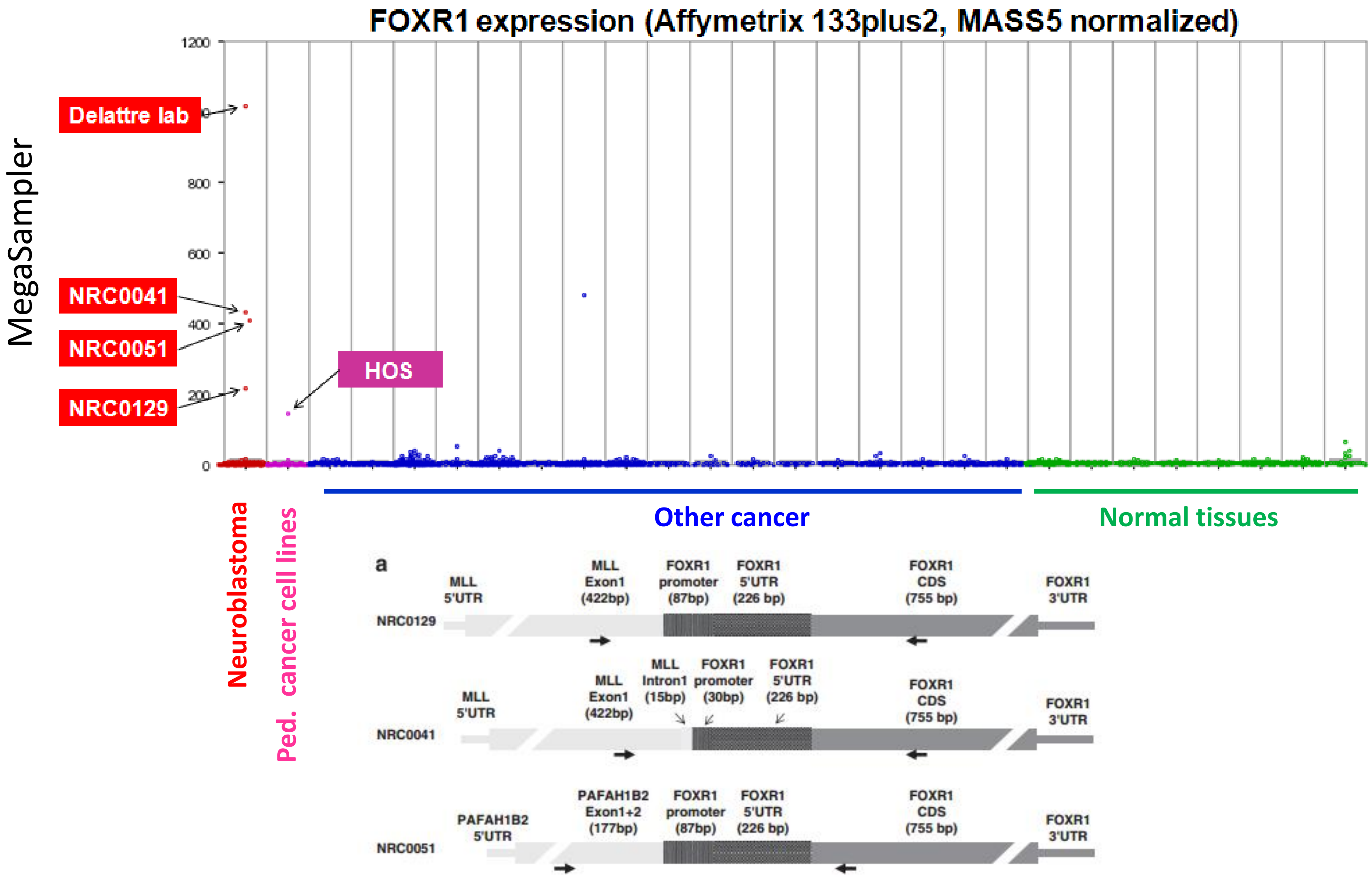
Forw

Rev



Santo et al, Oncogene, 2012

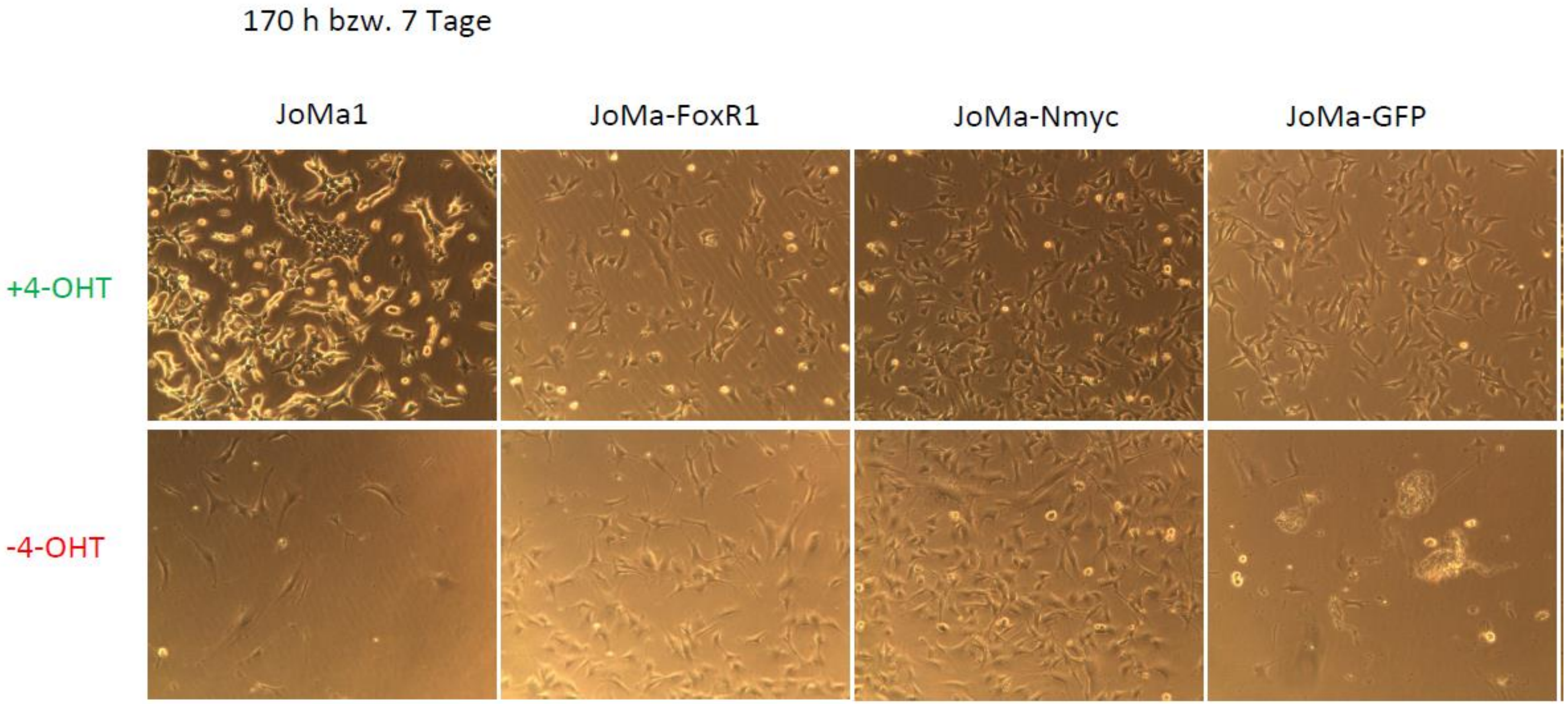
FOXR1 only expressed in combination with Structural Variation



R2-support@amsterda

Santo et al, Oncogene, 2012

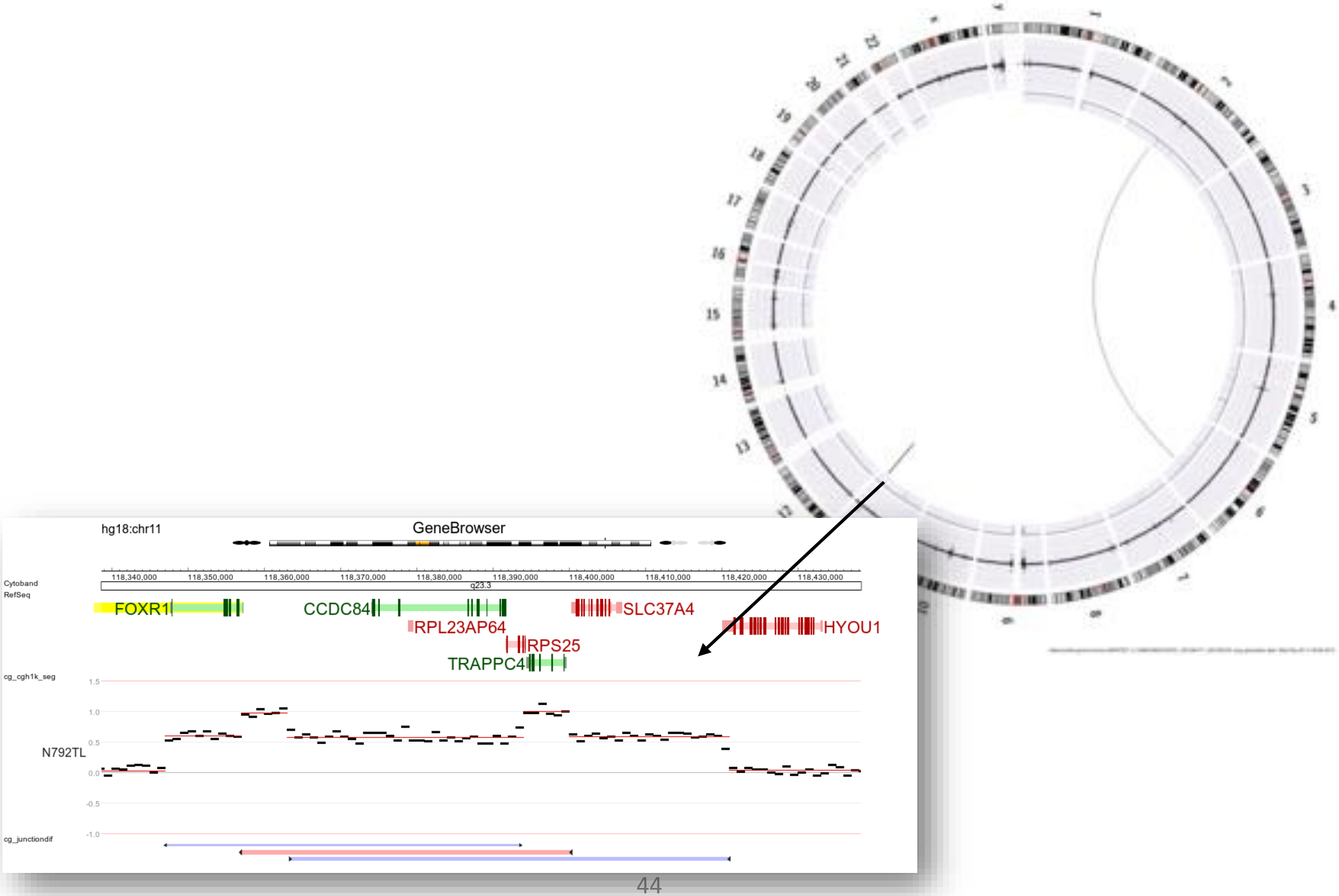
FOXR1 causes growth maintenance in non malignant mouse neuroblasts



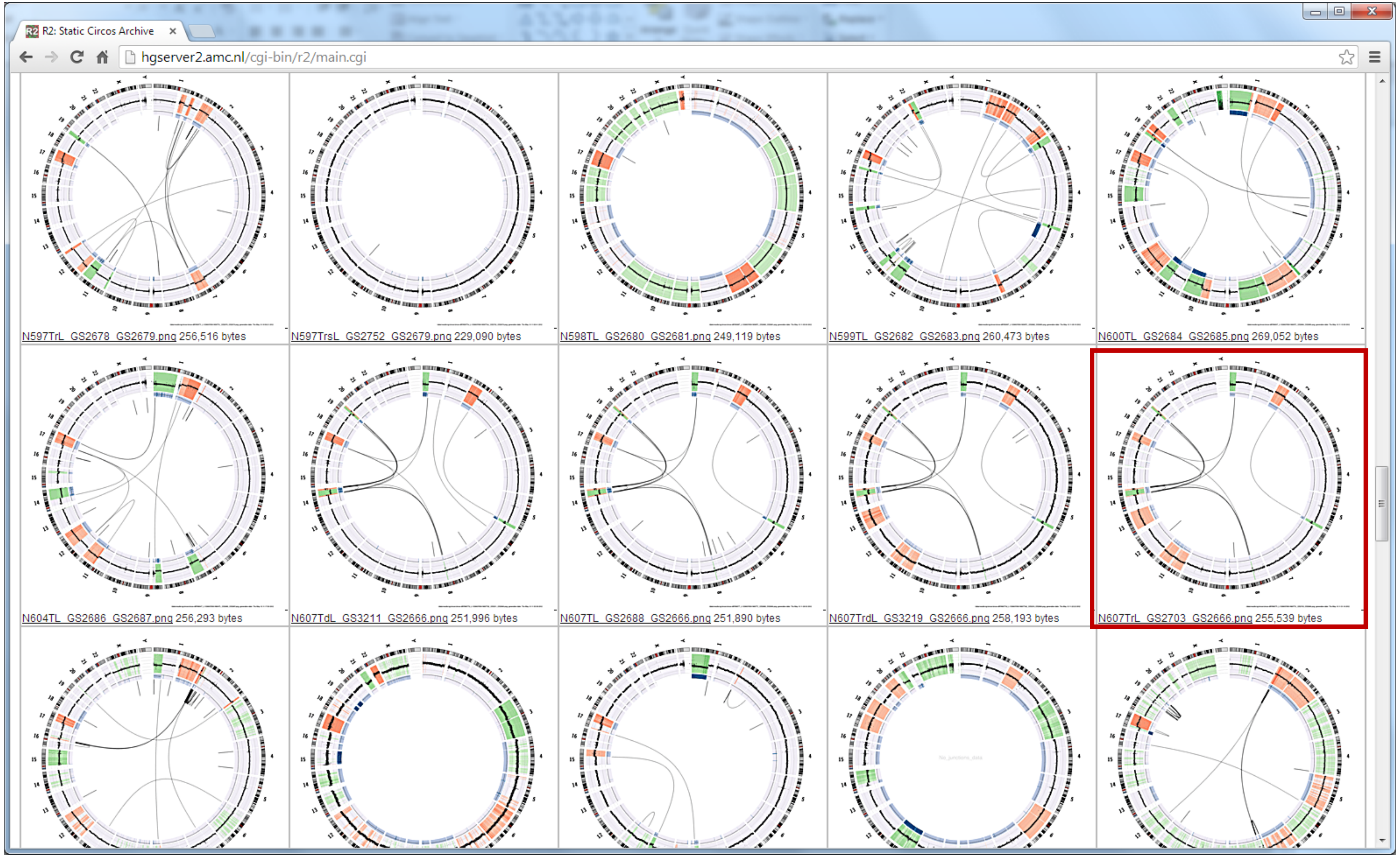
Immortalized by 4-oht regulated cMYC expression
Removal of 4-oht > terminal differentiation

Santo et al, Oncogene, 2012

Later on other patient with only a FOXR1 event



Tumor board Patient overview



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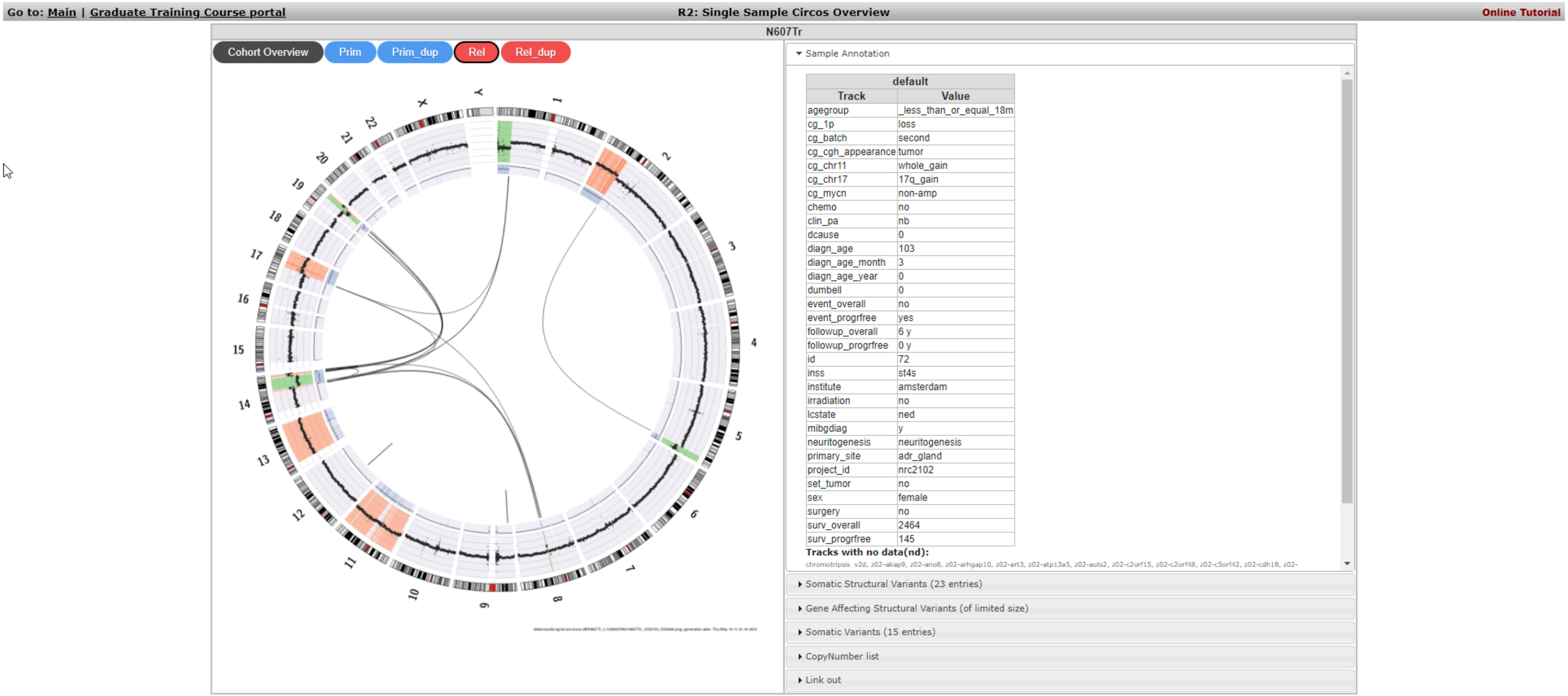
N607TrdL_GS3219_GS2666.png 258,193 bytes

N607TrL_GS2703_GS2666.png 255,539 bytes

R2-support@amsterdamumc.nl

R2-Platform

Patient overview

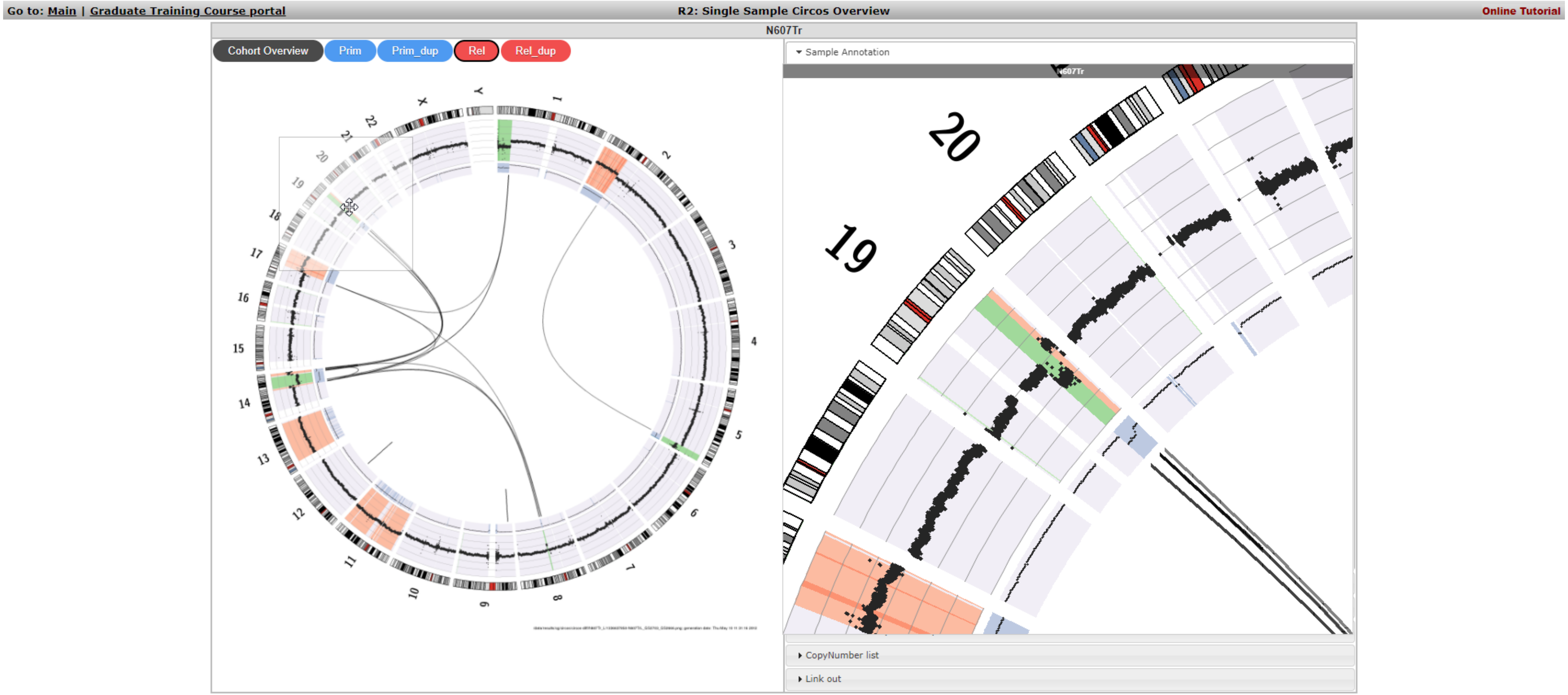


default	
Track	**Value**
agegroup	_less_than_or_equal_18m
cg_1p	loss
cg_batch	second
cg_cgh_appearance	tumor
cg_chr11	whole_gain
cg_chr17	17q_gain
cg_mycn	non-amp
chemo	no
clin_pa	nb
dcause	0
diagn_age	103
diagn_age_month	3
diagn_age_year	0
dumbell	0
event_overall	no
event_progrfree	yes
followup_overall	6 y
followup_progrfree	0 y
id	72
inss	st4s
institute	amsterdam
irradiation	no
lcstate	ned
mibgdiag	y
neuritogenesis	neuritogenesis
primary_site	adr_gland
project_id	nrc2102
set_tumor	no
sex	female
surgery	no
surv_overall	2464
surv_progrfree	145

Tracks with no data(nd):

chromotripsis_v2d, z02-akap9, z02-ano8, z02-arhgap10, z02-art3, z02-atp13a5, z02-auts2, z02-c2orf15, z02-c2orf48, z02-c5orf42, z02-cdh18, z02-

Patient overview



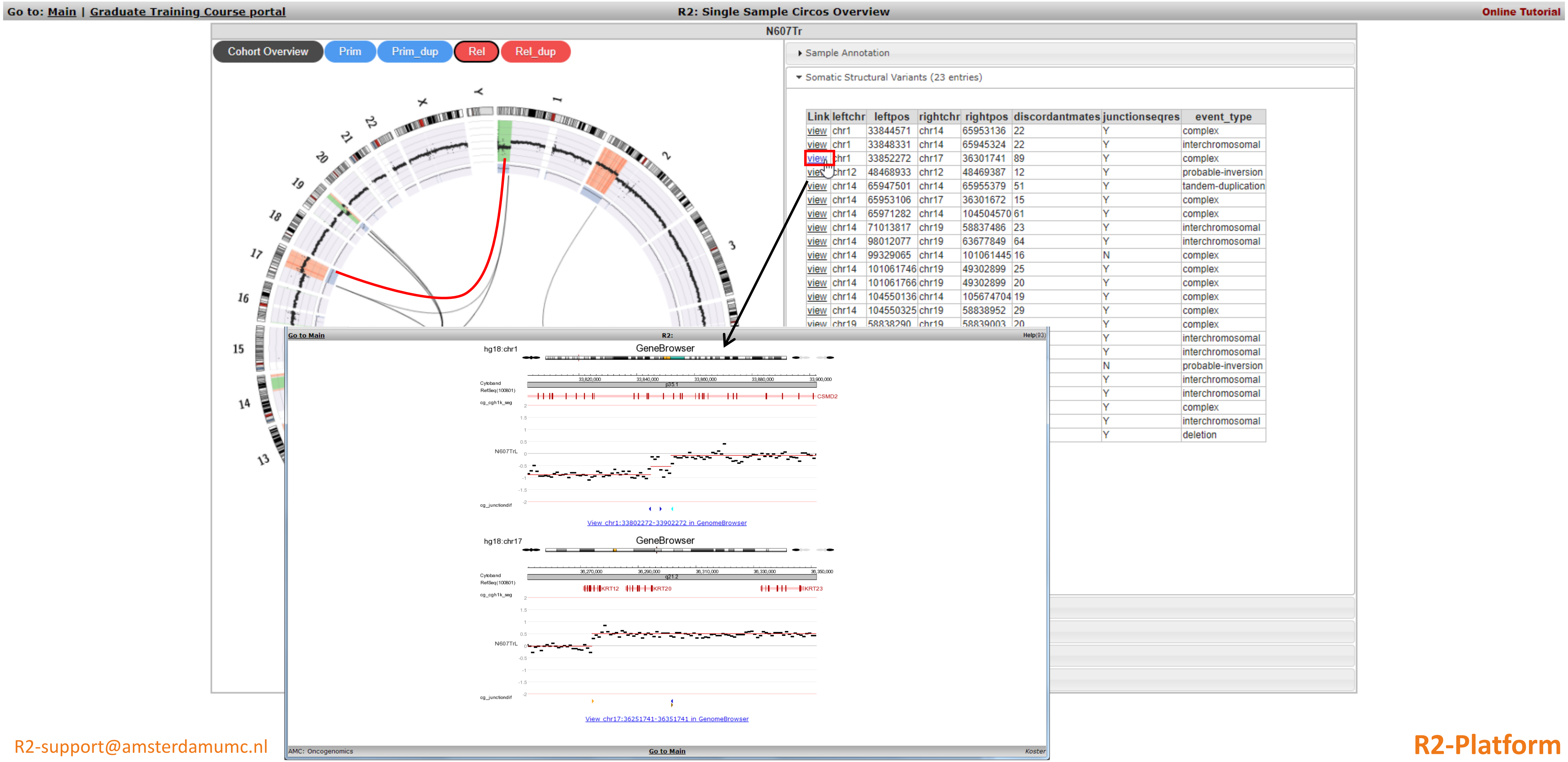
Go to: Main | Graduate Training Course portal

R2: Single Sample Circos Overview

Online Tutorial

N607Tr

Patient overview



Link	leftchr	leftpos	rightchr	rightpos	discordantmates	junctionseqres	event_type
view	chr1	33844571	chr14	65953136	22	Y	complex
view	chr1	33848331	chr14	65945324	22	Y	interchromosomal
view	chr1	33852272	chr17	36301741	89	Y	complex
view	chr12	48468933	chr12	48469387	12	Y	probable-inversion
view	chr14	65947501	chr14	65955379	51	Y	tandem-duplication
view	chr14	65953106	chr17	36301672	15	Y	complex
view	chr14	65971282	chr14	104504570	61	Y	complex
view	chr14	71013817	chr19	58837486	23	Y	interchromosomal
view	chr14	98012077	chr19	63677849	64	Y	interchromosomal
view	chr14	99329065	chr14	101061445	16	N	complex
view	chr14	101061746	chr19	49302899	25	Y	complex
view	chr14	101061766	chr19	49302899	20	Y	complex
view	chr14	104550136	chr14	105674704	19	Y	complex
view	chr14	104550325	chr19	58838952	29	Y	complex
view	chr19	58838290	chr19	58839003	20	Y	complex
						Y	interchromosomal
						Y	interchromosomal
						N	probable-inversion
						Y	interchromosomal
						Y	interchromosomal
						Y	complex
						Y	interchromosomal
						Y	deletion

View chr1:33802272-33902272 in GenomeBrowser

View chr17:36251741-36351741 in GenomeBrowser

Patient overview

R2:

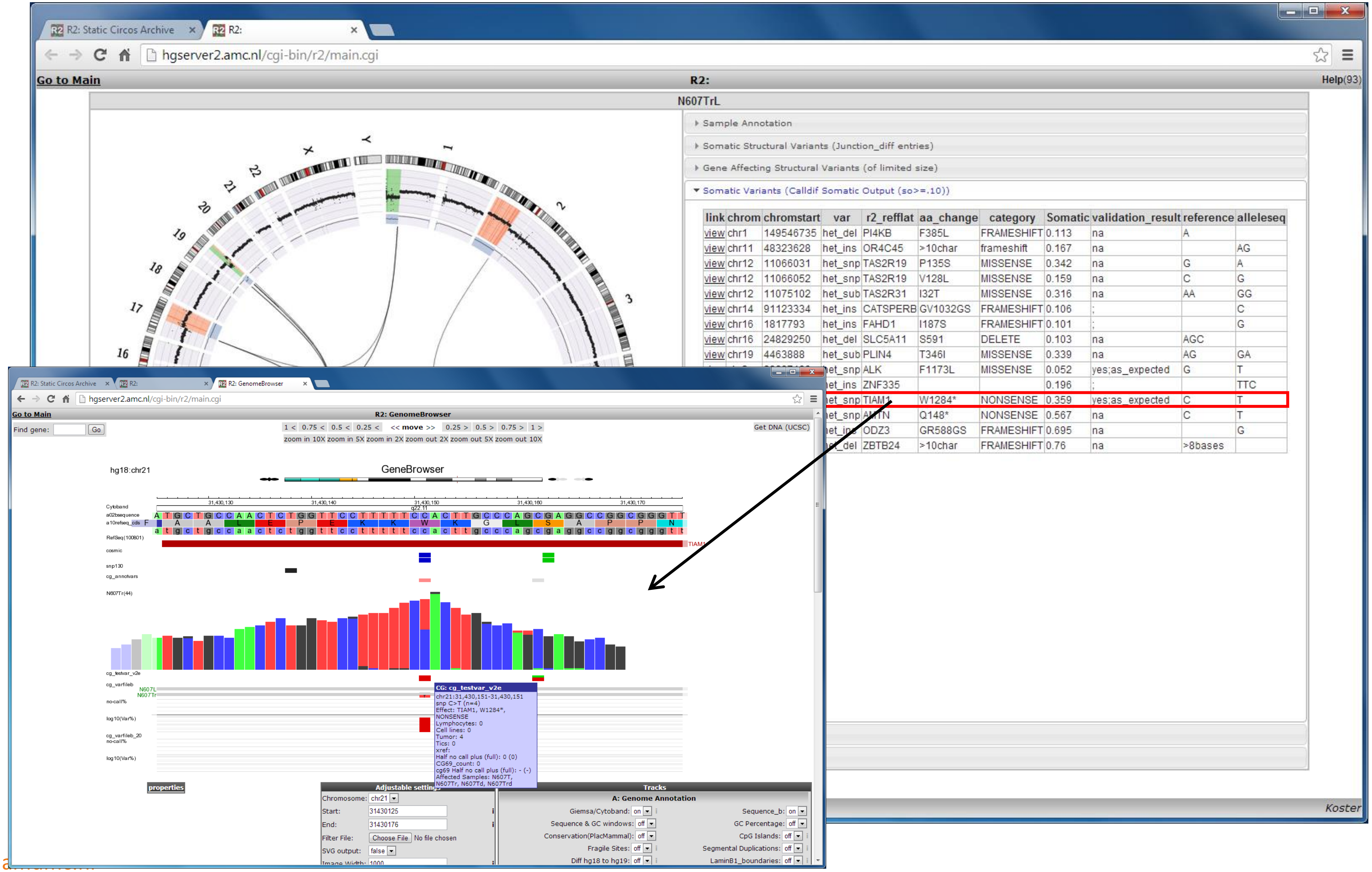
N607TrL

- Sample Annotation
- Somatic Structural Variants (Junction_diff entries)
- Gene Affecting Structural Variants (of limited size)

int_class	leftid	rightid	str_con	distance	mates	seqres	event_type	left_r2gene	right_r2_gene	exon_bite
potential_fusion-strand_match	chr8:63719834 -	chr17:36274286 +	N	0	72	Y	interchr	NKAIN3:+	KRT12:-	-
genes_in_region (<2mb)	chr14:99329065 -	chr14:101061445 -	Y	1732380	16	N	complex			-
genes_in_region (<2mb)	chr14:104550136 +	chr14:105674704 -	N	1124568	19	Y	complex	CDCA4:-		-
potential_fusion-strand_mismatch	chr8:63952839 +	chr14:70593474 -	N	0	26	Y	interchr	NKAIN3:+	PCNX:+	-

- Somatic Variants (Calldif Somatic Output (so>=.10))
- ITHER
- Link out

Patient overview



hgserver2.amc.nl/cgi-bin/r2/main.cgi

Go to Main — R2: — Help(93)

N607TrL

- Sample Annotation
- Somatic Structural Variants (Junction_diff entries)
- Gene Affecting Structural Variants (of limited size)
- Somatic Variants (Calldif Somatic Output (so>=.10))

link	chrom	chromstart	var	r2_refflat	aa_change	category	Somatic	validation_result	reference	alleleseq
view	chr1	149546735	het_del	PI4KB	F385L	FRAMESHIFT	0.113	na	A	
view	chr11	48323628	het_ins	OR4C45	>10char	frameshift	0.167	na		AG
view	chr12	11066031	het_snp	TAS2R19	P135S	MISSENSE	0.342	na	G	A
view	chr12	11066052	het_snp	TAS2R19	V128L	MISSENSE	0.159	na	C	G
view	chr12	11075102	het_sub	TAS2R31	I32T	MISSENSE	0.316	na	AA	GG
view	chr14	91123334	het_ins	CATSPERB	GV1032GS	FRAMESHIFT	0.106	;		C
view	chr16	1817793	het_ins	FAHD1	I187S	FRAMESHIFT	0.101	;		G
view	chr16	24829250	het_del	SLC5A11	S591	DELETE	0.103	na	AGC	
view	chr19	4463888	het_sub	PLIN4	T346I	MISSENSE	0.339	na	AG	GA
			et_snp	ALK	F1173L	MISSENSE	0.052	yes;as_expected	G	T
			et_ins	ZNF335			0.196	;		TTC
			et_snp	TIAM1	W1284*	NONSENSE	0.359	yes;as_expected	C	T
			et_snp	AMTN	Q148*	NONSENSE	0.567	na	C	T
			et_ins	ODZ3	GR588GS	FRAMESHIFT	0.695	na		G
			et_del	ZBTB24	>10char	FRAMESHIFT	0.76	na	>8bases	

R2: GenomeBrowser

Find gene: Go

Get DNA (UCSC)

hg18:chr21

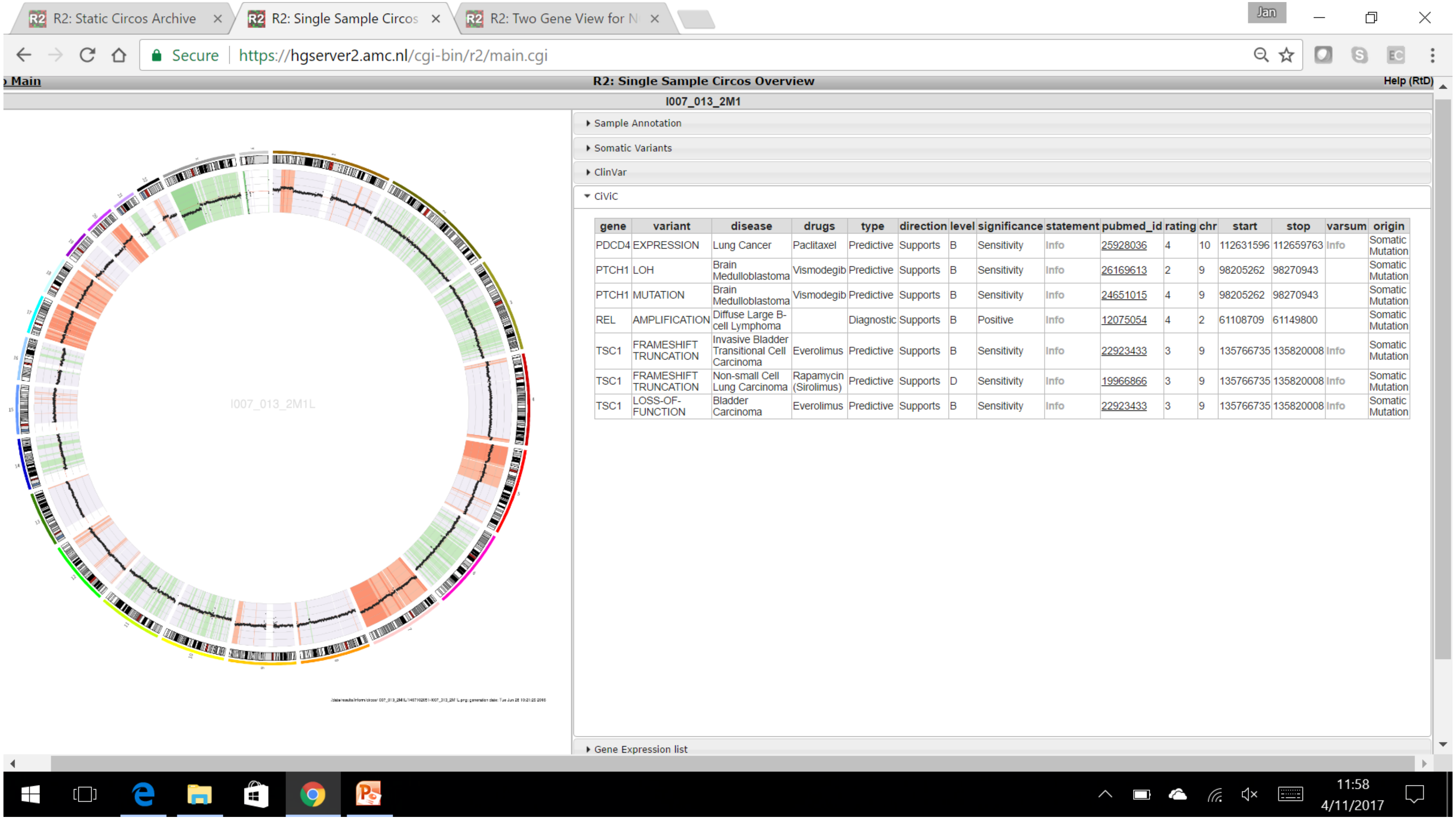
GeneBrowser

CG: cg_testvar_v2e
chr21:31,430,151-31,430,151
snp C>T (n=4)
Effect: TIAM1, W1284*,
NONSENSE
Lymphocytes: 0
Cell lines: 0
Tumor: 4
Tics: 0
xref:
Half no call plus (full): 0 (0)
CG69_count: 0
cg69 Half no call plus (full): - (-)
Affected Samples: N607T,
N607Tr, N607Td, N607Trd

Adjustable settings

Chromosome: chr21
Start: 31430125
End: 31430176
Filter File: Choose File No file chosen
SVG output: false

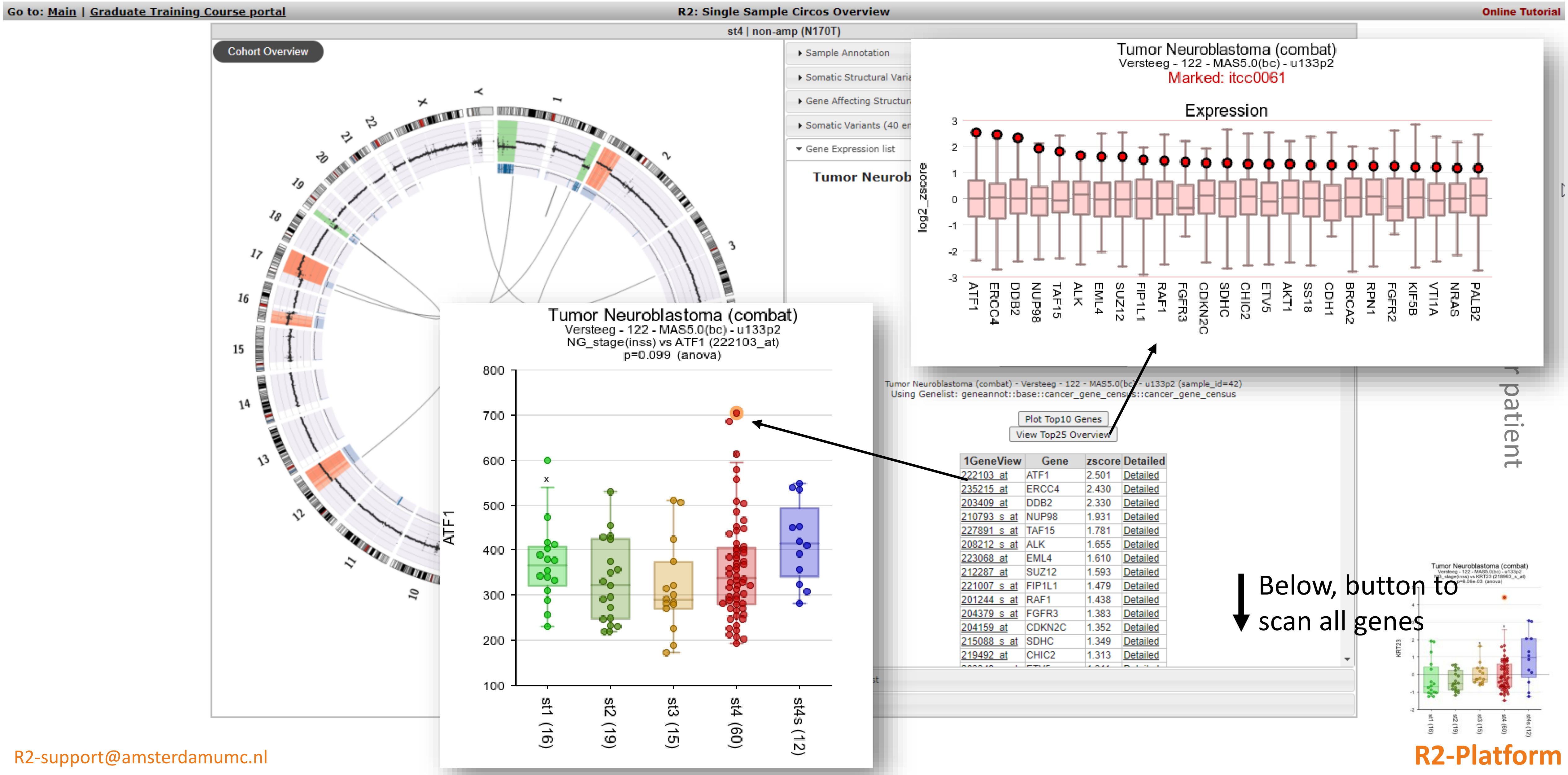
CiViC / Clinvar



gene	variant	disease	drugs	type	direction	level	significance	statement	pubmed_id	rating	chr	start	stop	varsum	origin
PDCD4	EXPRESSION	Lung Cancer	Paclitaxel	Predictive	Supports	B	Sensitivity	Info	25928036	4	10	112631596	112659763	Info	Somatic Mutation
PTCH1	LOH	Brain Medulloblastoma	Vismodegib	Predictive	Supports	B	Sensitivity	Info	26169613	2	9	98205262	98270943		Somatic Mutation
PTCH1	MUTATION	Brain Medulloblastoma	Vismodegib	Predictive	Supports	B	Sensitivity	Info	24651015	4	9	98205262	98270943		Somatic Mutation
REL	AMPLIFICATION	Diffuse Large B-cell Lymphoma		Diagnostic	Supports	B	Positive	Info	12075054	4	2	61108709	61149800		Somatic Mutation
TSC1	FRAMESHIFT TRUNCATION	Invasive Bladder Transitional Cell Carcinoma	Everolimus	Predictive	Supports	B	Sensitivity	Info	22923433	3	9	135766735	135820008	Info	Somatic Mutation
TSC1	FRAMESHIFT TRUNCATION	Non-small Cell Lung Carcinoma	Rapamycin (Sirolimus)	Predictive	Supports	D	Sensitivity	Info	19966866	3	9	135766735	135820008	Info	Somatic Mutation
TSC1	LOSS-OF-FUNCTION	Bladder Carcinoma	Everolimus	Predictive	Supports	B	Sensitivity	Info	22923433	3	9	135766735	135820008	Info	Somatic Mutation

Other patient

Gene Expression

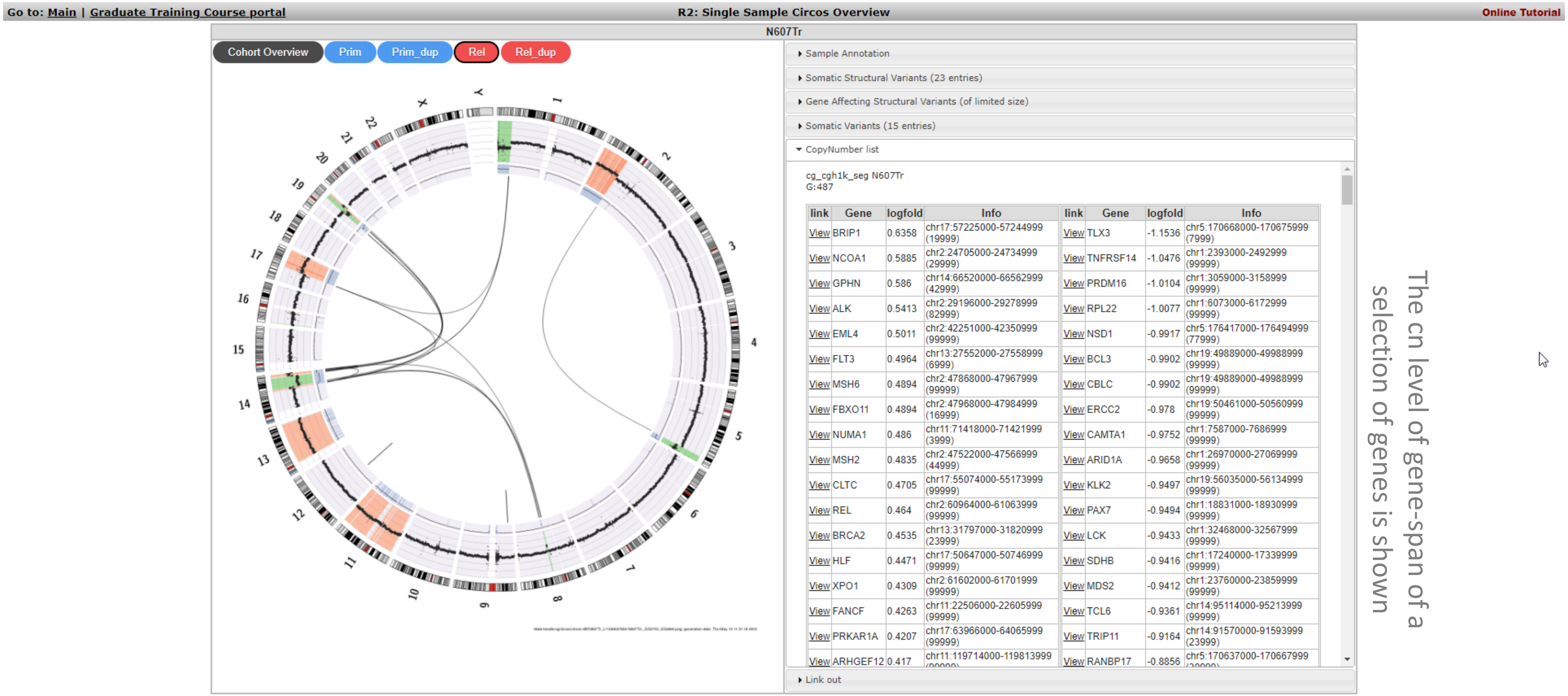


Tumor Neuroblastoma (combat) - Versteeg - 122 - MAS5.0(bc) - u133p2 (sample_id=42)
Using Genelist: geneannot::base::cancer_gene_census::cancer_gene_census

1GeneView	Gene	zscore	Detailed
222103_at	ATF1	2.501	Detailed
235215_at	ERCC4	2.430	Detailed
203409_at	DDB2	2.330	Detailed
210793_s_at	NUP98	1.931	Detailed
227891_s_at	TAF15	1.781	Detailed
208212_s_at	ALK	1.655	Detailed
223068_at	EML4	1.610	Detailed
212287_at	SUZ12	1.593	Detailed
221007_s_at	FIP1L1	1.479	Detailed
201244_s_at	RAF1	1.438	Detailed
204379_s_at	FGFR3	1.383	Detailed
204159_at	CDKN2C	1.352	Detailed
215088_s_at	SDHC	1.349	Detailed
219492_at	CHIC2	1.313	Detailed

Below, button to scan all genes

Copy number events by genes



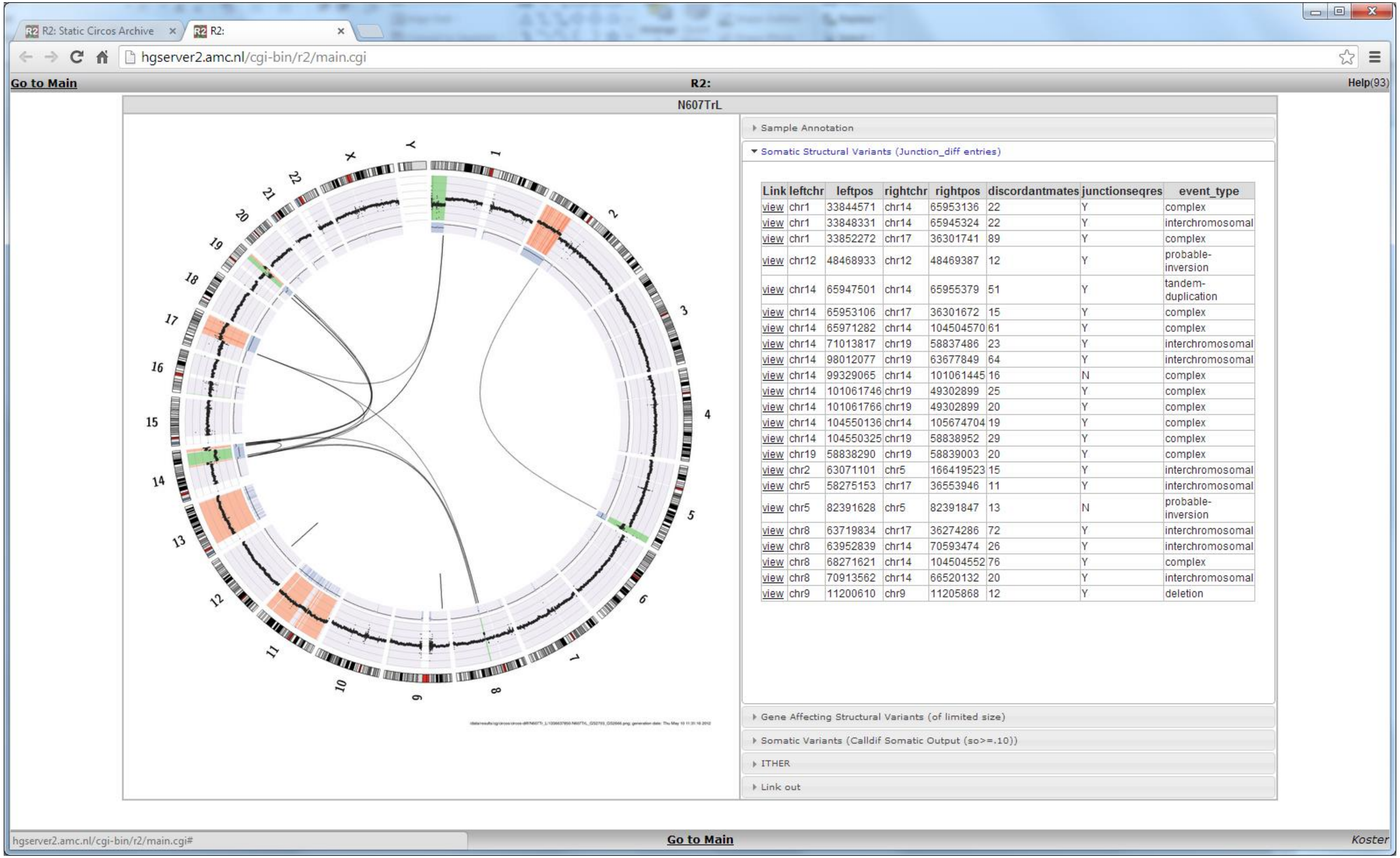
cg_cgh1k_seg N607Tr
G:487

link	Gene	logfold	Info
View	BRIP1	0.6358	chr17:57225000-57244999 (19999)
View	NCOA1	0.5885	chr2:24705000-24734999 (29999)
View	GPHN	0.586	chr14:66520000-66562999 (42999)
View	ALK	0.5413	chr2:29196000-29278999 (82999)
View	EML4	0.5011	chr2:42251000-42350999 (99999)
View	FLT3	0.4964	chr13:27552000-27558999 (6999)
View	MSH6	0.4894	chr2:47868000-47967999 (99999)
View	FBXO11	0.4894	chr2:47968000-47984999 (16999)
View	NUMA1	0.486	chr11:71418000-71421999 (3999)
View	MSH2	0.4835	chr2:47522000-47566999 (44999)
View	CLTC	0.4705	chr17:55074000-55173999 (99999)
View	REL	0.464	chr2:60964000-61063999 (99999)
View	BRCA2	0.4535	chr13:31797000-31820999 (23999)
View	HLF	0.4471	chr17:50647000-50746999 (99999)
View	XPO1	0.4309	chr2:61602000-61701999 (99999)
View	FANCF	0.4263	chr11:22506000-22605999 (99999)
View	PRKAR1A	0.4207	chr17:63966000-64065999 (99999)
View	ARHGEF12	0.417	chr11:119714000-119813999

link	Gene	logfold	Info
View	TLX3	-1.1536	chr5:170668000-170675999 (7999)
View	TNFRSF14	-1.0476	chr1:2393000-2492999 (99999)
View	PRDM16	-1.0104	chr1:3059000-3158999 (99999)
View	RPL22	-1.0077	chr1:6073000-6172999 (99999)
View	NSD1	-0.9917	chr5:176417000-176494999 (77999)
View	BCL3	-0.9902	chr19:49889000-49988999 (99999)
View	CBLC	-0.9902	chr19:49889000-49988999 (99999)
View	ERCC2	-0.978	chr19:50461000-50560999 (99999)
View	CAMTA1	-0.9752	chr1:7587000-7686999 (99999)
View	ARID1A	-0.9658	chr1:26970000-27069999 (99999)
View	KLK2	-0.9497	chr19:56035000-56134999 (99999)
View	PAX7	-0.9494	chr1:18831000-18930999 (99999)
View	LCK	-0.9433	chr1:32468000-32567999 (99999)
View	SDHB	-0.9416	chr1:17240000-17339999 (99999)
View	MDS2	-0.9412	chr1:23760000-23859999 (99999)
View	TCL6	-0.9361	chr14:95114000-95213999 (99999)
View	TRIP11	-0.9164	chr14:91570000-91593999 (23999)
View	RANBP17	-0.8856	chr5:170637000-170667999

The cn level of gene-span of a selection of genes is shown

Structural Variations



Somatic Structural Variants (Junction_diff entries)

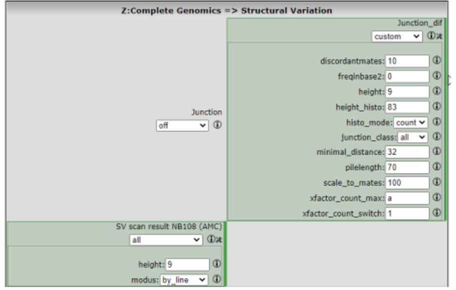
Link	leftchr	leftpos	rightchr	rightpos	discordantmates	junctionseqres	event_type
view	chr1	33844571	chr14	65953136	22	Y	complex
view	chr1	33848331	chr14	65945324	22	Y	interchromosomal
view	chr1	33852272	chr17	36301741	89	Y	complex
view	chr12	48468933	chr12	48469387	12	Y	probable-inversion
view	chr14	65947501	chr14	65955379	51	Y	tandem-duplication
view	chr14	65953106	chr17	36301672	15	Y	complex
view	chr14	65971282	chr14	104504570	61	Y	complex
view	chr14	71013817	chr19	58837486	23	Y	interchromosomal
view	chr14	98012077	chr19	63677849	64	Y	interchromosomal
view	chr14	99329065	chr14	101061445	16	N	complex
view	chr14	101061746	chr19	49302899	25	Y	complex
view	chr14	101061766	chr19	49302899	20	Y	complex
view	chr14	104550136	chr14	105674704	19	Y	complex
view	chr14	104550325	chr19	58838952	29	Y	complex
view	chr19	58838290	chr19	58839003	20	Y	complex
view	chr2	63071101	chr5	166419523	15	Y	interchromosomal
view	chr5	58275153	chr17	36553946	11	Y	interchromosomal
view	chr5	82391628	chr5	82391847	13	N	probable-inversion
view	chr8	63719834	chr17	36274286	72	Y	interchromosomal
view	chr8	63952839	chr14	70593474	26	Y	interchromosomal
view	chr8	68271621	chr14	104504552	76	Y	complex
view	chr8	70913562	chr14	66520132	20	Y	interchromosomal
view	chr9	11200610	chr9	11205868	12	Y	deletion

Valentijn & Koster et al, Nat. Genet, 2015

Scan for Enrichment in SV

- Are there hotspots of SV in the neuroblastoma genome?

R2 genome browser



Z:Complete Genomics => Structural Variation

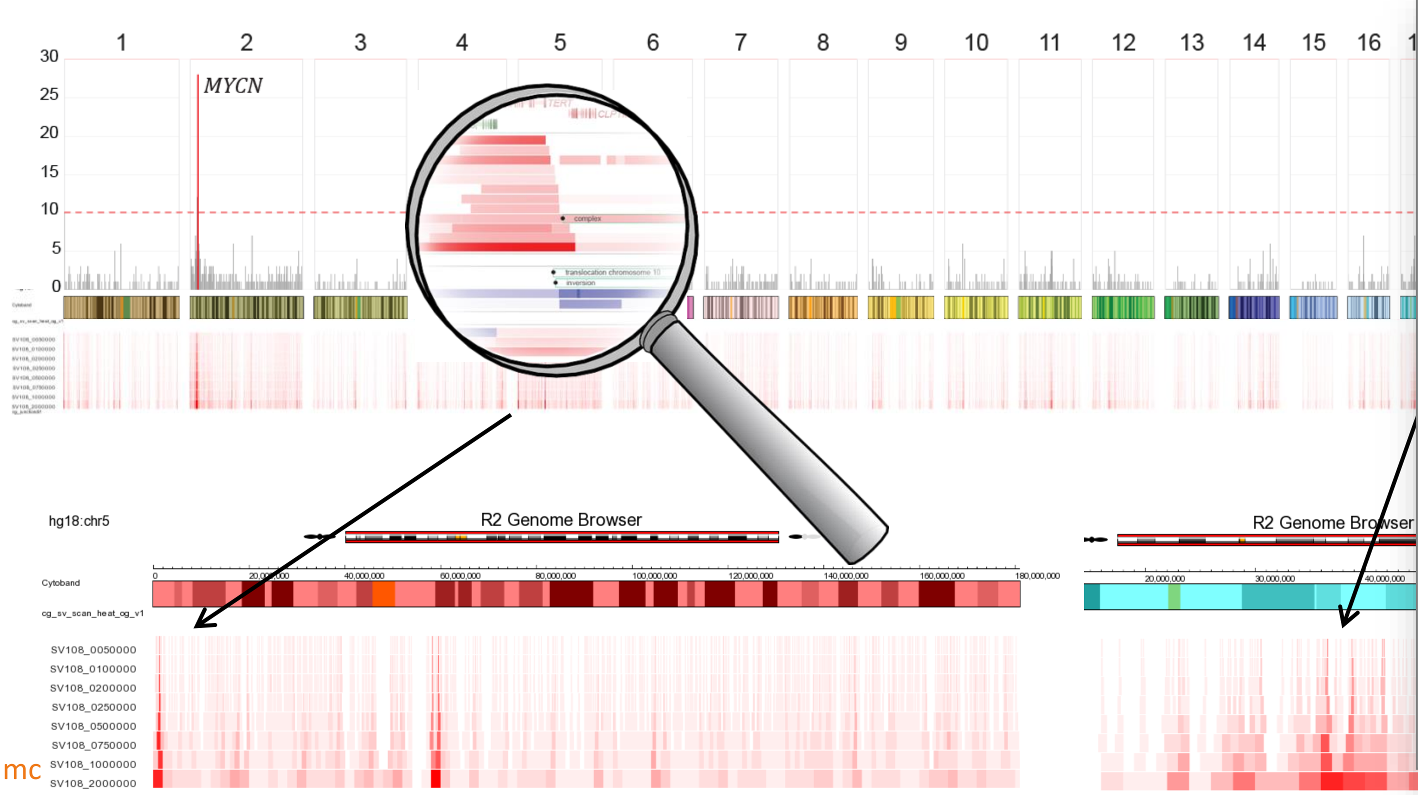
Junction: off

Junction_dif: custom

discordantmates: 10
freqinbase2: 0
height: 9
height_histo: 83
histo_mode: count
junction_class: all
minimal_distance: 32
pilelength: 70
scale_to_mates: 100
xfactor_count_max: a
xfactor_count_switch: 1

SV scan result NB108 (AMC): all

height: 9
modus: by_line



Gene	#_samples	Where
MYCN	28	SURR
TERT	13	US
ATRX	8	INTRA
TENM3	6	INTRA
PDE4D	6	INTRA
PTPRD	6	INTRA
GATA3	5	DS
CCND1	5	US
SHANK2	5	INTRA
PSEN1	5	US
ASCC2	5	INTRA
EIF4E	5	DS
MAML3	4	INTRA
CSMD2	3	INTRA
ADAM12	3	DS
UNC79	3	INTRA
ZFHX3	3	INTRA
ASIC2	3	INTRA
STAG2	3	INTRA

108 selected cases

TERT region has gains, losses and inversions in 23% of high stage NB

Y:Complete Genomics => cgCGH

cgh1k_seg

custom

height:

highest: a

linewidth_segment: a

lowest: -2

modus: colorcode

Valentijn & Koster et al 2015 Nat. Genet

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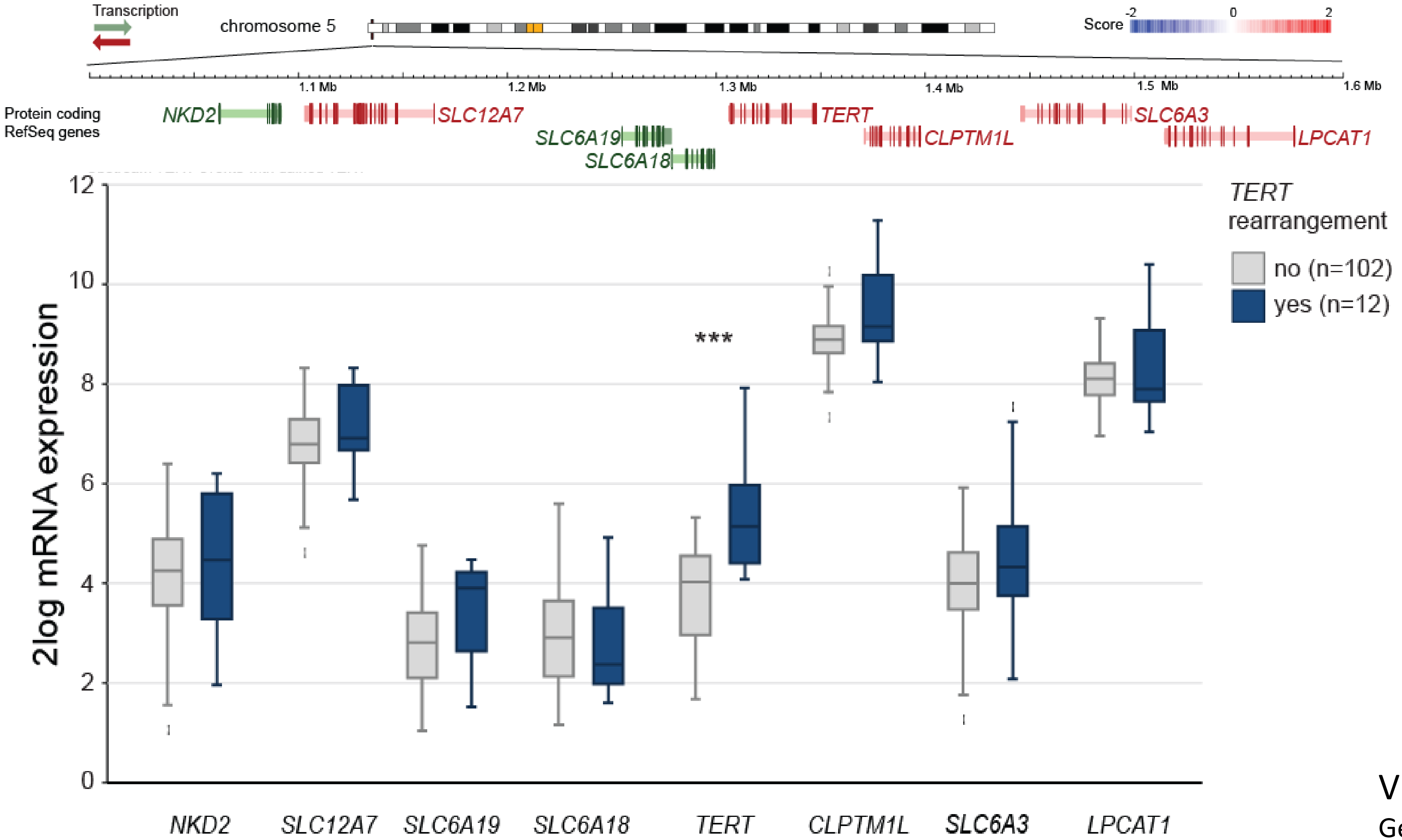
Amsterdam UMC
University Medical Centers

TERT expression affected

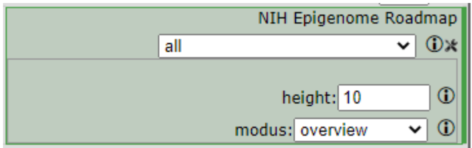


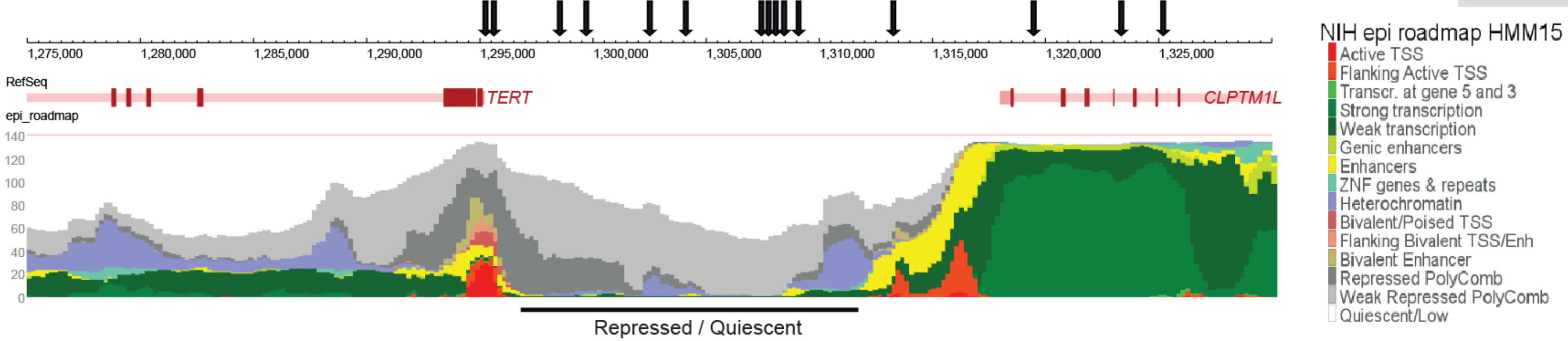
Valentijn & Koster et al 2015 Nat. Genet

View Multiple Genes

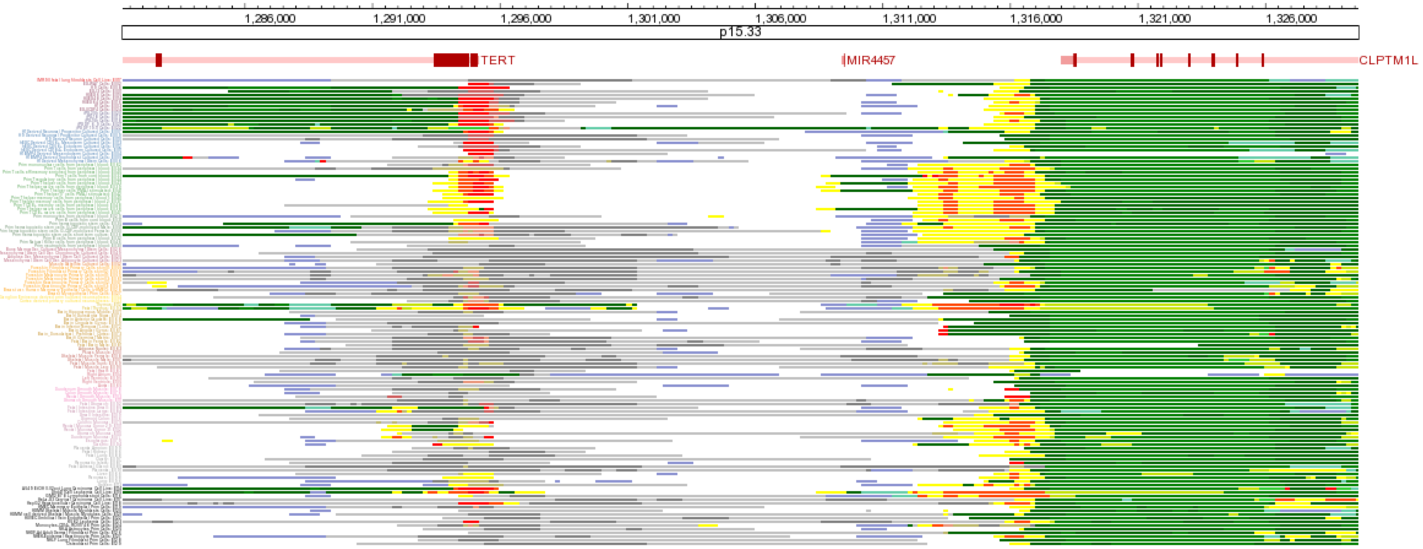
Genes in order of genome

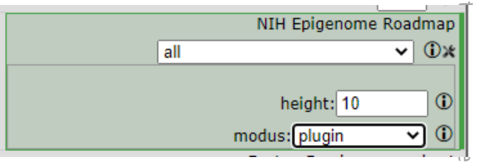
TERT upstream region mostly quiescent / repressed


NIH Epigenome Roadmap
all
height: 10
modus: overview



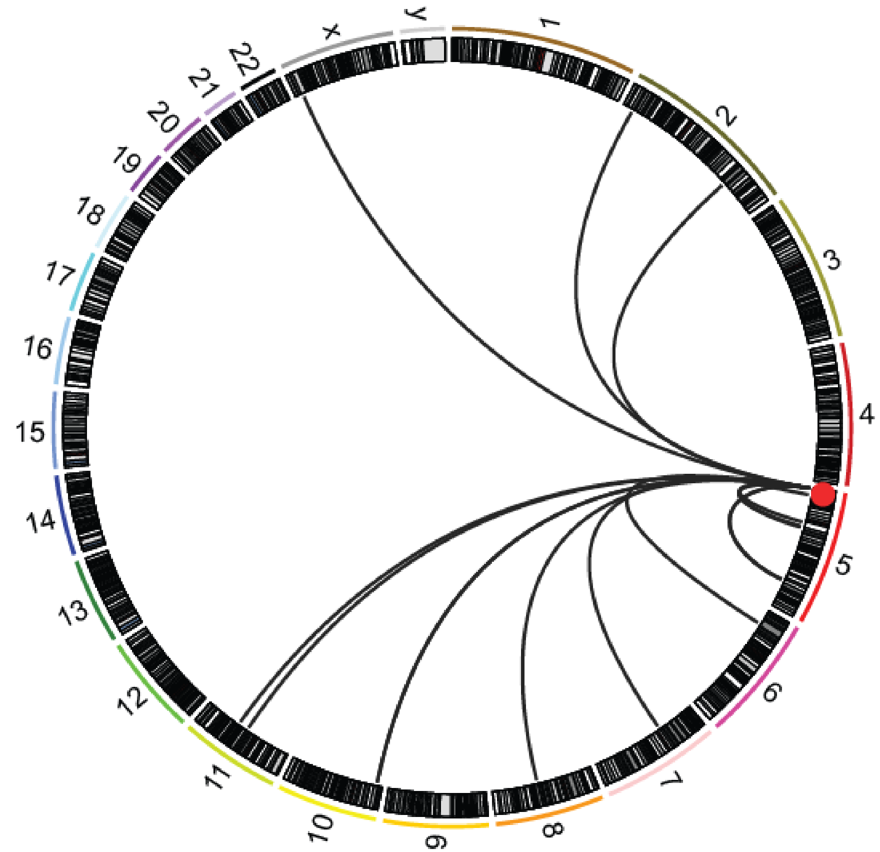
Repressed / Quiescent




NIH Epigenome Roadmap
all
height: 10
modus: plugin

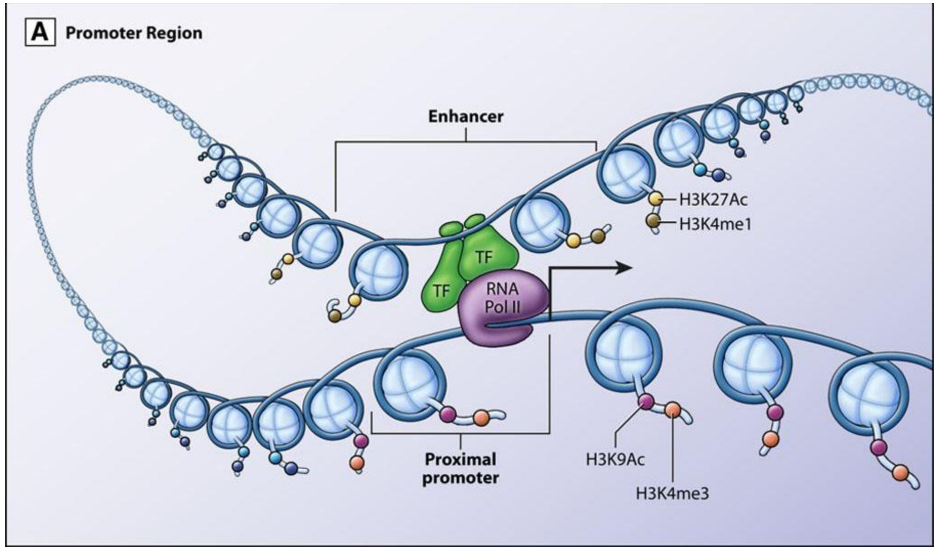
Valentijn & Koster et

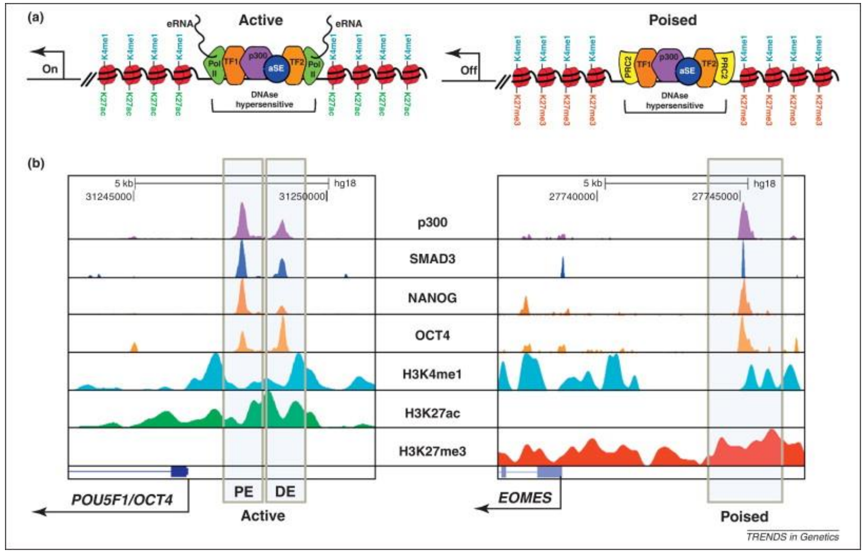
TERT rearrangements have many different translocation partners



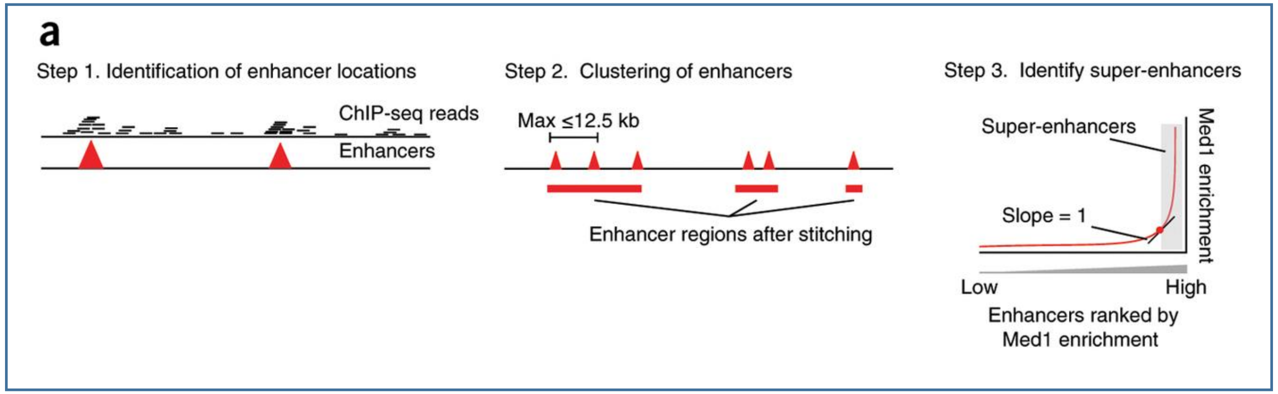
Valentijn & Koster et al 2015 Nat. Genet

Enhancers





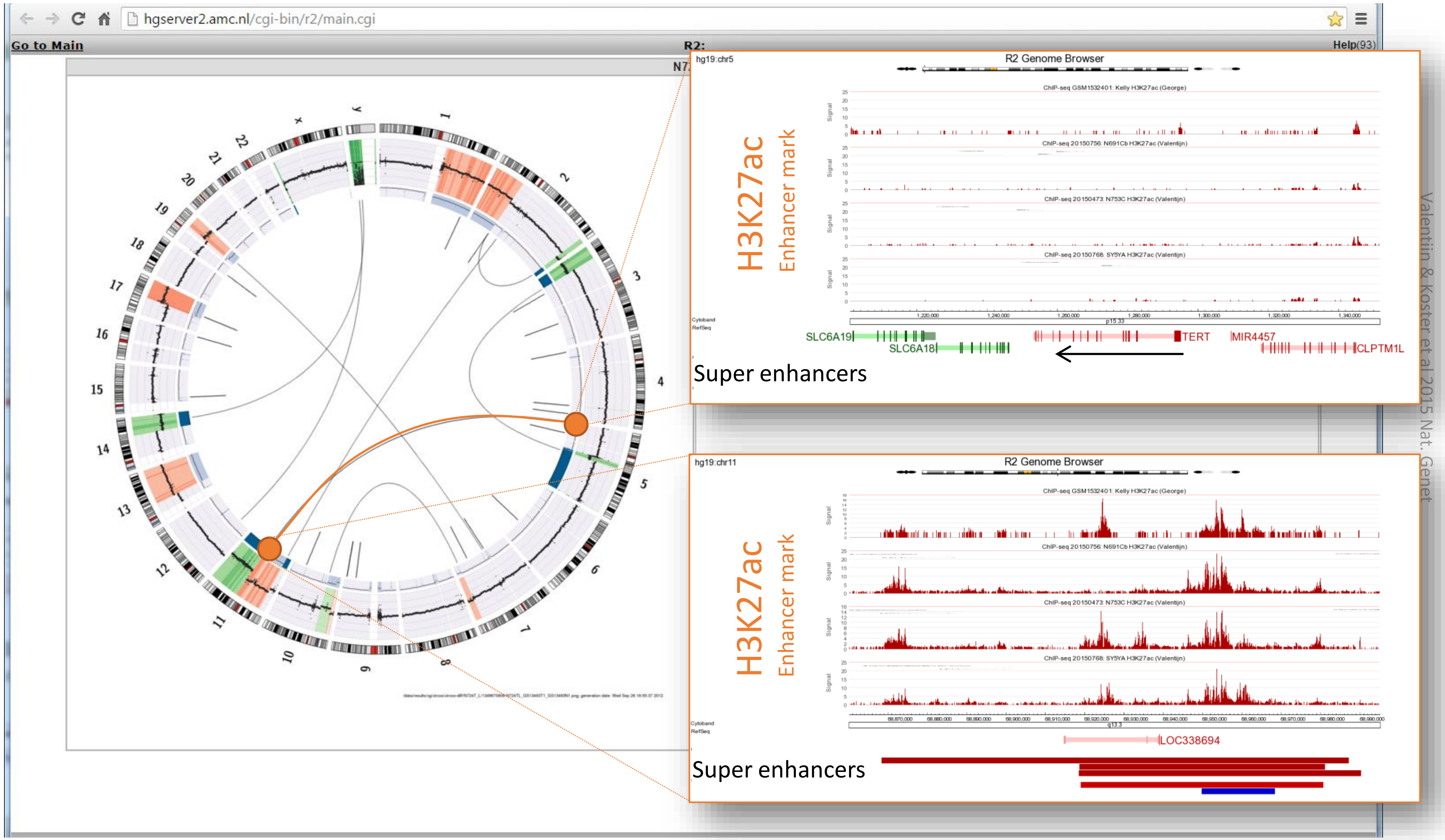
Active enhancers are marked by H3K27Ac



Super Enhancers are the most ‘active / enriched’ enhancers

http://atvb.ahajournals.org/content/35/11/2297
http://www.nature.com/ng/journal/v47/n1/full/ng.3167.html
http://www.cell.com/trends/genetics/fulltext/S0168-9525(12)00033-9

TERT translocates to super-enhancers



Valentijn & Koster et al 2015 Nat. Genet

We will cover ChIP profiles later

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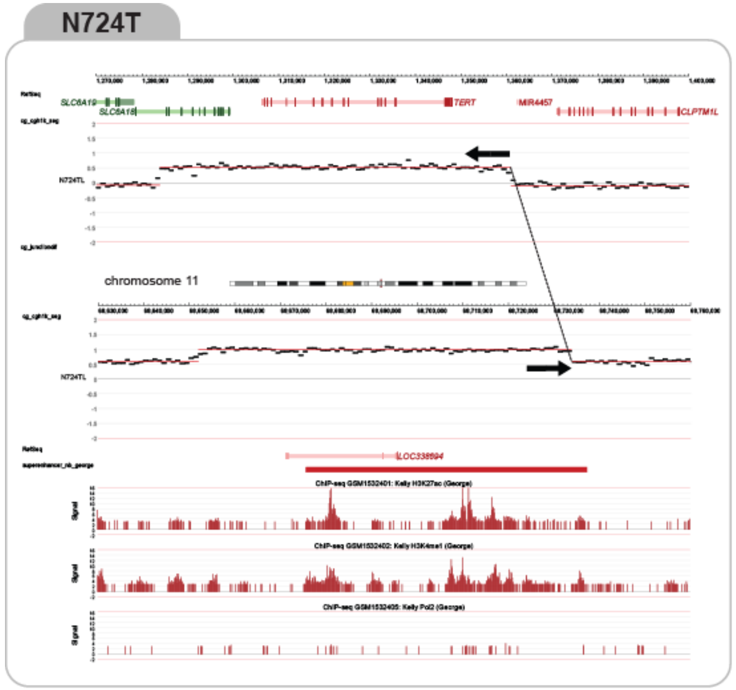
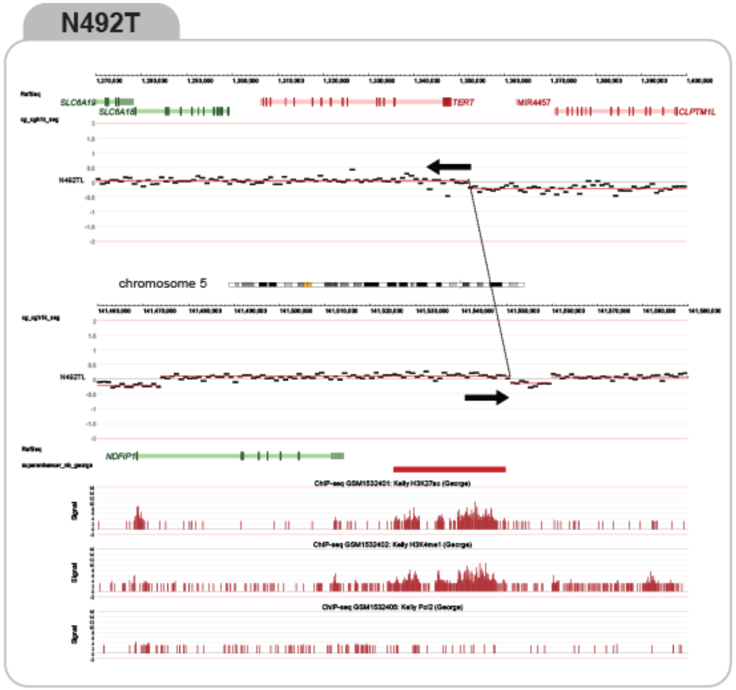
R2-Platform

TERT translocates to super-enhancers

Valentijn & Koster et al, Nat. Genet, 2015

TERT translocates to super-enhancers



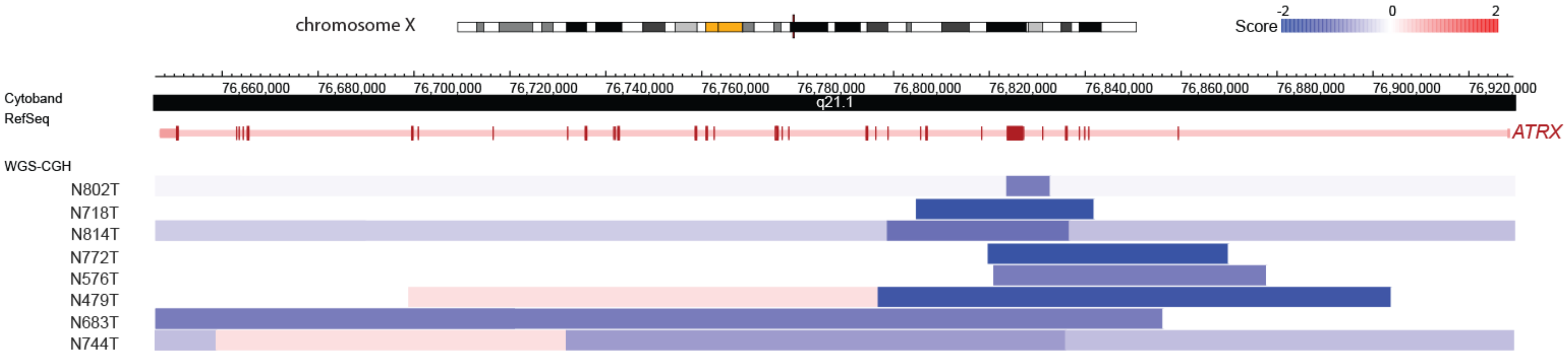


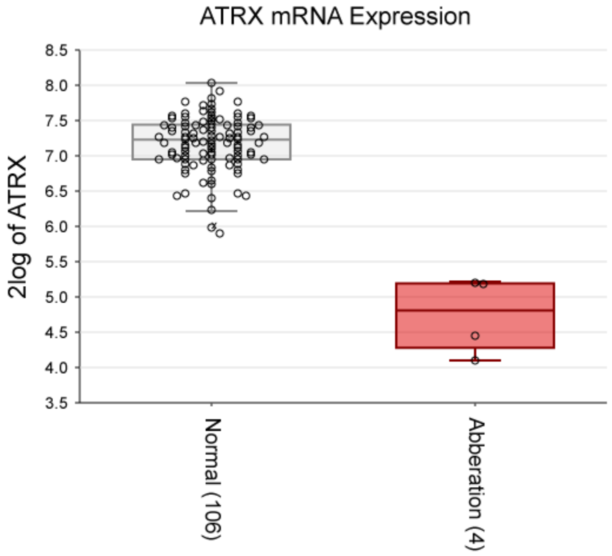
Valentijn & Koster et al 2015 Nat. Genet

	r100k	r250k	r500k	r750k	r1000k
p count>=5	0.00034				
p count>=6		0.0011			
p count>=7			0.00306		
p count>=9				0.00045	0.00234

100,000 iterations of random breakpoints

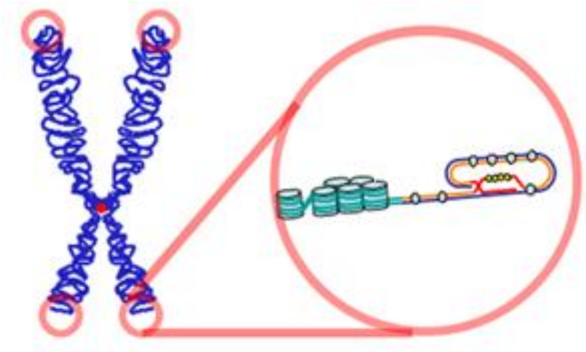
ATRX impairment => ALT





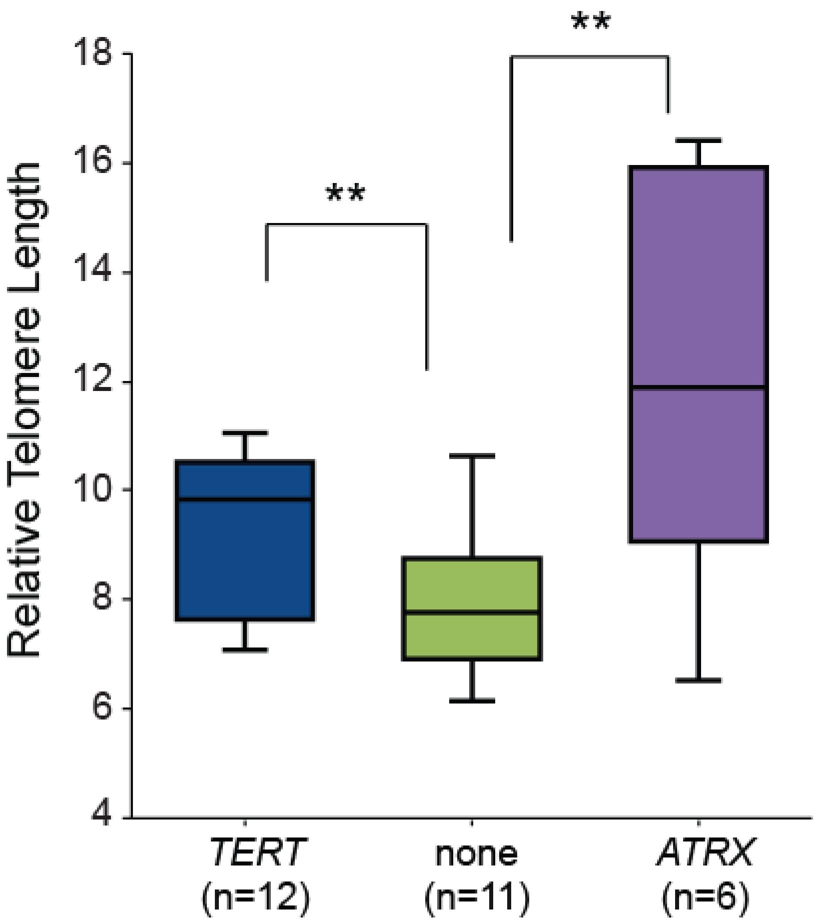
Valentijn & Koster et al 2015 Nat. Genet

Telomeres length NGS



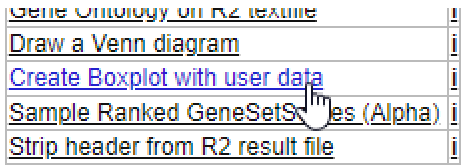
Telomeres are $(TTAGGG)_n$

Search for reads containing multiple instances (>=4) of this sequence and relate to total reads



Valentijn & Koster et al 2015 Nat. Genet

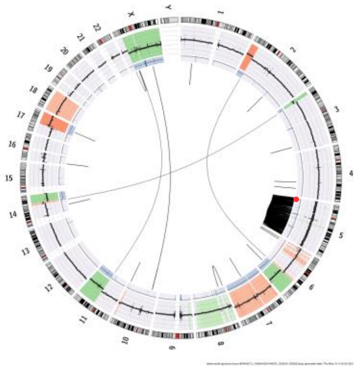
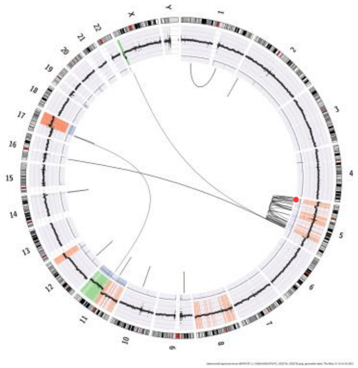
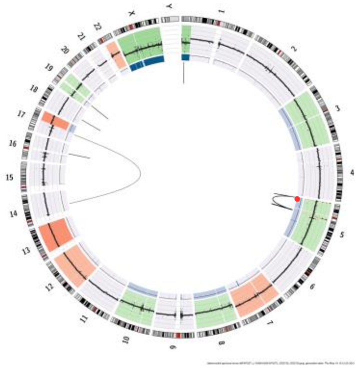
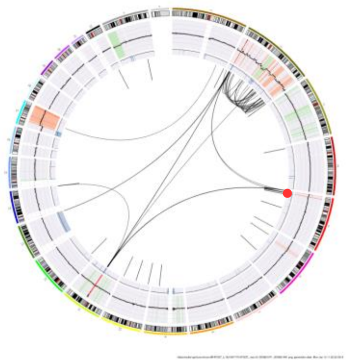
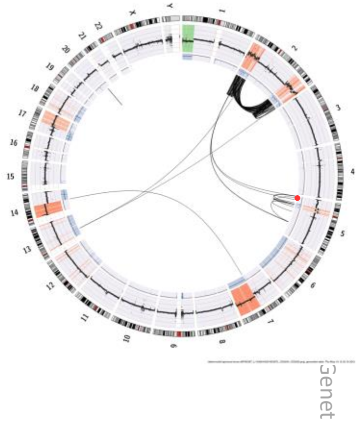
Small Tools



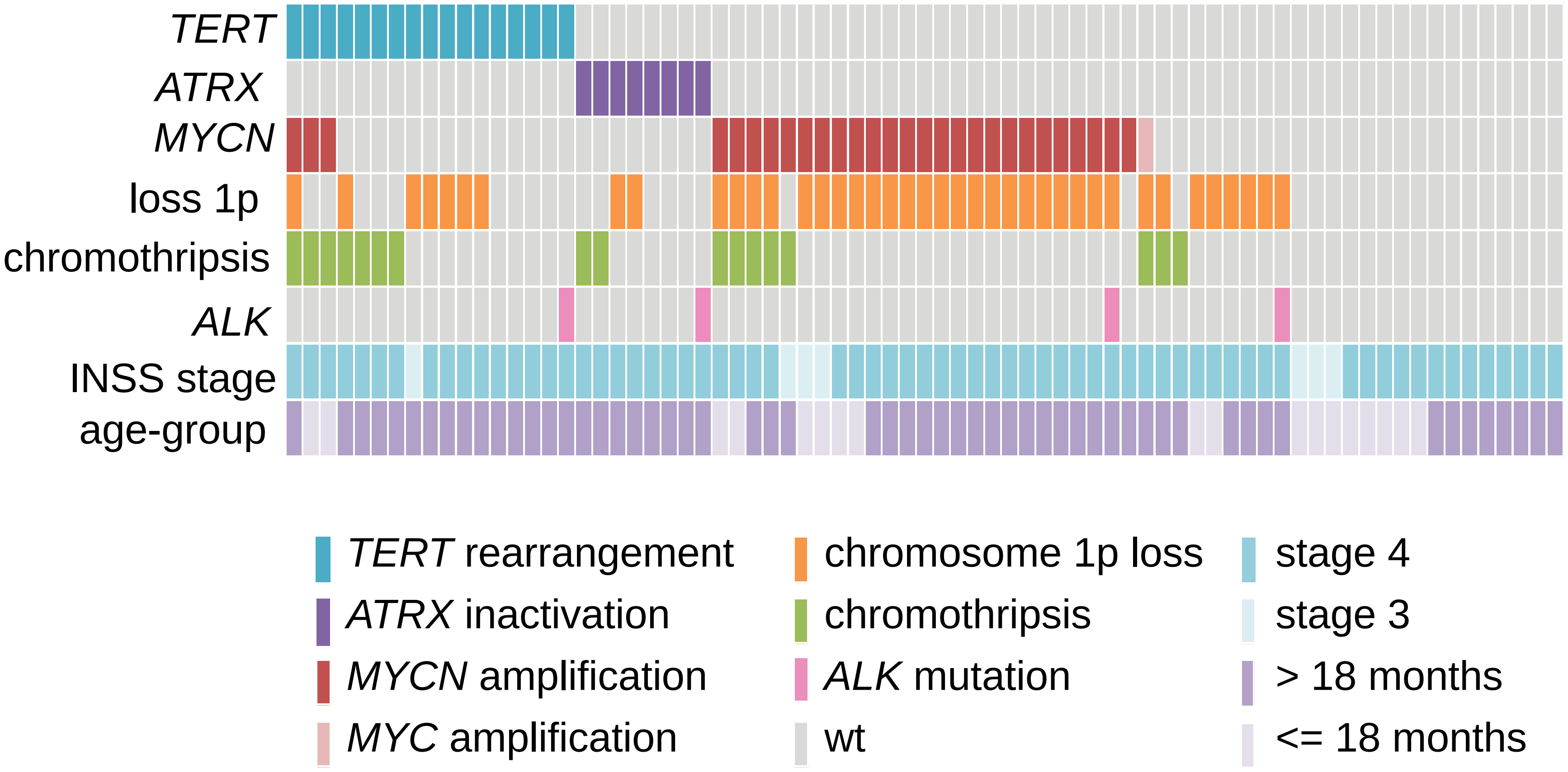
Gene Ontology on R2 textfile
Draw a Venn diagram
Create Boxplot with user data
Sample Ranked GeneSetS es (Alpha)
Strip header from R2 result file

Chromothripsis

- 5 chromothripsis cases directly affect TERT

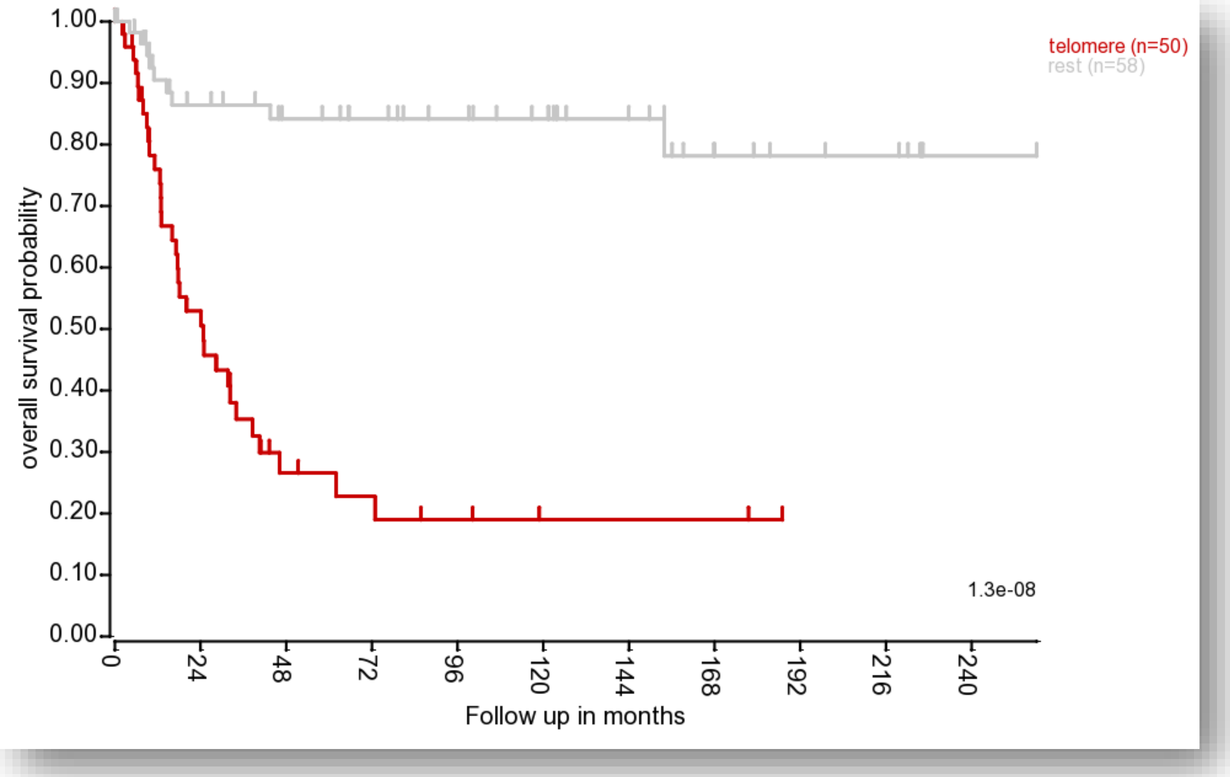
Clinical / Molecular association



Valentijn & Koster et al 2015 Nat. Genet

Annotation Plotter

Clinical / Molecular association



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Kaplan by groups

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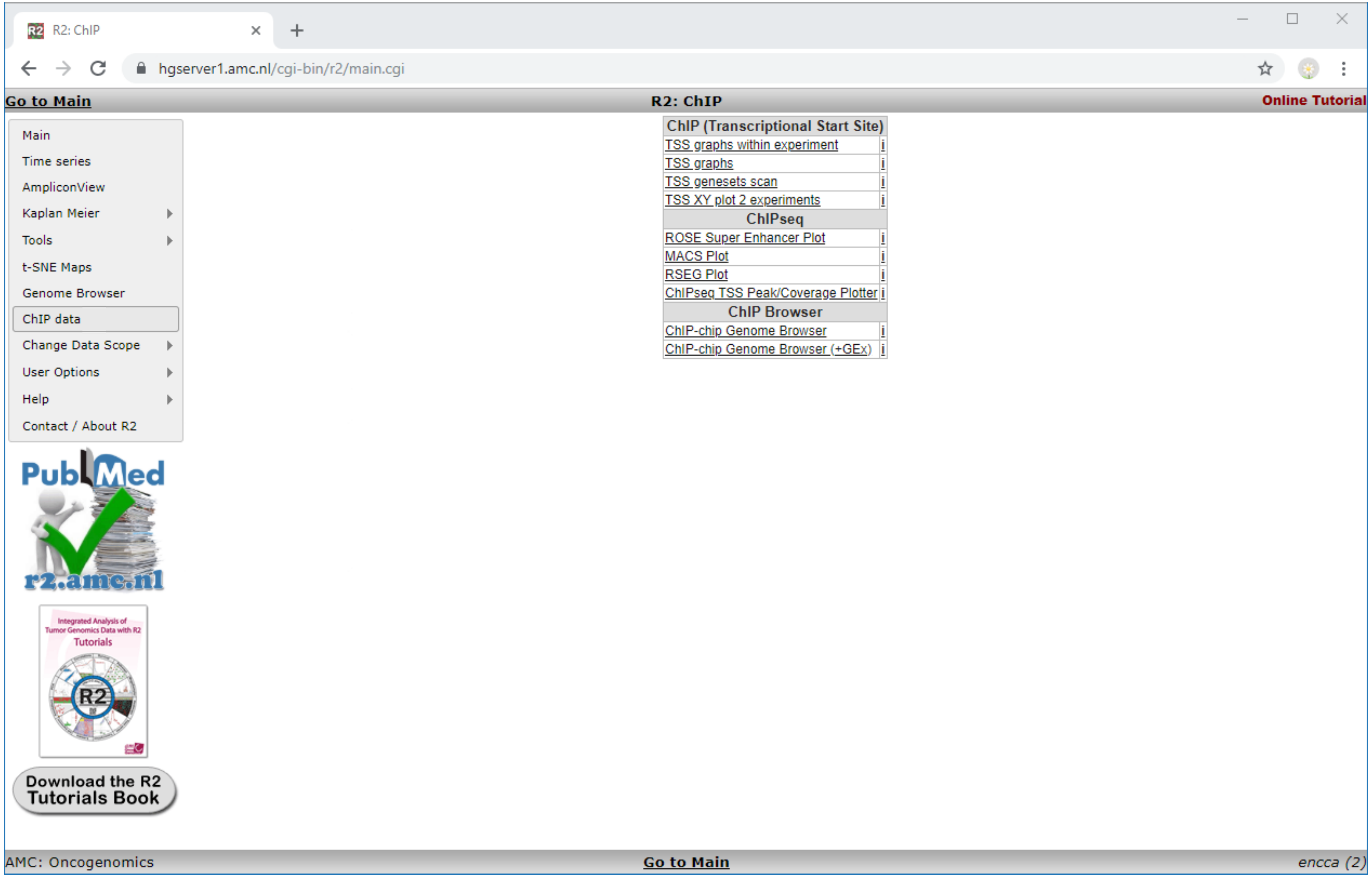
ChIPseq analysis

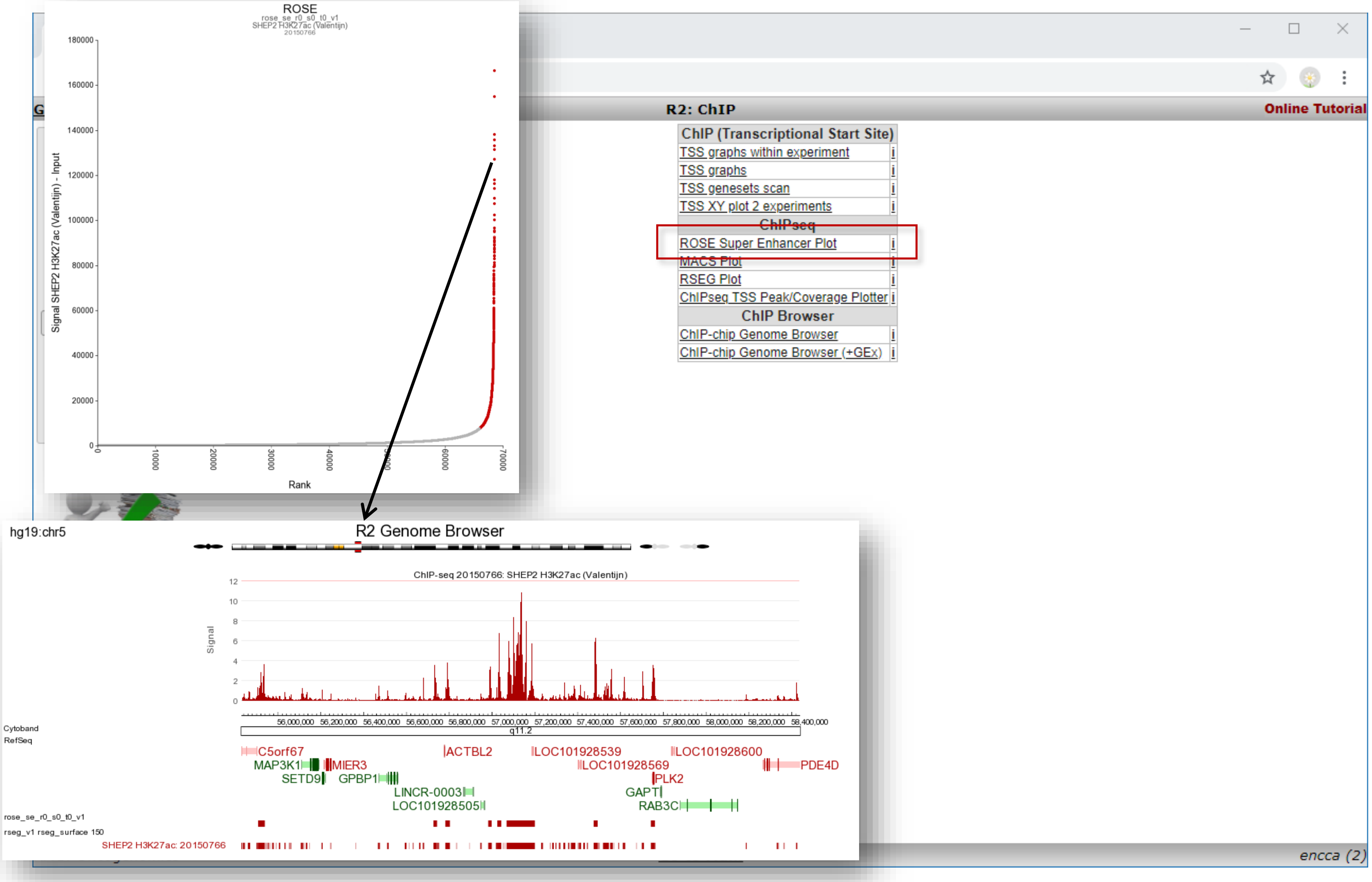


ChIP (Transcriptional Start Site)
- TSS graphs within experiment i
- TSS graphs i
- TSS genesets scan i
- TSS XY plot 2 experiments i

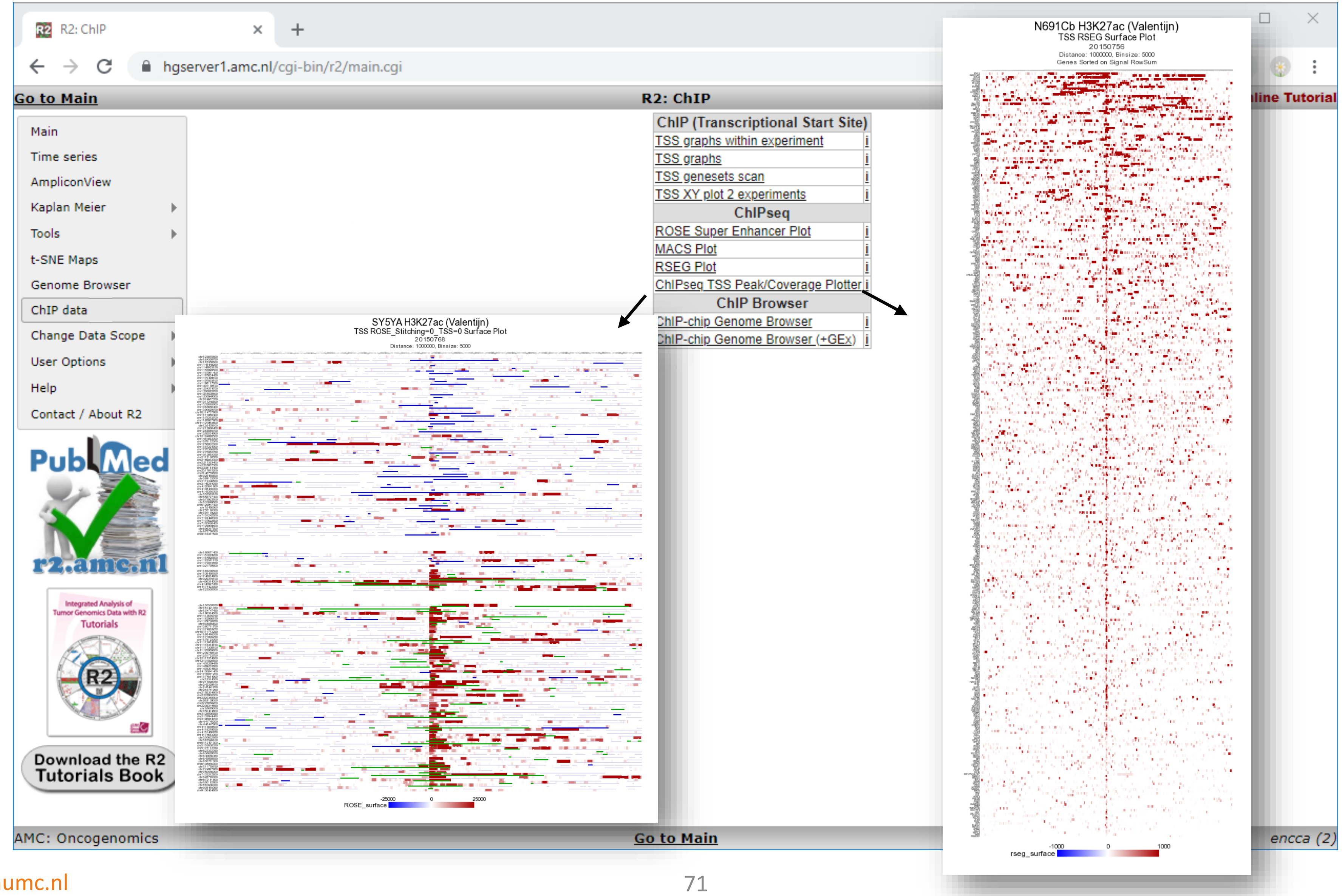
ChIPseq
- ROSE Super Enhancer Plot i
- MACS Plot i
- RSEG Plot i
- ChIPseq TSS Peak/Coverage Plotter i

ChIP Browser
- ChIP-chip Genome Browser i
- ChIP-chip Genome Browser (+GEx) i

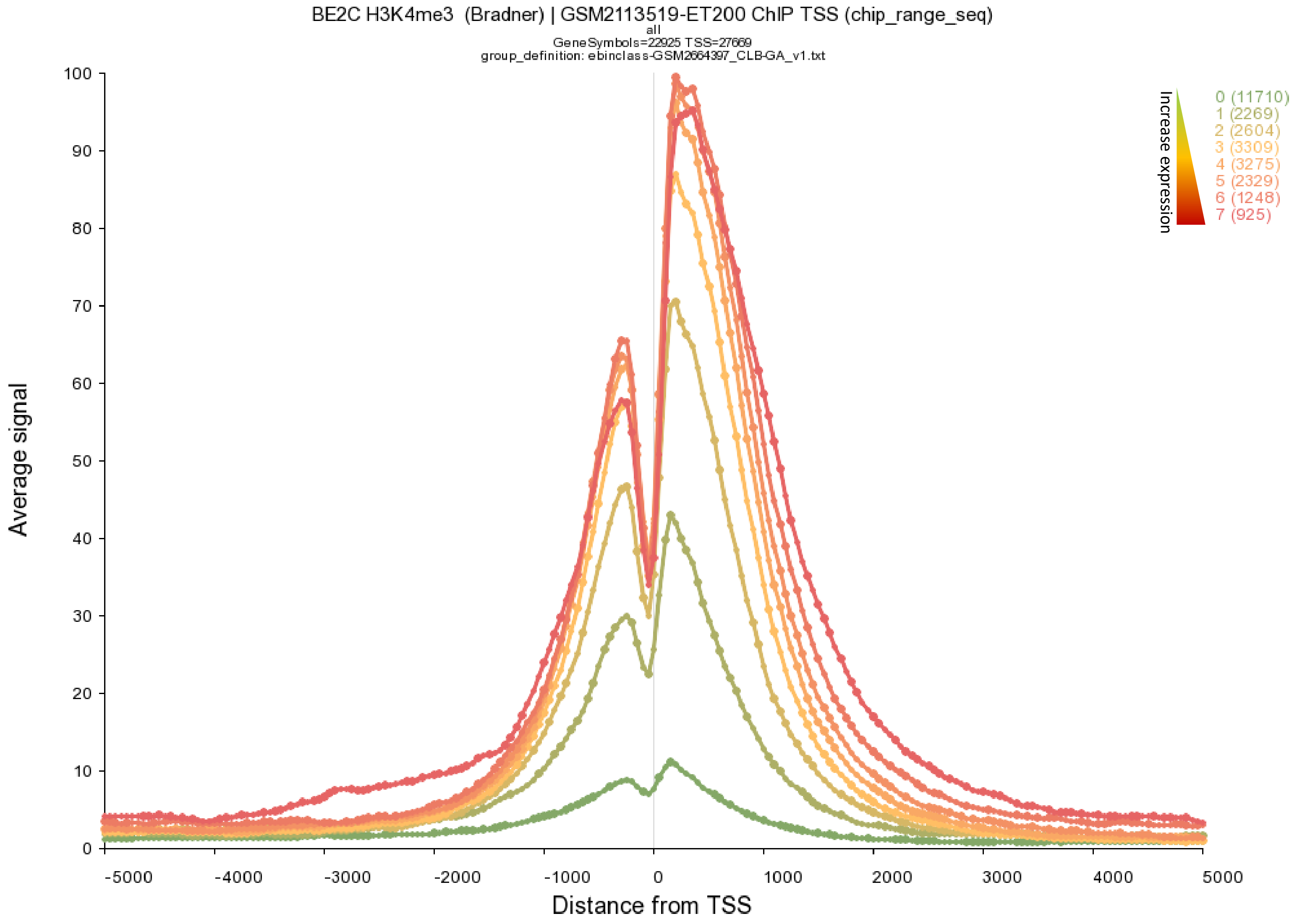
ChIPseq analysis



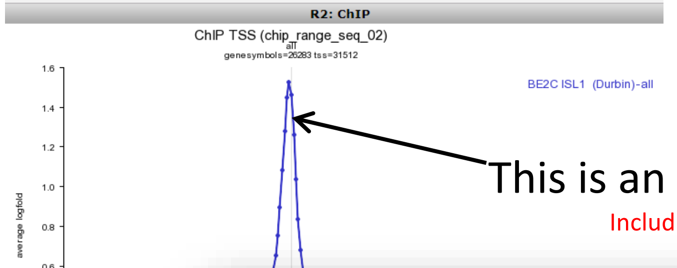
ChIPseq analysis



TSS graphs


BE2C H3K4me3 (Bradner) | GSM2113519-ET200 ChIP TSS (chip_range_seq)
all
GeneSymbols=22925 TSS=27669
group_definition: ebinclass-GSM2664397_CLB-GA_v1.txt
Average signal
0
10
20
30
40
50
60
70
80
90
100
Distance from TSS
-5000
-4000
-3000
-2000
-1000
0
1000
2000
3000
4000
5000
Increase expression
0 (11710)
1 (2269)
2 (2604)
3 (3309)
4 (3275)
5 (2329)
6 (1248)
7 (925)

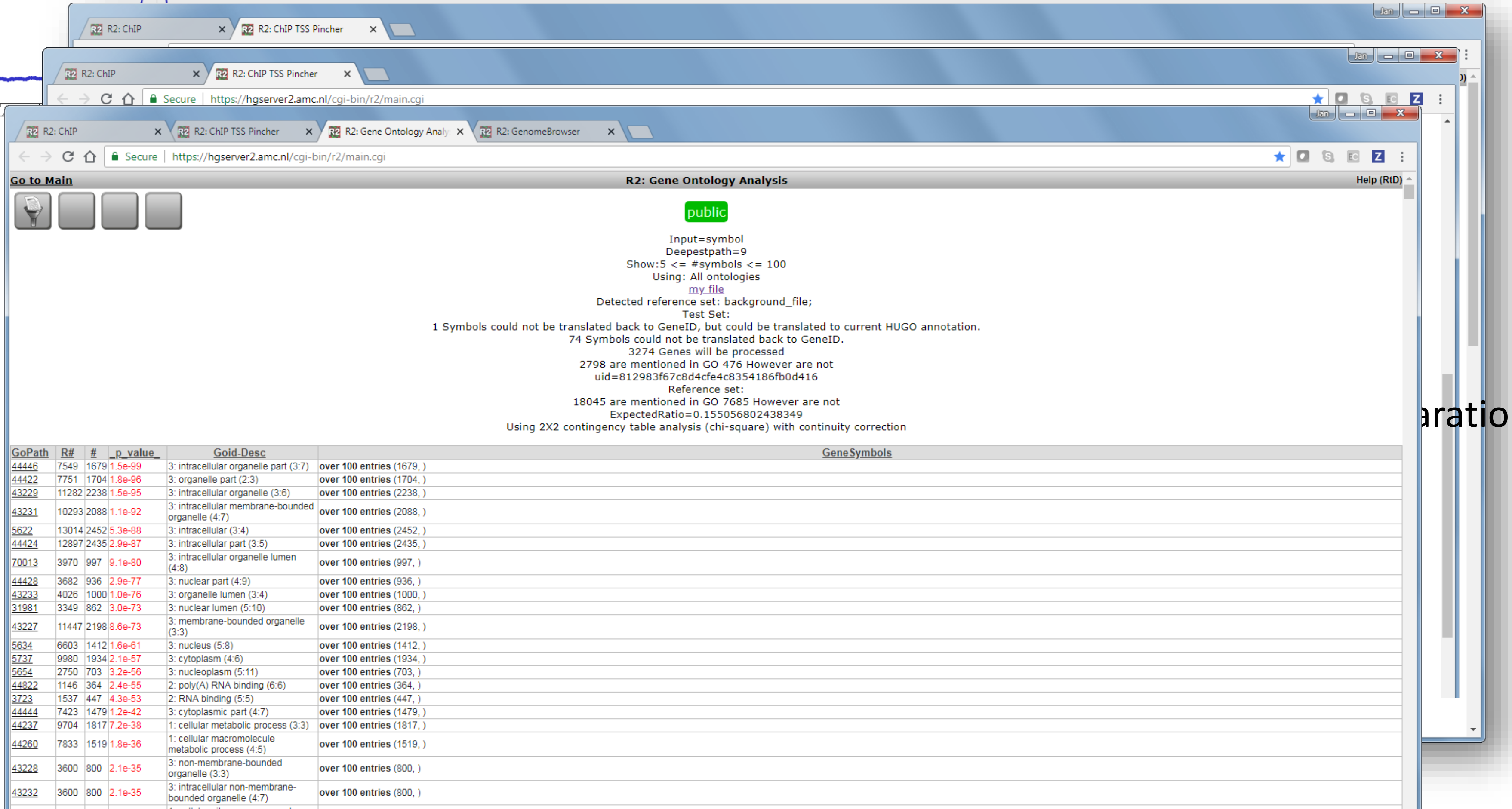
ChIP Pincher



This is an average of ALL

Including silent TSSes

aration



Input=symbol
Deepestpath=9
Show:5 <= #symbols <= 100
Using: All ontologies
my file
Detected reference set: background_file;
Test Set:
1 Symbols could not be translated back to GeneID, but could be translated to current HUGO annotation.
74 Symbols could not be translated back to GeneID.
3274 Genes will be processed
2798 are mentioned in GO 476 However are not
uid=812983f67c8d4cfe4c8354186fb0d416
Reference set:
18045 are mentioned in GO 7685 However are not
ExpectedRatio=0.155056802438349
Using 2X2 contingency table analysis (chi-square) with continuity correction

GoPath	R#	#	_p_value_	Goid-Desc	GeneSymbols
44446	7549	1679	1.5e-99	3: intracellular organelle part (3:7)	**over 100 entries** (1679,)
44422	7751	1704	1.8e-96	3: organelle part (2:3)	**over 100 entries** (1704,)
43229	11282	2238	1.5e-95	3: intracellular organelle (3:6)	**over 100 entries** (2238,)
43231	10293	2088	1.1e-92	3: intracellular membrane-bounded organelle (4:7)	**over 100 entries** (2088,)
5622	13014	2452	5.3e-88	3: intracellular (3:4)	**over 100 entries** (2452,)
44424	12897	2435	2.9e-87	3: intracellular part (3:5)	**over 100 entries** (2435,)
70013	3970	997	9.1e-80	3: intracellular organelle lumen (4:8)	**over 100 entries** (997,)
44428	3682	936	2.9e-77	3: nuclear part (4:9)	**over 100 entries** (936,)
43233	4026	1000	1.0e-76	3: organelle lumen (3:4)	**over 100 entries** (1000,)
31981	3349	862	3.0e-73	3: nuclear lumen (5:10)	**over 100 entries** (862,)
43227	11447	2198	8.6e-73	3: membrane-bounded organelle (3:3)	**over 100 entries** (2198,)
5634	6603	1412	1.6e-61	3: nucleus (5:8)	**over 100 entries** (1412,)
5737	9980	1934	2.1e-57	3: cytoplasm (4:6)	**over 100 entries** (1934,)
5654	2750	703	3.2e-56	3: nucleoplasm (5:11)	**over 100 entries** (703,)
44822	1146	364	2.4e-55	2: poly(A) RNA binding (6:6)	**over 100 entries** (364,)
3723	1537	447	4.3e-53	2: RNA binding (5:5)	**over 100 entries** (447,)
44444	7423	1479	1.2e-42	3: cytoplasmic part (4:7)	**over 100 entries** (1479,)
44237	9704	1817	7.2e-38	1: cellular metabolic process (3:3)	**over 100 entries** (1817,)
44260	7833	1519	1.8e-36	1: cellular macromolecule metabolic process (4:5)	**over 100 entries** (1519,)
43228	3600	800	2.1e-35	3: non-membrane-bounded organelle (3:3)	**over 100 entries** (800,)
43232	3600	800	2.1e-35	3: intracellular non-membrane-bounded organelle (4:7)	**over 100 entries** (800,)

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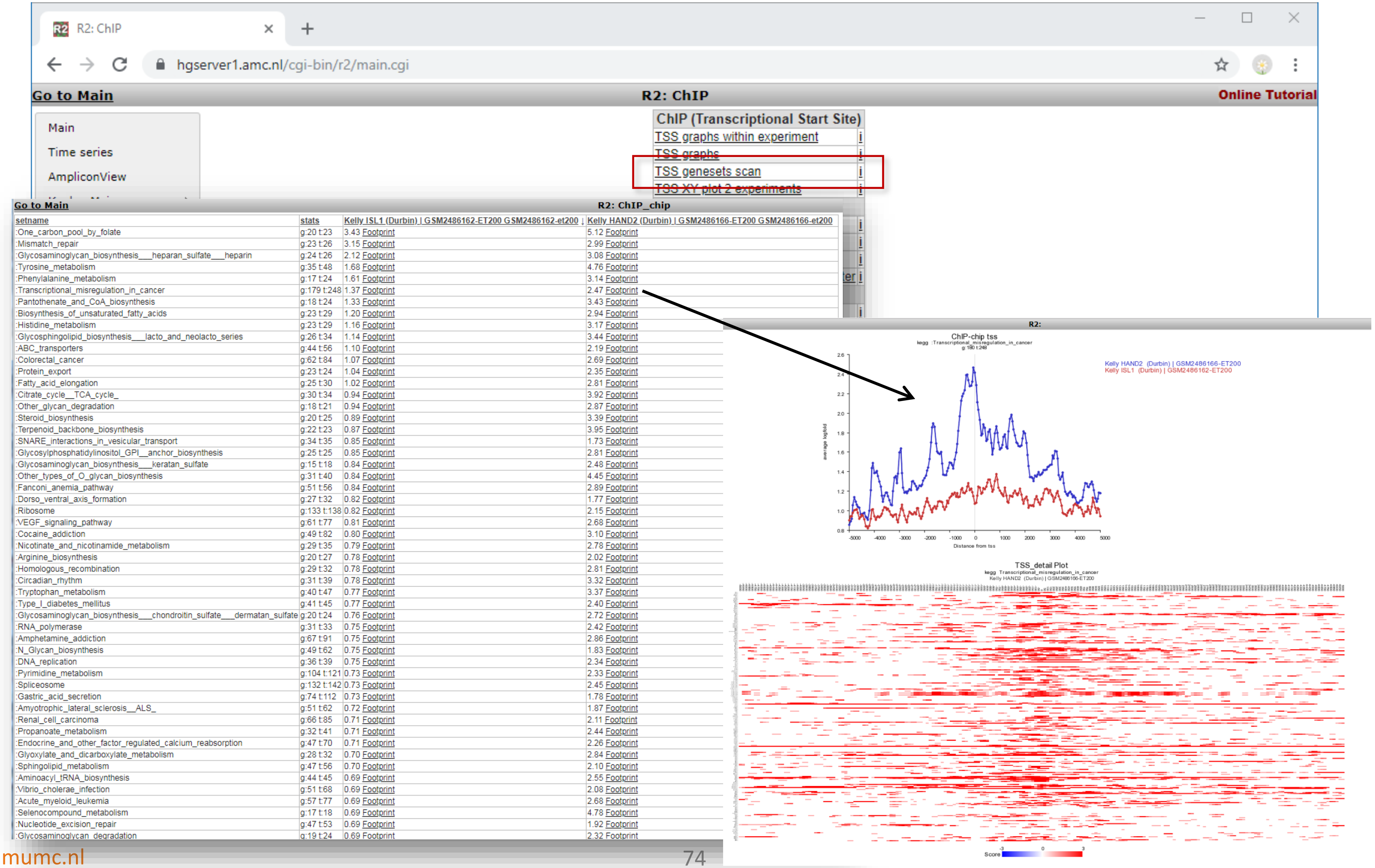
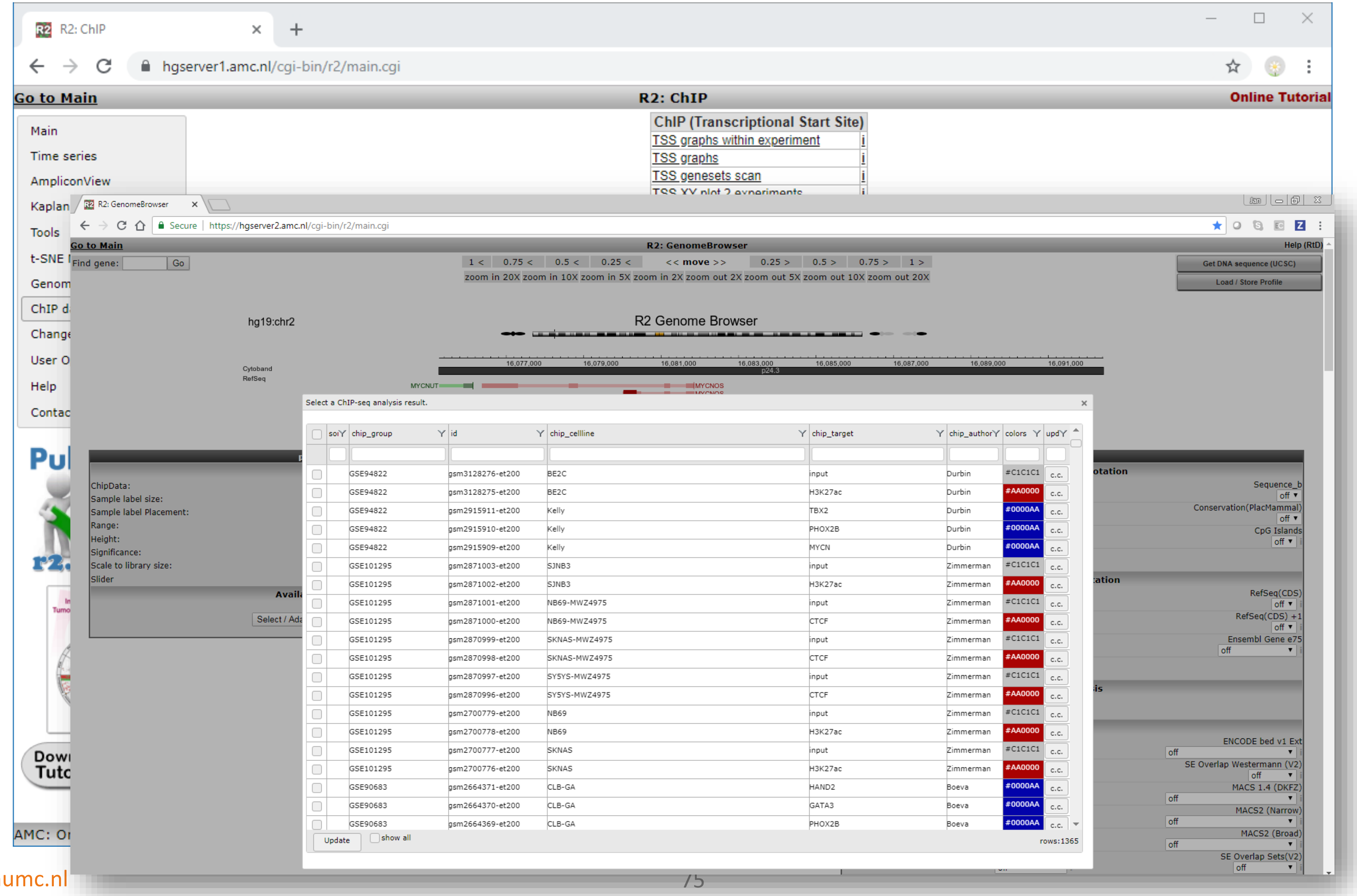
R2-Platform

TSS geneset scans



setname	stats	Kelly ISL1 (Durbin) | GSM2486162-ET200 GSM2486162-et200 ↓	Kelly HAND2 (Durbin) | GSM2486166-ET200 GSM2486166-et200
:One_carbon_pool_by_folate	g:20 t:23	3.43 Footprint	5.12 Footprint
:Mismatch_repair	g:23 t:26	3.15 Footprint	2.99 Footprint
:Glycosaminoglycan_biosynthesis___heparan_sulfate___heparin	g:24 t:26	2.12 Footprint	3.08 Footprint
:Tyrosine_metabolism	g:35 t:48	1.68 Footprint	4.76 Footprint
:Phenylalanine_metabolism	g:17 t:24	1.61 Footprint	3.14 Footprint
:Transcriptional_misregulation_in_cancer	g:179 t:248	1.37 Footprint	2.47 Footprint
:Pantothenate_and_CoA_biosynthesis	g:18 t:24	1.33 Footprint	3.43 Footprint
:Biosynthesis_of_unsaturated_fatty_acids	g:23 t:29	1.20 Footprint	2.94 Footprint
:Histidine_metabolism	g:23 t:29	1.16 Footprint	3.17 Footprint
:Glycosphingolipid_biosynthesis___lacto_and_neolacto_series	g:26 t:34	1.14 Footprint	3.44 Footprint
:ABC_transporters	g:44 t:56	1.10 Footprint	2.19 Footprint
:Colorectal_cancer	g:62 t:84	1.07 Footprint	2.69 Footprint
:Protein_export	g:23 t:24	1.04 Footprint	2.35 Footprint
:Fatty_acid_elongation	g:25 t:30	1.02 Footprint	2.81 Footprint
:Citrate_cycle__TCA_cycle_	g:30 t:34	0.94 Footprint	3.92 Footprint
:Other_glycan_degradation	g:18 t:21	0.94 Footprint	2.87 Footprint
:Steroid_biosynthesis	g:20 t:25	0.89 Footprint	3.39 Footprint
:Terpenoid_backbone_biosynthesis	g:22 t:23	0.87 Footprint	3.95 Footprint
:SNARE_interactions_in_vesicular_transport	g:34 t:35	0.85 Footprint	1.73 Footprint
:Glycosylphosphatidylinositol_GPI__anchor_biosynthesis	g:25 t:25	0.85 Footprint	2.81 Footprint
:Glycosaminoglycan_biosynthesis___keratan_sulfate	g:15 t:18	0.84 Footprint	2.48 Footprint
:Other_types_of_O_glycan_biosynthesis	g:31 t:40	0.84 Footprint	4.45 Footprint
:Fanconi_anemia_pathway	g:51 t:56	0.84 Footprint	2.89 Footprint
:Dorso_ventral_axis_formation	g:27 t:32	0.82 Footprint	1.77 Footprint
:Ribosome	g:133 t:138	0.82 Footprint	2.15 Footprint
:VEGF_signaling_pathway	g:61 t:77	0.81 Footprint	2.68 Footprint
:Cocaine_addiction	g:49 t:82	0.80 Footprint	3.10 Footprint
:Nicotinate_and_nicotinamide_metabolism	g:29 t:35	0.79 Footprint	2.78 Footprint
:Arginine_biosynthesis	g:20 t:27	0.78 Footprint	2.02 Footprint
:Homologous_recombination	g:29 t:32	0.78 Footprint	2.81 Footprint
:Circadian_rhythm	g:31 t:39	0.78 Footprint	3.32 Footprint
:Tryptophan_metabolism	g:40 t:47	0.77 Footprint	3.37 Footprint
:Type_I_diabetes_mellitus	g:41 t:45	0.77 Footprint	2.40 Footprint
:Glycosaminoglycan_biosynthesis___chondroitin_sulfate___dermatan_sulfate	g:20 t:24	0.76 Footprint	2.72 Footprint
:RNA_polymerase	g:31 t:33	0.75 Footprint	2.42 Footprint
:Amphetamine_addiction	g:67 t:91	0.75 Footprint	2.86 Footprint
:N_Glycan_biosynthesis	g:49 t:62	0.75 Footprint	1.83 Footprint
:DNA_replication	g:36 t:39	0.75 Footprint	2.34 Footprint
:Pyrimidine_metabolism	g:104 t:121	0.73 Footprint	2.33 Footprint
:Spliceosome	g:132 t:142	0.73 Footprint	2.45 Footprint
:Gastric_acid_secretion	g:74 t:112	0.73 Footprint	1.78 Footprint
:Amyotrophic_lateral_sclerosis__ALS_	g:51 t:62	0.72 Footprint	1.87 Footprint
:Renal_cell_carcinoma	g:66 t:85	0.71 Footprint	2.11 Footprint
:Propanoate_metabolism	g:32 t:41	0.71 Footprint	2.44 Footprint
:Endocrine_and_other_factor_regulated_calcium_reabsorption	g:47 t:70	0.71 Footprint	2.26 Footprint
:Glyoxylate_and_dicarboxylate_metabolism	g:28 t:32	0.70 Footprint	2.84 Footprint
:Sphingolipid_metabolism	g:47 t:56	0.70 Footprint	2.10 Footprint
:Aminoacyl_tRNA_biosynthesis	g:44 t:45	0.69 Footprint	2.55 Footprint
:Vibrio_cholerae_infection	g:51 t:68	0.69 Footprint	2.08 Footprint
:Acute_myeloid_leukemia	g:57 t:77	0.69 Footprint	2.68 Footprint
:Selenocompound_metabolism	g:17 t:18	0.69 Footprint	4.78 Footprint
:Nucleotide_excision_repair	g:47 t:53	0.69 Footprint	1.92 Footprint
:Glycosaminoglycan_degradation	g:19 t:24	0.69 Footprint	2.32 Footprint

ChIPseq genome browser

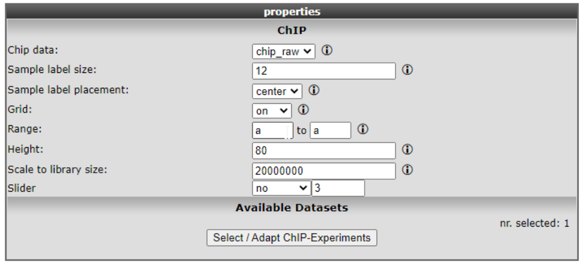


Select a ChIP-seq analysis result.

☐	soi	chip_group	id	chip_cellline	chip_target	chip_author	colors	upd
☐		GSE94822	gsm3128276-et200	BE2C	input	Durbin	#C1C1C1	c.c.
☐		GSE94822	gsm3128275-et200	BE2C	H3K27ac	Durbin	#AA0000	c.c.
☐		GSE94822	gsm2915911-et200	Kelly	TBX2	Durbin	#0000AA	c.c.
☐		GSE94822	gsm2915910-et200	Kelly	PHOX2B	Durbin	#0000AA	c.c.
☐		GSE94822	gsm2915909-et200	Kelly	MYCN	Durbin	#0000AA	c.c.
☐		GSE101295	gsm2871003-et200	SJNB3	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2871002-et200	SJNB3	H3K27ac	Zimmerman	#AA0000	c.c.
☐		GSE101295	gsm2871001-et200	NB69-MWZ4975	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2871000-et200	NB69-MWZ4975	CTCF	Zimmerman	#AA0000	c.c.
☐		GSE101295	gsm2870999-et200	SKNAS-MWZ4975	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2870998-et200	SKNAS-MWZ4975	CTCF	Zimmerman	#AA0000	c.c.
☐		GSE101295	gsm2870997-et200	SY5YS-MWZ4975	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2870996-et200	SY5YS-MWZ4975	CTCF	Zimmerman	#AA0000	c.c.
☐		GSE101295	gsm2700779-et200	NB69	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2700778-et200	NB69	H3K27ac	Zimmerman	#AA0000	c.c.
☐		GSE101295	gsm2700777-et200	SKNAS	input	Zimmerman	#C1C1C1	c.c.
☐		GSE101295	gsm2700776-et200	SKNAS	H3K27ac	Zimmerman	#AA0000	c.c.
☐		GSE90683	gsm2664371-et200	CLB-GA	HAND2	Boeva	#0000AA	c.c.
☐		GSE90683	gsm2664370-et200	CLB-GA	GATA3	Boeva	#0000AA	c.c.
☐		GSE90683	gsm2664369-et200	CLB-GA	PHOX2B	Boeva	#0000AA	c.c.

Update ☐ show all rows:1365

Multiple ChIP profiles



properties

ChIP

Chip data: chip_raw

Sample label size: 12

Sample label placement: center

Grid: on

Range: a to a

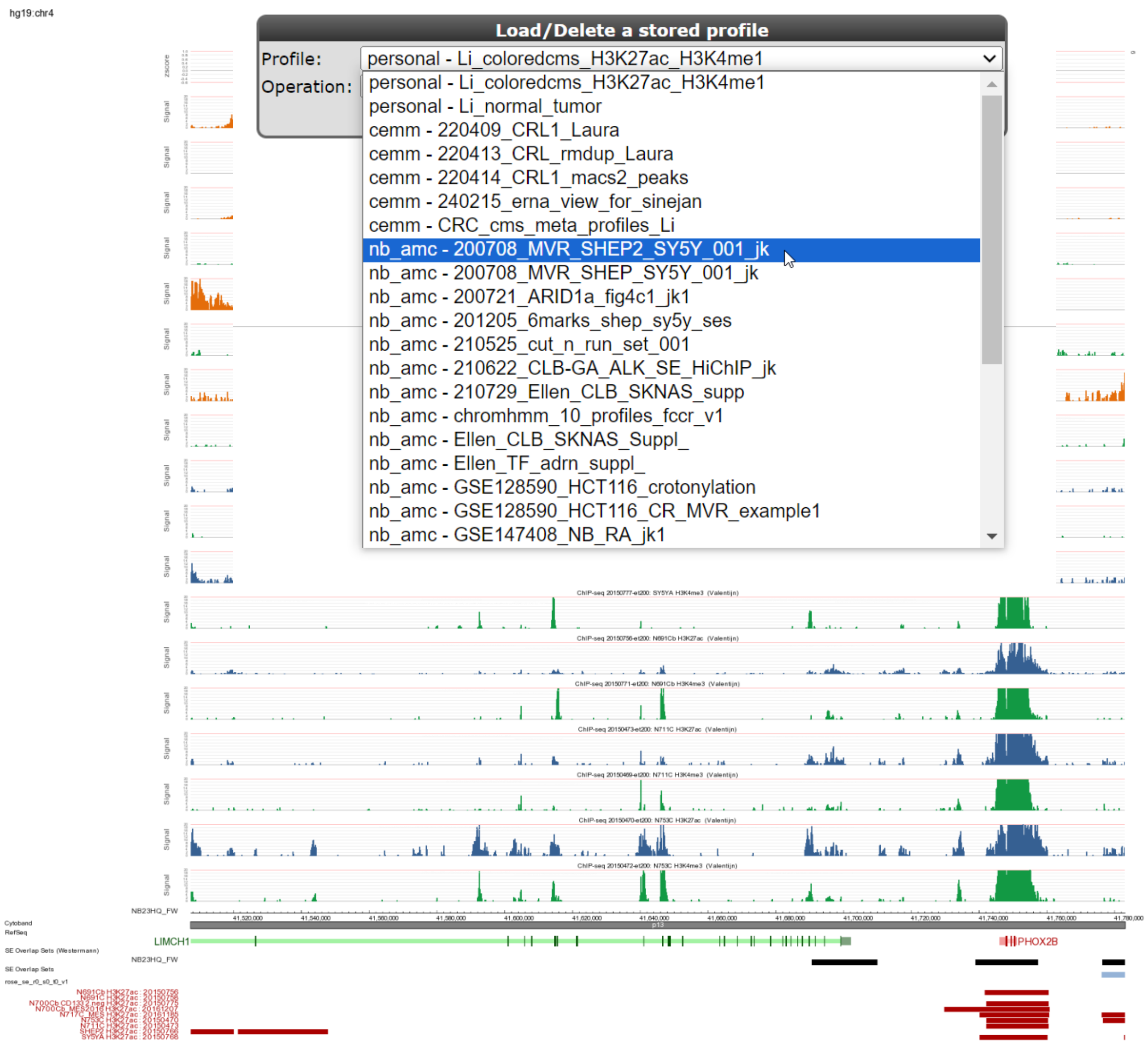
Height: 80

Scale to library size: 20000000

Slider no 3

Available Datasets

nr. selected: 1



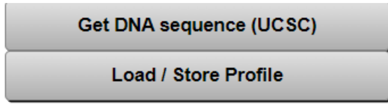
hg19:chr4

Load/Delete a stored profile

Profile: personal - Li_coloredcms_H3K27ac_H3K4me1

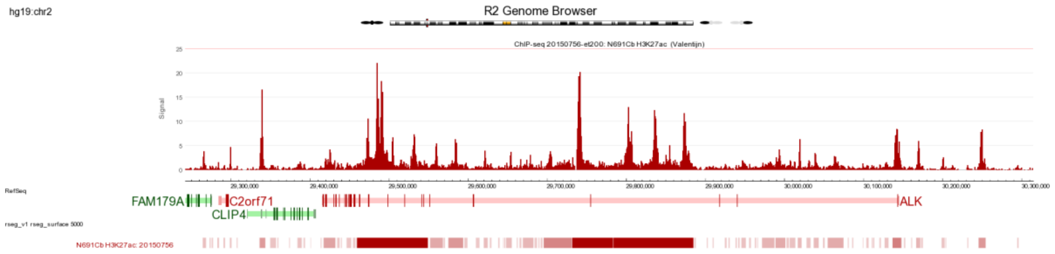
Operation:

- personal - Li_coloredcms_H3K27ac_H3K4me1
- personal - Li_normal_tumor
- cemm - 220409_CRL1_Laura
- cemm - 220413_CRL_rmdup_Laura
- cemm - 220414_CRL1_macs2_peaks
- cemm - 240215_erna_view_for_sinejan
- cemm - CRC_cms_meta_profiles_Li
- nb_amc - 200708_MVR_SHEP2_SY5Y_001_jk
- nb_amc - 200708_MVR_SHEP_SY5Y_001_jk
- nb_amc - 200721_ARID1a_fig4c1_jk1
- nb_amc - 201205_6marks_shep_sy5y_ses
- nb_amc - 210525_cut_n_run_set_001
- nb_amc - 210622_CLB-GA_ALK_SE_HiChIP_jk
- nb_amc - 210729_Ellen_CLB_SKNAS_supp
- nb_amc - chromhmm_10_profiles_fccr_v1
- nb_amc - Ellen_CLB_SKNAS_Suppl_
- nb_amc - Ellen_TF_adrn_suppl_
- nb_amc - GSE128590_HCT116_crotonylation
- nb_amc - GSE128590_HCT116_CR_MVR_example1
- nb_amc - GSE147408_NB_RA_jk1



Enhancer Landscape

- ROSE SE data of multiple samples
  - Find overlapping SE's and assemble set of SE's seen more than once

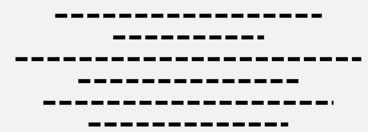


E.g. 4 sets of ROSE SE regions

🟥
🟨
🟩
🟦

Overlay all sets and determine regions

Align regions SE>= 2 cell lines



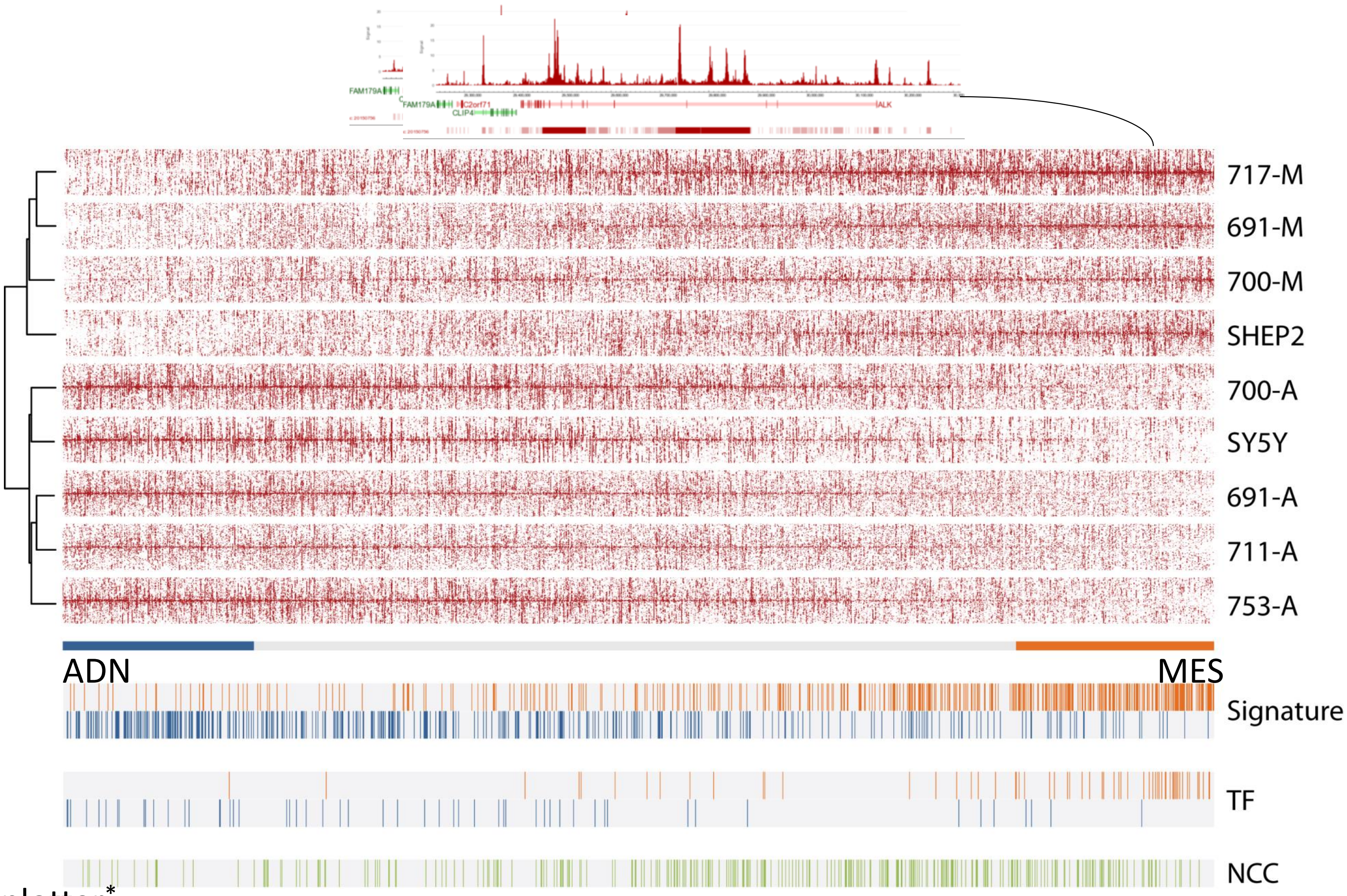
Cluster Profiles

Exclude transcription induced signals
Merge to point estimates
Cluster on samples
Order on diff. Signals (MES/ADN)

Prepare for visualization

Replace point estimates by SE peak profiles (+/- 1mb)

SuperEnhancer Landscape MES/ADN

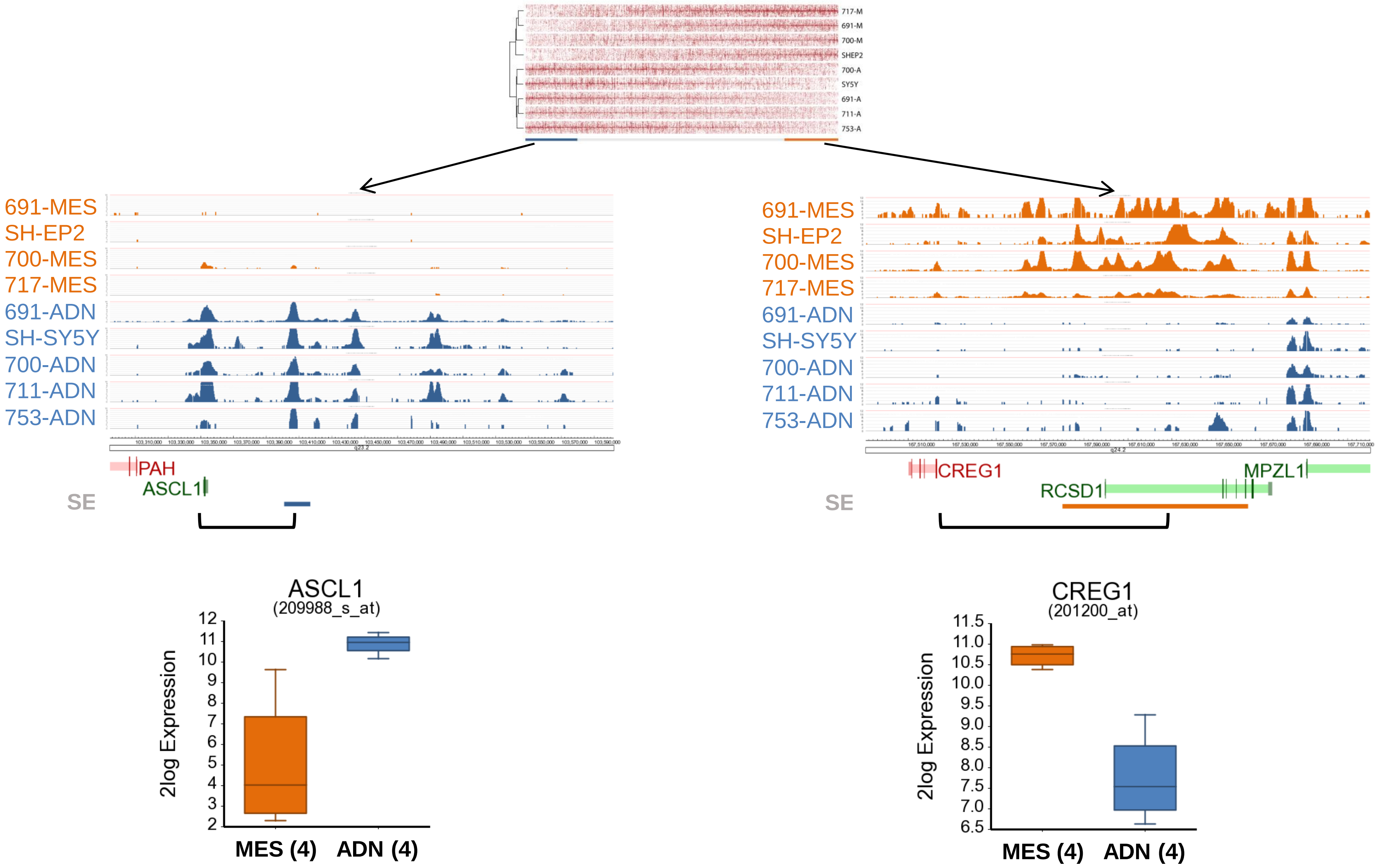


van Groningen & Koster et al 2017 Nat. Genet

TSS peak coverage plotter*

R2-support@amsterdamumc.nl

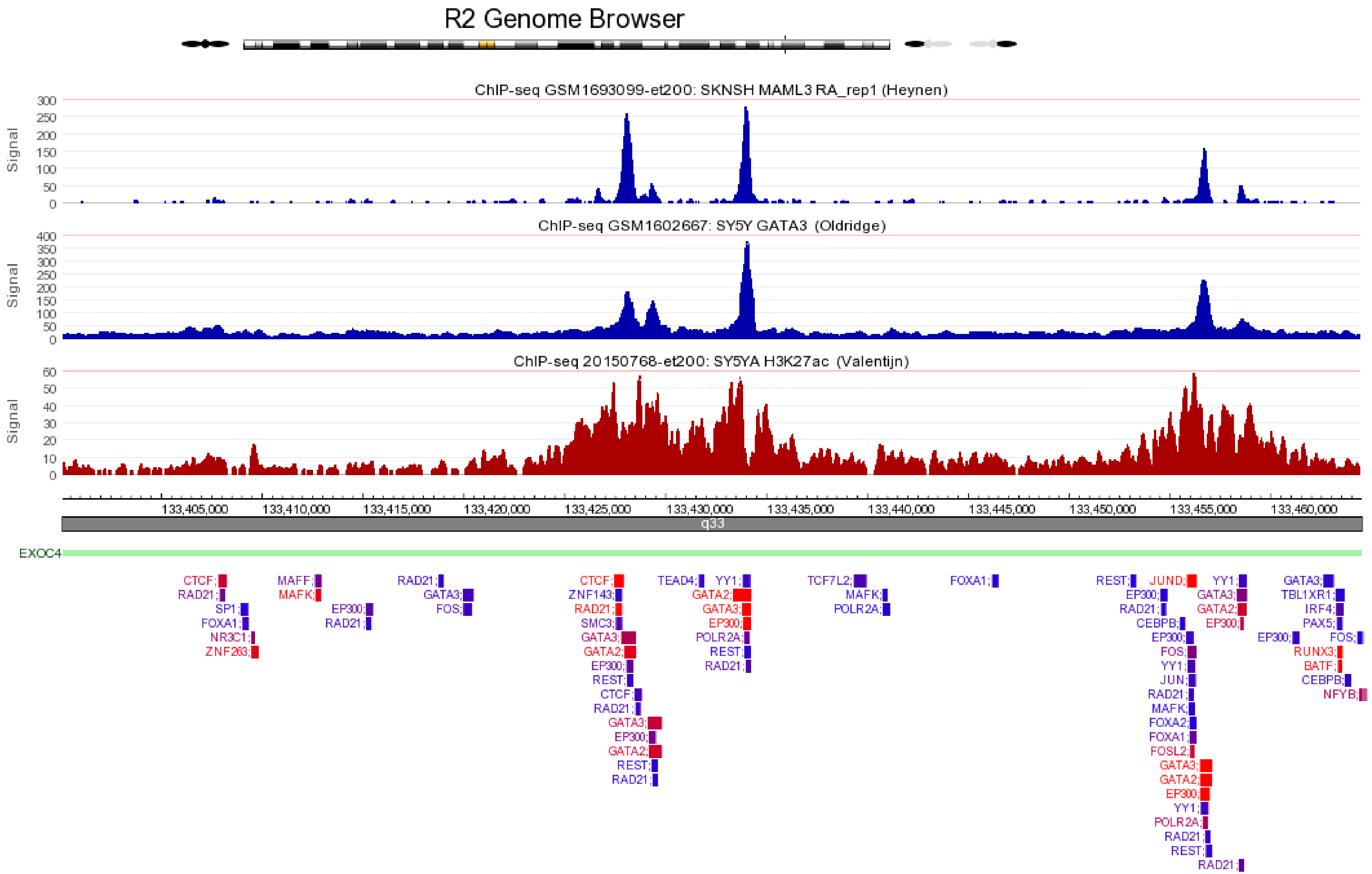
SuperEnhancer Landscape MES/ADN



van Groningen & Koster et al 2017 Nat. Genet

ChIPseq analysis

hg19:chr7



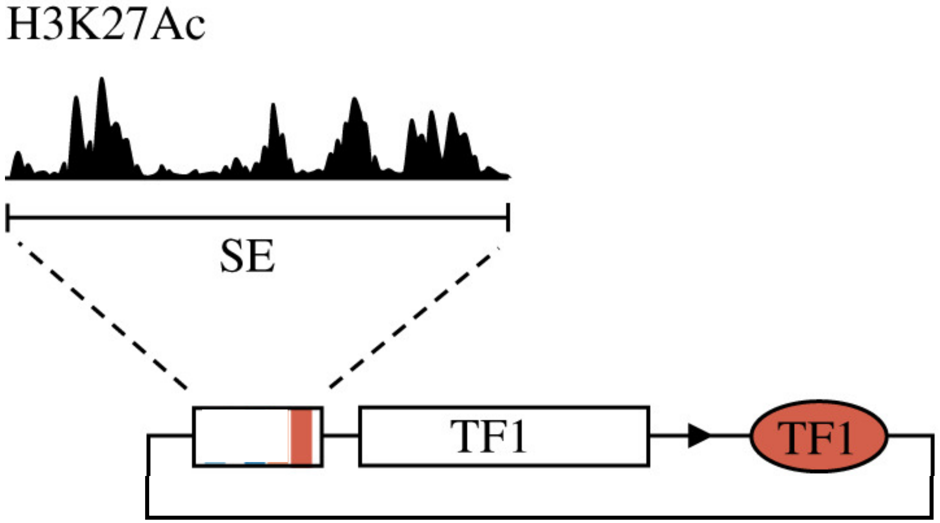
ENCODE re-analysis

Peaks for **161 transcription factors** in **91 cell types** are combined here into clusters to produce a summary display showing occupancy regions for each factor and motif sites within the regions when identified.

Scores were assigned to peaks by multiplying the input signal values by a normalization factor calculated as the ratio of the maximum score value (1000) to the signal value at one standard deviation from the mean. The cluster score is the highest score for any peak contributing to the cluster

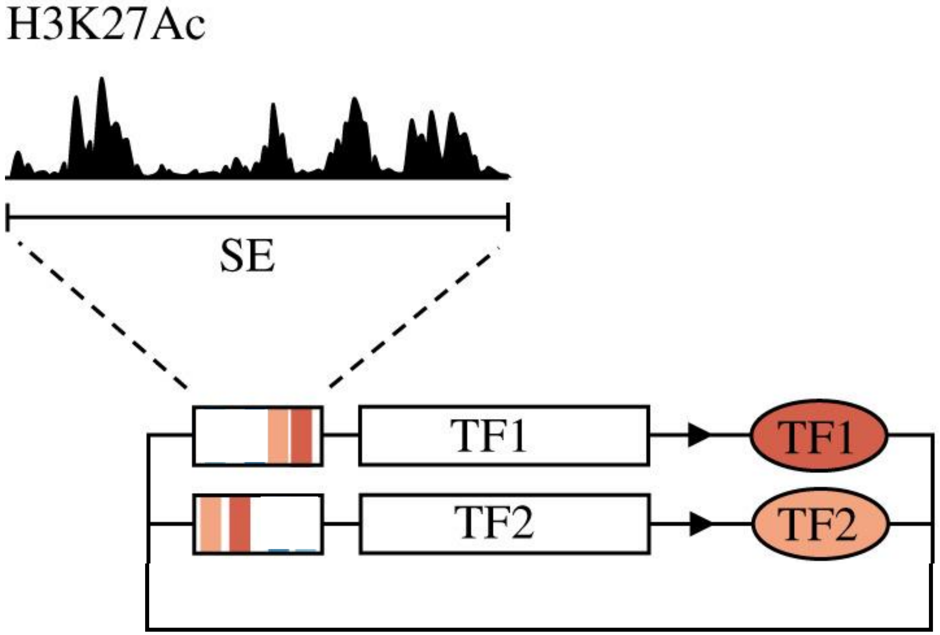
http://genome.ucsc.edu/cgi-bin/hgTrackUi?db=hg19&g=wgEncodeRegTfbsClusteredV3

Core Regulatory Circuitries (CRC)



https://royalsocietypublishing.org/doi/10.1098/rsob.200121

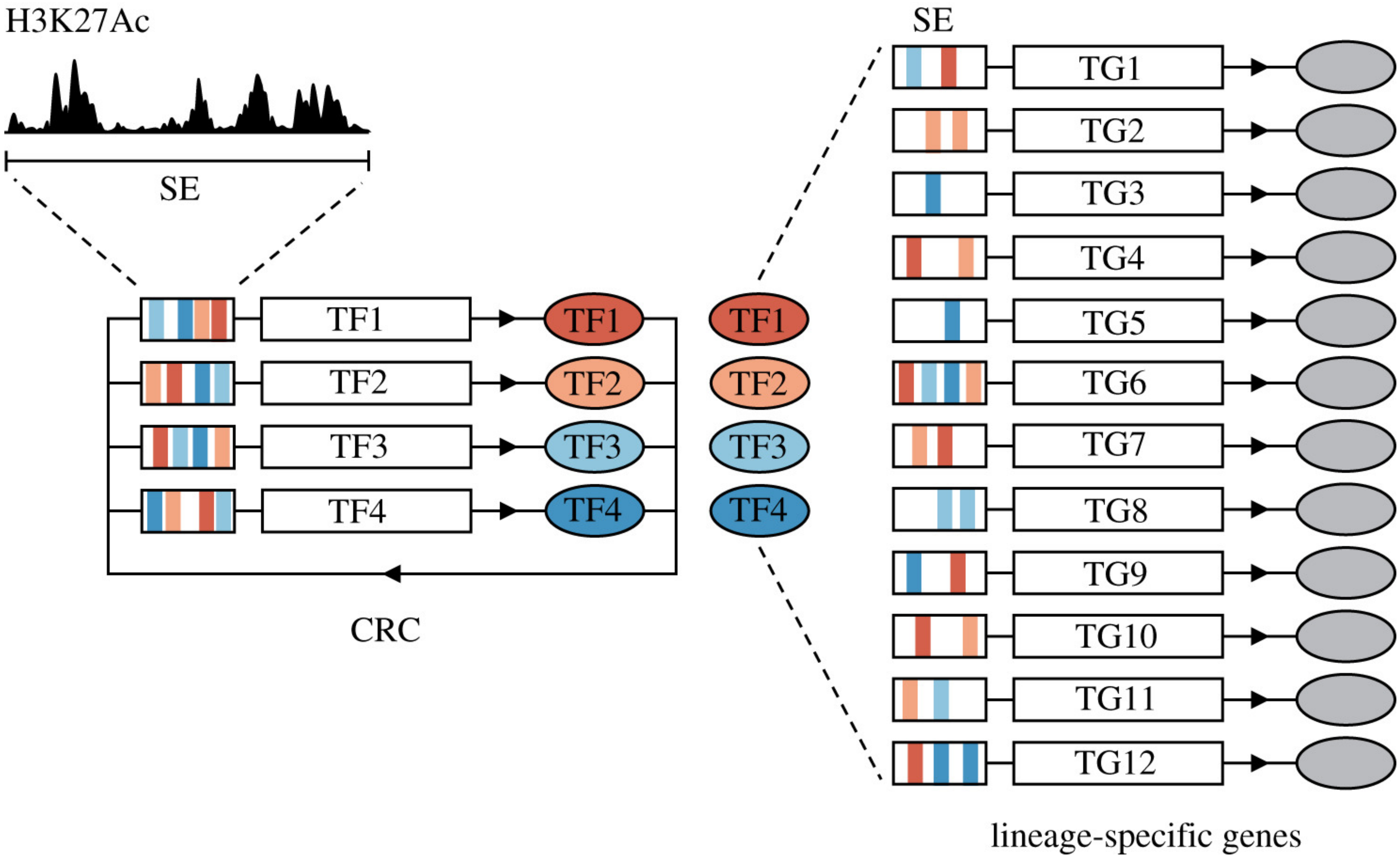
Core Regulatory Circuitries (CRC)



R2-support@amsterdamumc.nl

https://royalsocietypublishing.org/doi/10.1098/rsob.200121

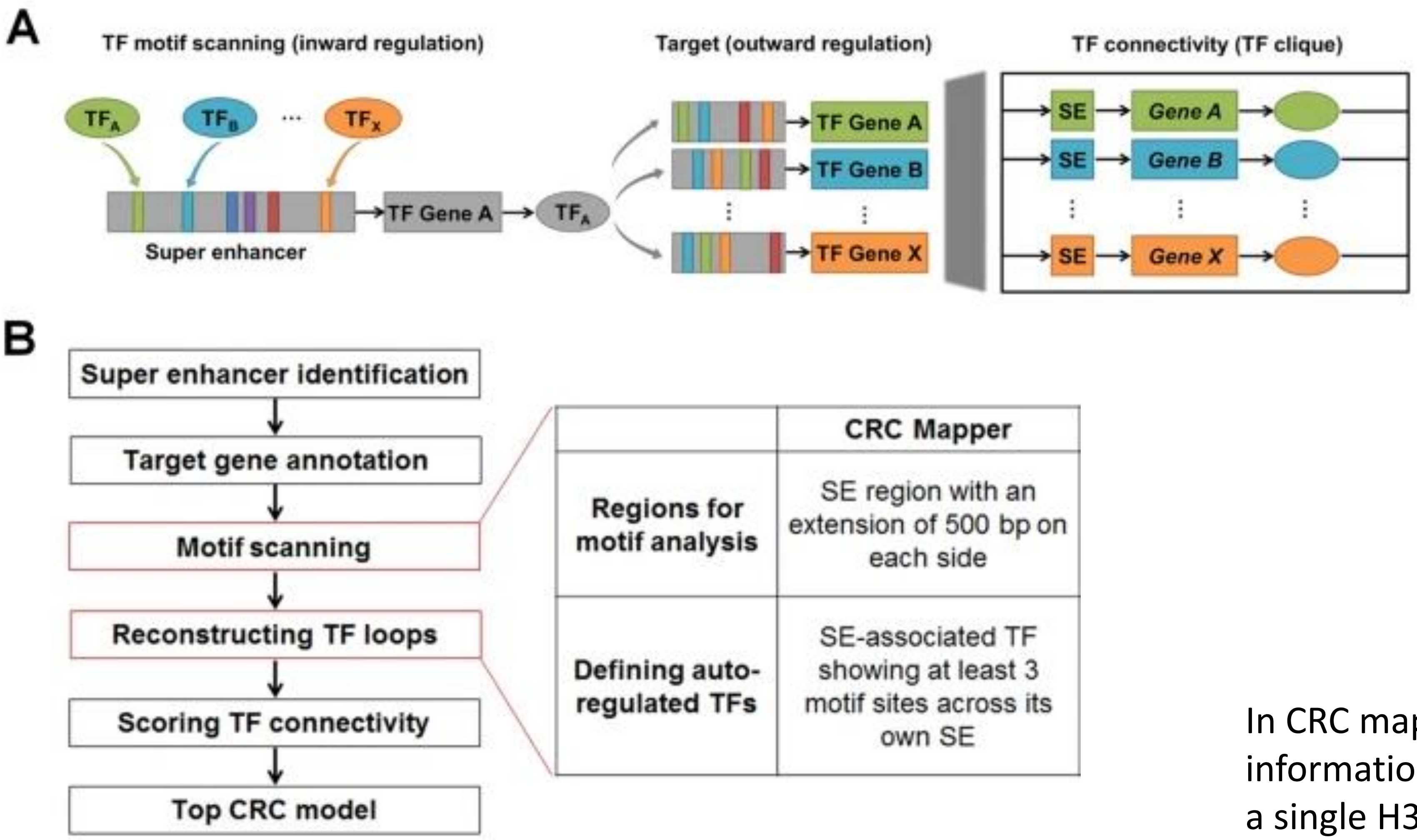
Core Regulatory Circuitries (CRC)



https://royalsocietypublishing.org/doi/10.1098/rsob.200121

Identification of CRCs with CRC-Mapper

Fig. 2: Modeling of core transcriptional regulatory circuitry.

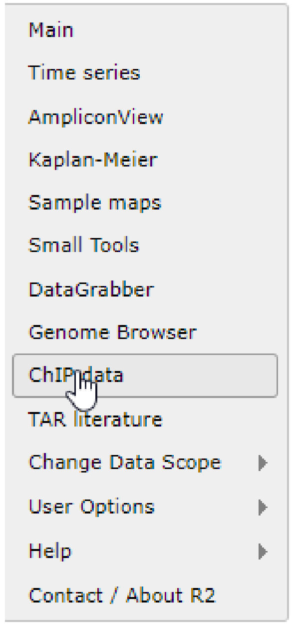


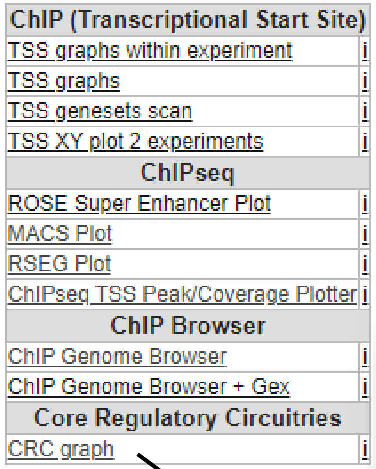
	CRC Mapper
Regions for motif analysis	SE region with an extension of 500 bp on each side
Defining auto-regulated TFs	SE-associated TF showing at least 3 motif sites across its own SE

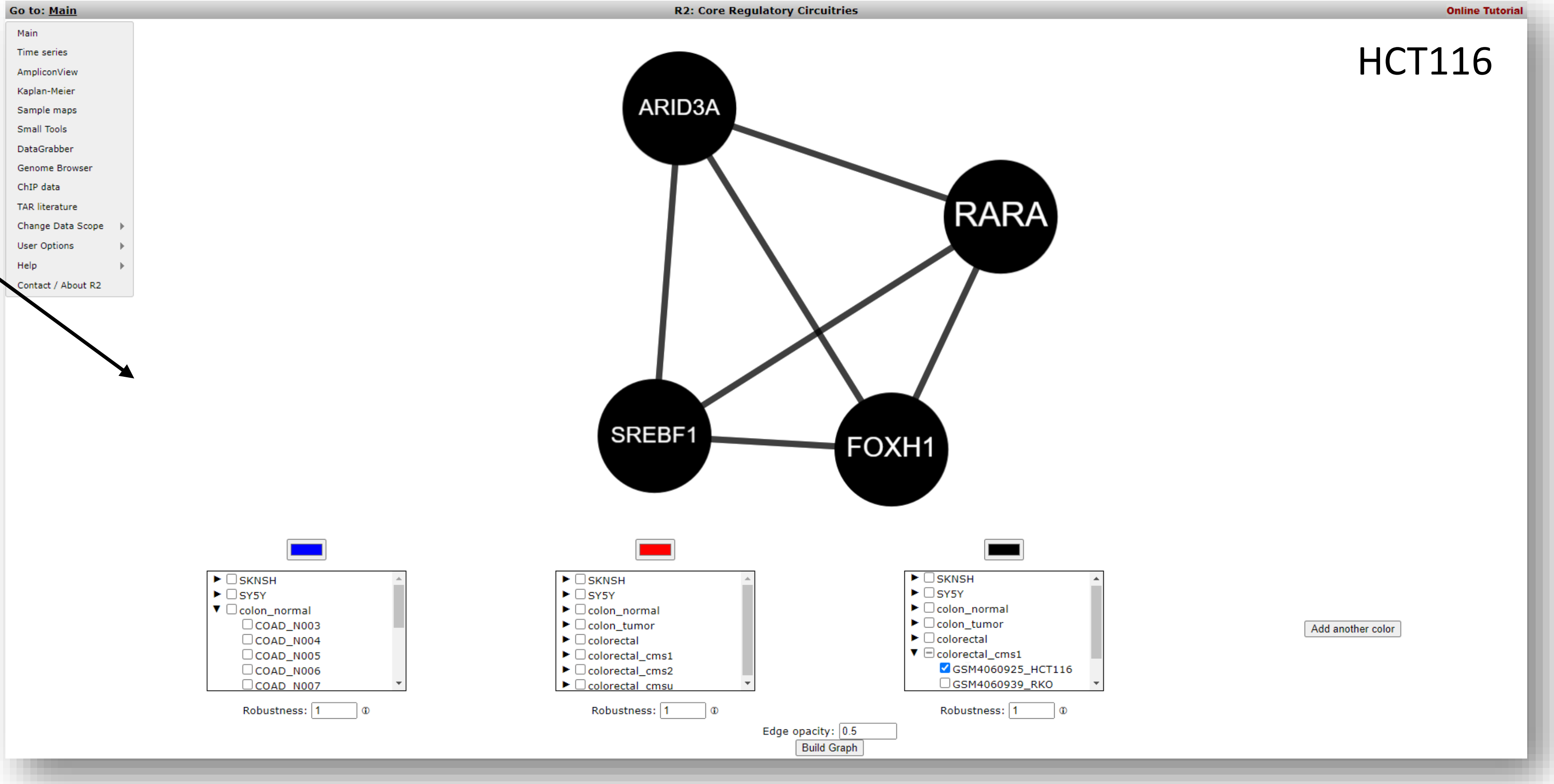
In CRC mapper all information is inferred from a single H3K27ac profile

https://www.nature.com/articles/s41388-020-01459-w

CRC graph in R2







Robustness: 1

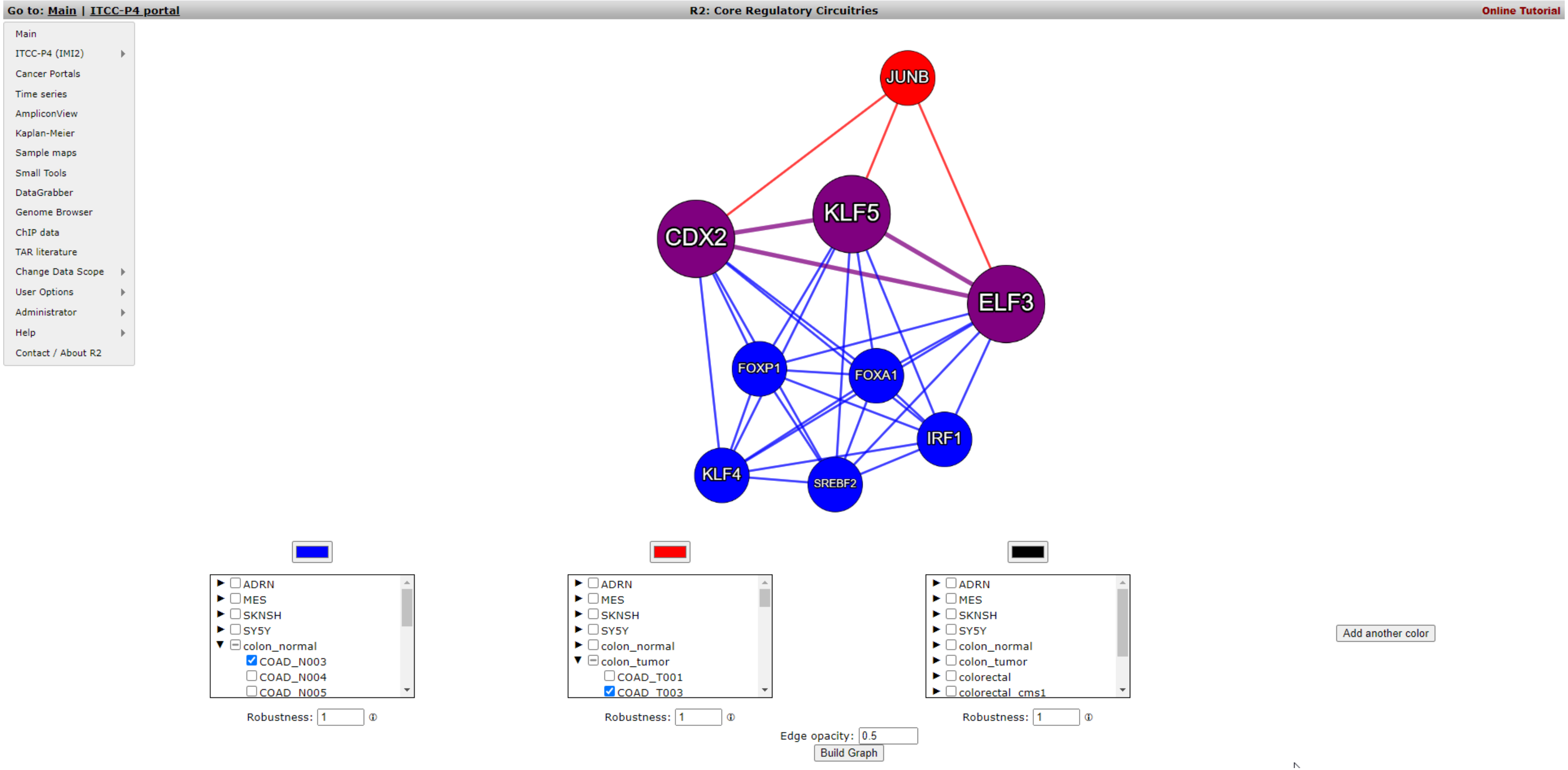
Robustness: 1

Robustness: 1

Edge opacity: 0.5

HCT116

CRC normal vs colon tumor



🟦

▶ ☐ ADRN
▶ ☐ MES
▶ ☐ SKNSH
▶ ☐ SY5Y
▼ ⊟ colon_normal
☑ COAD_N003
☐ COAD_N004
☐ COAD_N005

Robustness: 1

🟥

▶ ☐ ADRN
▶ ☐ MES
▶ ☐ SKNSH
▶ ☐ SY5Y
▶ ☐ colon_normal
▼ ⊟ colon_tumor
☐ COAD_T001
☑ COAD_T003

Robustness: 1

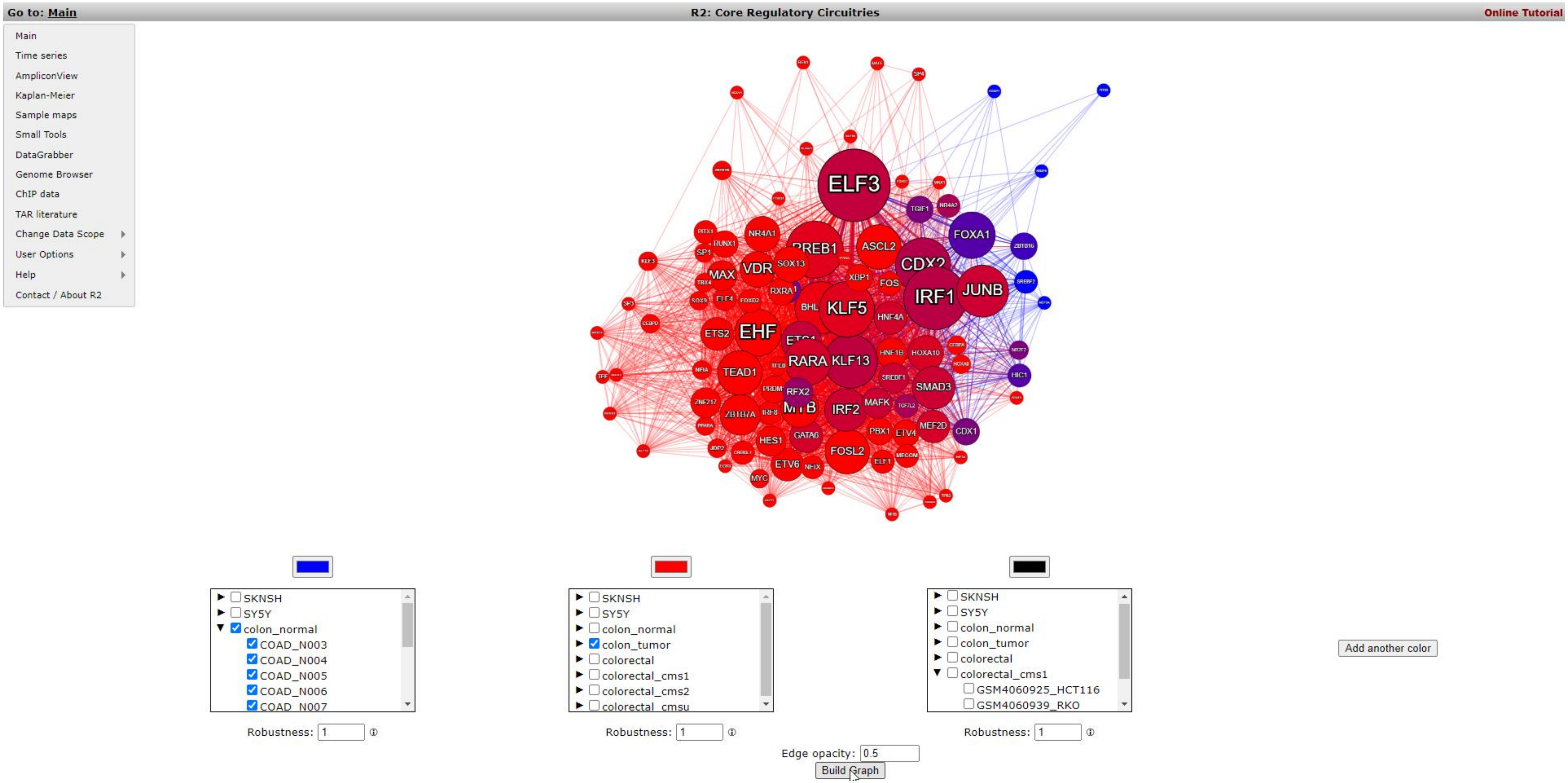
⬛

▶ ☐ ADRN
▶ ☐ MES
▶ ☐ SKNSH
▶ ☐ SY5Y
▶ ☐ colon_normal
▶ ☐ colon_tumor
▶ ☐ colorectal
▶ ☐ colorectal_cms1

Robustness: 1

Edge opacity: 0.5

CRC normal vs colon tumors



🟦
- ☐ SKNSH
- ☐ SY5Y
- ☑ colon_normal
  - ☑ COAD_N003
  - ☑ COAD_N004
  - ☑ COAD_N005
  - ☑ COAD_N006
  - ☑ COAD_N007

Robustness: 1

🟥
- ☐ SKNSH
- ☐ SY5Y
- ☐ colon_normal
- ☑ colon_tumor
- ☐ colorectal
- ☐ colorectal_cms1
- ☐ colorectal_cms2
- ☐ colorectal_cmsu

Robustness: 1

⬛
- ☐ SKNSH
- ☐ SY5Y
- ☐ colon_normal
- ☐ colon_tumor
- ☐ colorectal
- ☐ colorectal_cms1
  - ☐ GSM4060925_HCT116
  - ☐ GSM4060939_RKO

Robustness: 1

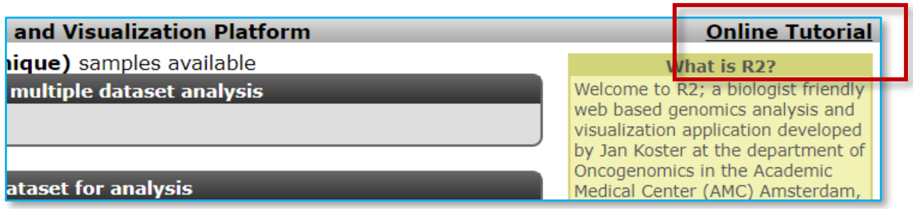
Edge opacity: 0.5

Work in progress

Fun things to do:

Tutorial

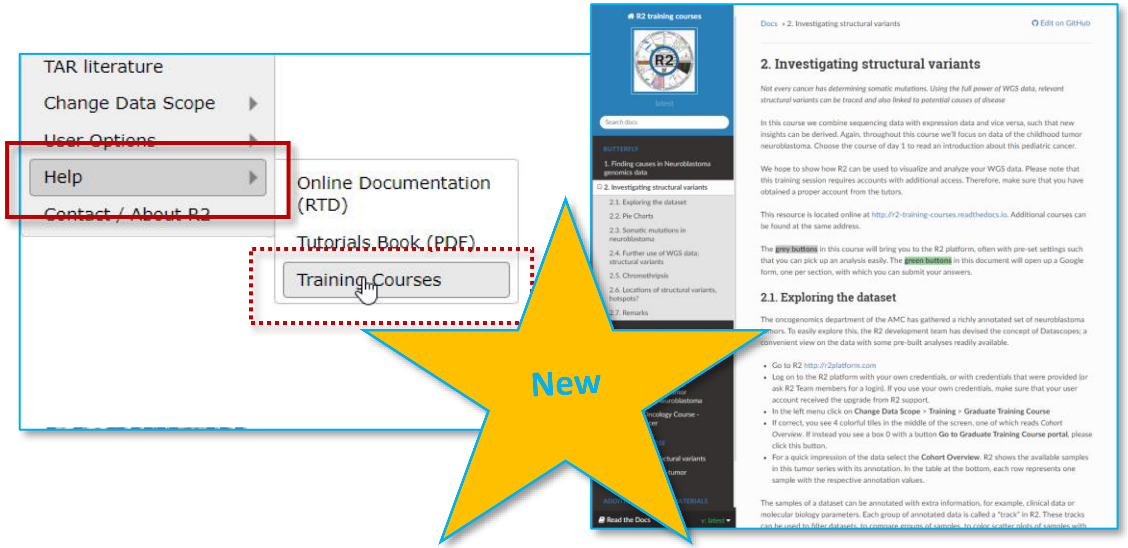
- Go to a chapter of interest and follow the examples
- Toy around with a similar pipeline on a different dataset
- Perform a follow up analysis from the tutorial



Welcome to R2; a biologist friendly web based genomics analysis and visualization application developed by Jan Koster at the department of Oncogenomics in the Academic Medical Center (AMC) Amsterdam,

R2 Butterfly Training Courses

- Help => Training Courses => Butterfly Training Courses
- Read carefully and follow the research line step by step
- Feel free to toy around
  - Who knows



Docs » 2. Investigating structural variants

Edit on GitHub

2. Investigating structural variants

Not every cancer has determining somatic mutations. Using the full power of WGS data, relevant structural variants can be traced and also linked to potential causes of disease

In this course we combine sequencing data with expression data and vice versa, such that new insights can be derived. Again, throughout this course we'll focus on data of the childhood tumor neuroblastoma. Choose the course of day 1 to read an introduction about this pediatric cancer.

We hope to show how R2 can be used to visualize and analyze your WGS data. Please note that this training session requires accounts with additional access. Therefore, make sure that you have obtained a proper account from the tutors.

This resource is located online at http://r2-training-courses.readthedocs.io. Additional courses can be found at the same address.

The **grey buttons** in this course will bring you to the R2 platform, often with pre-set settings such that you can pick up an analysis easily. The **green buttons** in this document will open up a Google form, one per section, with which you can submit your answers.

2.1. Exploring the dataset

The oncogenomics department of the AMC has gathered a richly annotated set of neuroblastoma tumors. To easily explore this, the R2 development team has devised the concept of Datascopes; a convenient view on the data with some pre-built analyses readily available.

- Go to R2 http://r2platform.com
- Log on to the R2 platform with your own credentials, or with credentials that were provided (or ask R2 Team members for a login). If you use your own credentials, make sure that your user account received the upgrade from R2 support.
- In the left menu click on **Change Data Scope** > **Training** > **Graduate Training Course**
- If correct, you see 4 colorful tiles in the middle of the screen, one of which reads *Cohort Overview*. If instead you see a box 0 with a button **Go to Graduate Training Course portal**, please click this button.
- For a quick impression of the data select the **Cohort Overview**. R2 shows the available samples in this tumor series with its annotation. In the table at the bottom, each row represents one sample with the respective annotation values.

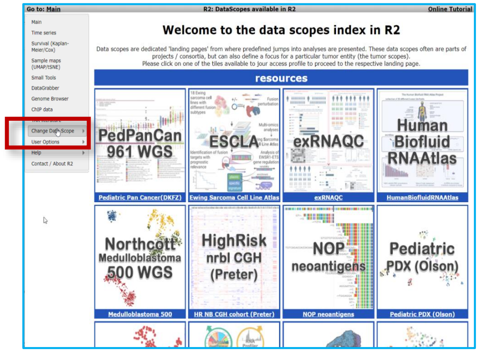
The samples of a dataset can be annotated with extra information, for example, clinical data or molecular biology parameters. Each group of annotated data is called a "track" in R2. These tracks

Do your own research

- Find a dataset of your interest
- Think about a good biological research question
- Try to find the analyses that can help you gain insight

Datascopes

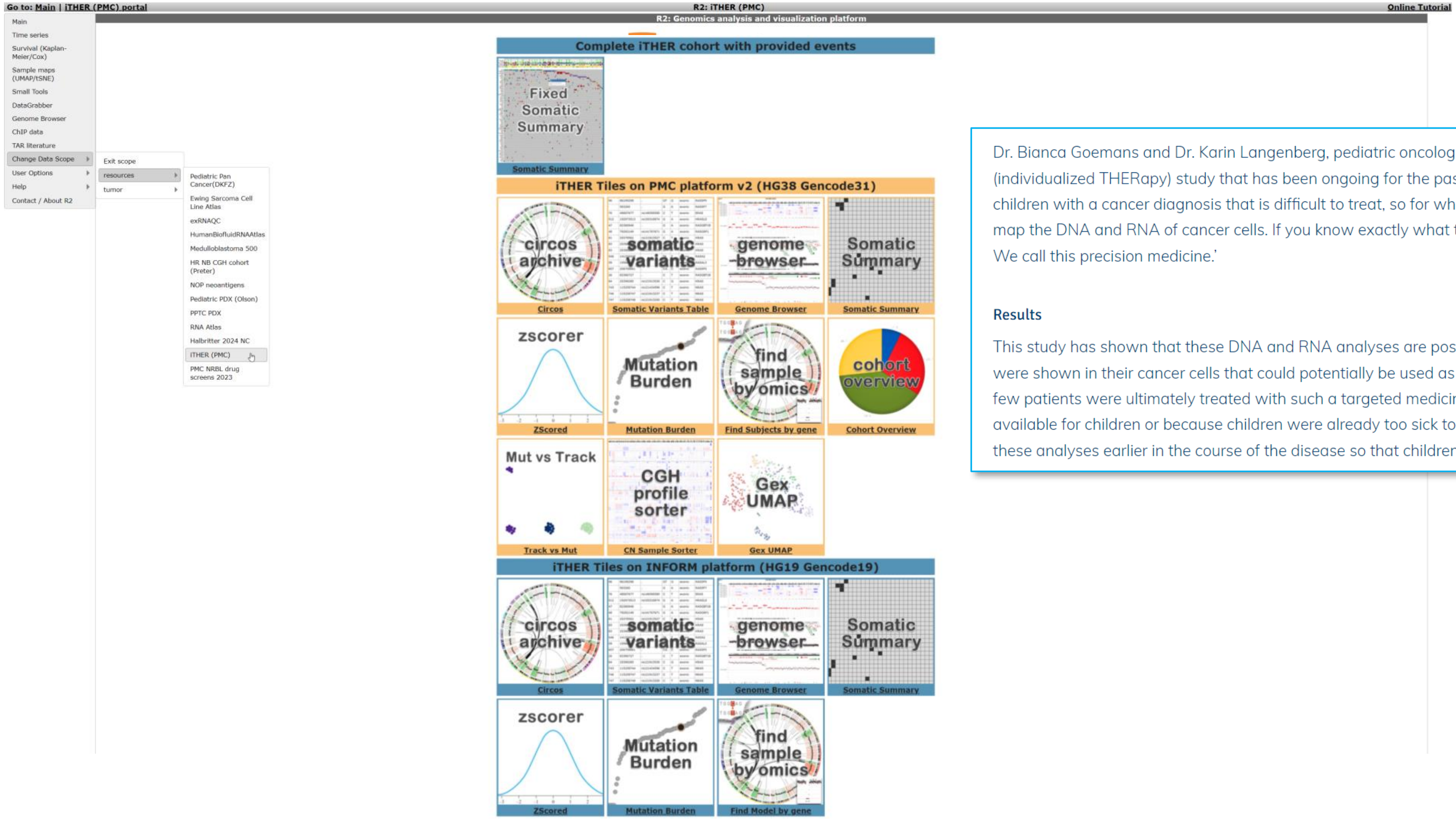
- Find an interesting datascope to dive into



Welcome to the data scopes index in R2

Data scopes are dedicated 'landing pages' from where predefined jumps into analyses are presented. These data scopes often are parts of projects / consortia, but can also define a focus for a particular tumor entity (the tumor scopes). Please click on one of the tiles available to jour access profile to proceed to the respective landing page.

Ither datascope



Dr. Bianca Goemans and Dr. Karin Langenberg, pediatric oncologists and researchers, are involved in the iTHER (individualized THERapy) study that has been ongoing for the past five years. Bianca Goemans says: ‘This study involved children with a cancer diagnosis that is difficult to treat, so for which there is no standard treatment available. We wanted to map the DNA and RNA of cancer cells. If you know exactly what that looks like, you can find leads for a targeted medicine. We call this precision medicine.’

Results

This study has shown that these DNA and RNA analyses are possible and that in the majority of patients (83%) changes were shown in their cancer cells that could potentially be used as a target for treatment. Bianca Goemans: ‘Unfortunately, few patients were ultimately treated with such a targeted medicine, partly because the medicine was often not (yet) available for children or because children were already too sick to participate in a clinical trial. That's why we want to do these analyses earlier in the course of the disease so that children may still qualify for a targeted treatment.’

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Tutorial

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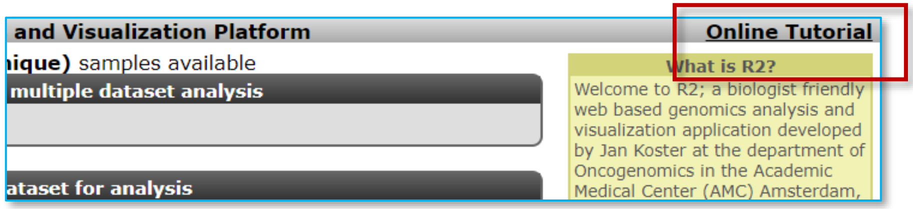
- Toy around with a similar pipeline on a different dataset
- Perform a follow up analysis from the tutorial



and Visualization Platform

ique) samples available

multiple dataset analysis

ataset for analysis

What is R2?

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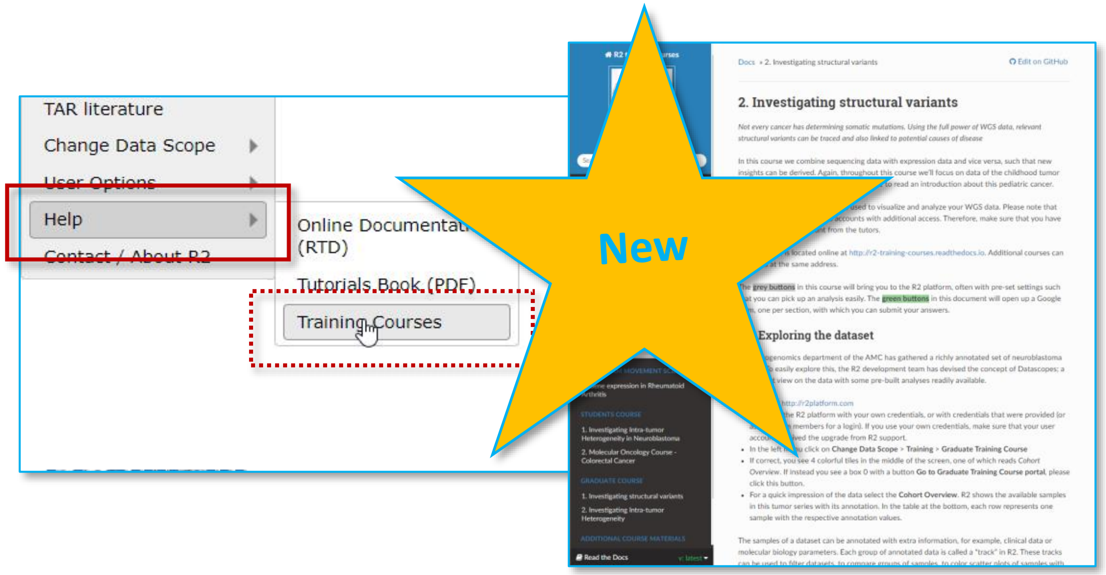

2. Investigating structural variants

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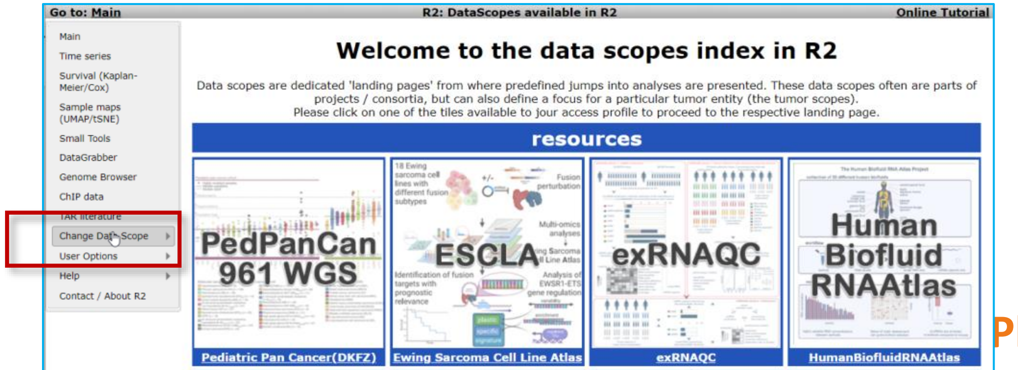

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Platform

Amsterdam UMC
University Medical Centers

http://r2platform.com

R2 Platform Team

Rianne van Drimmelen

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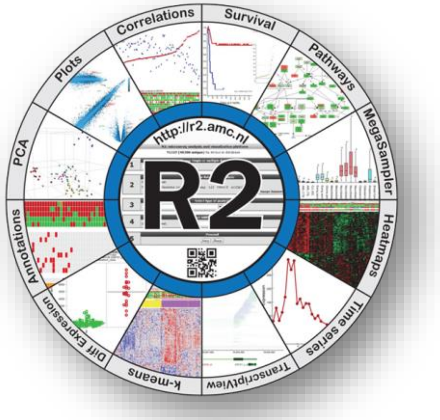

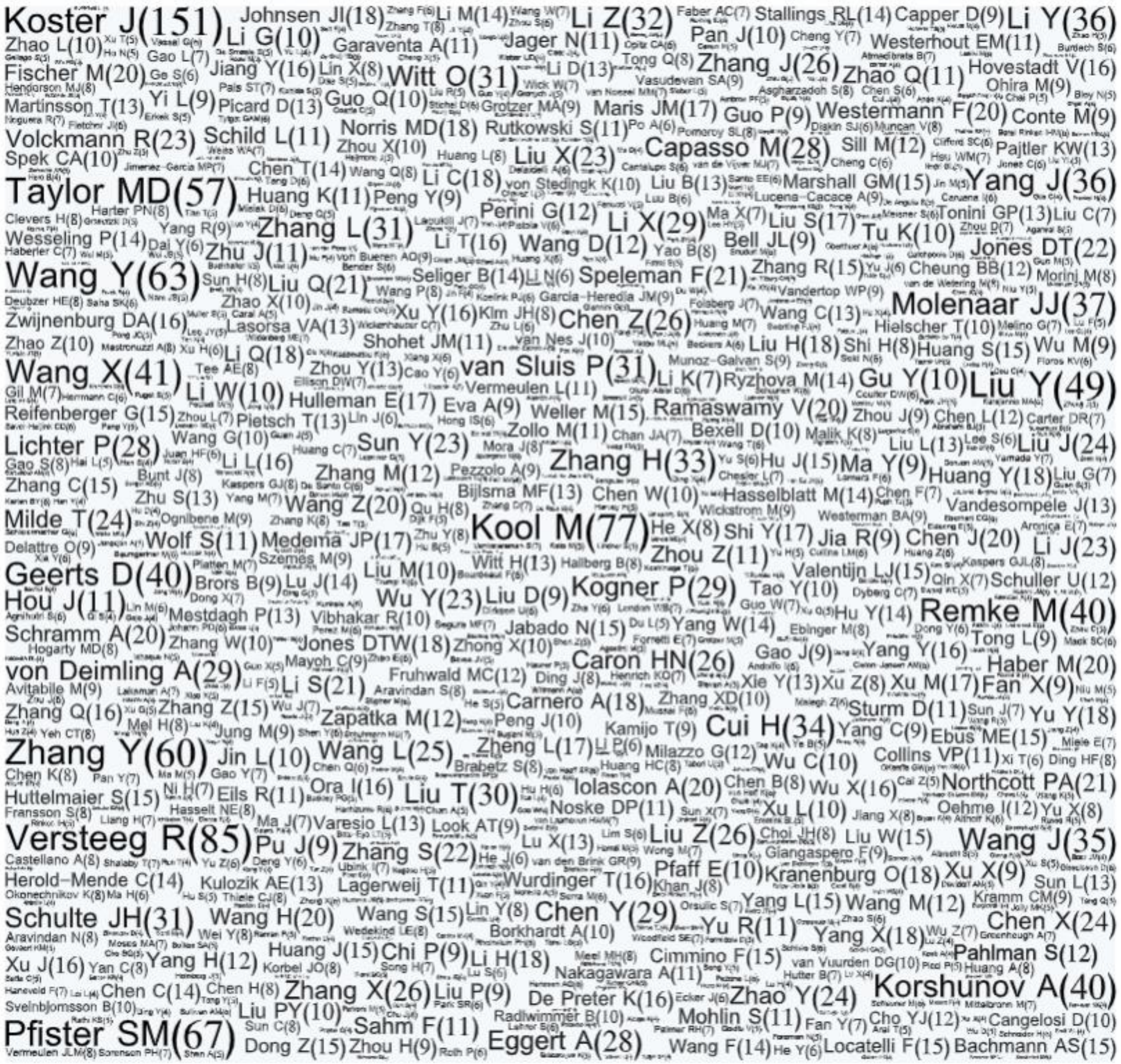

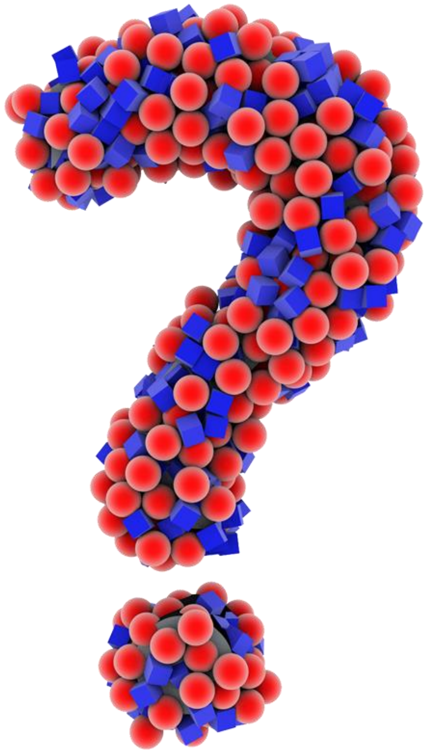

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