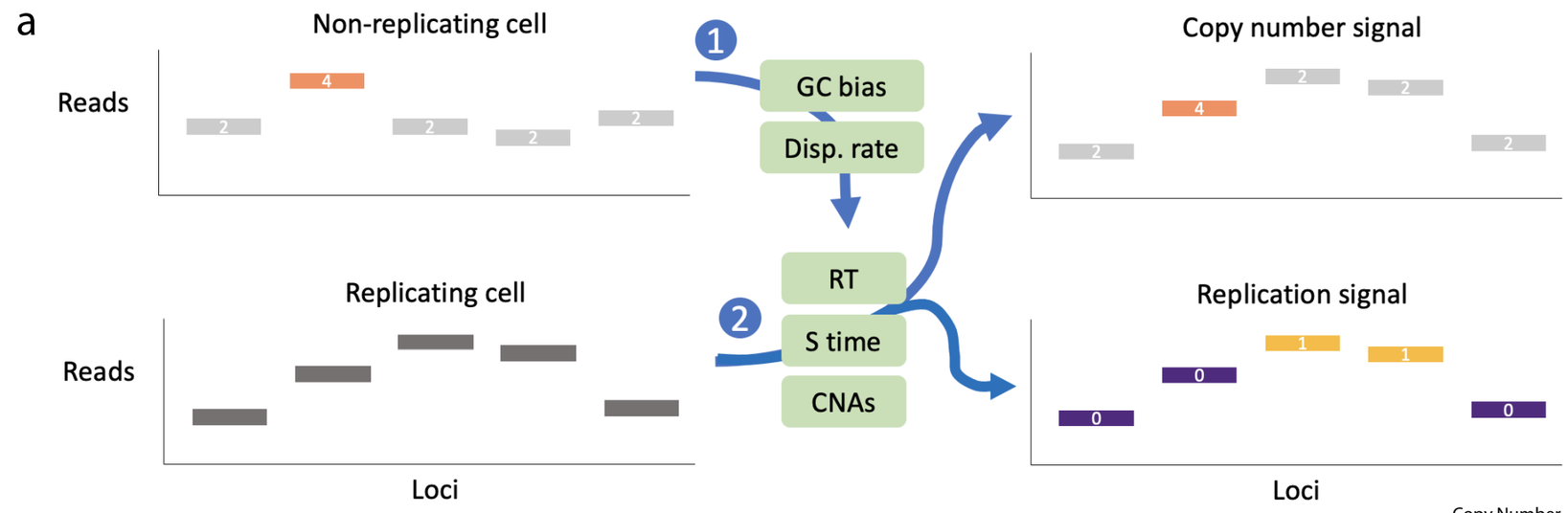
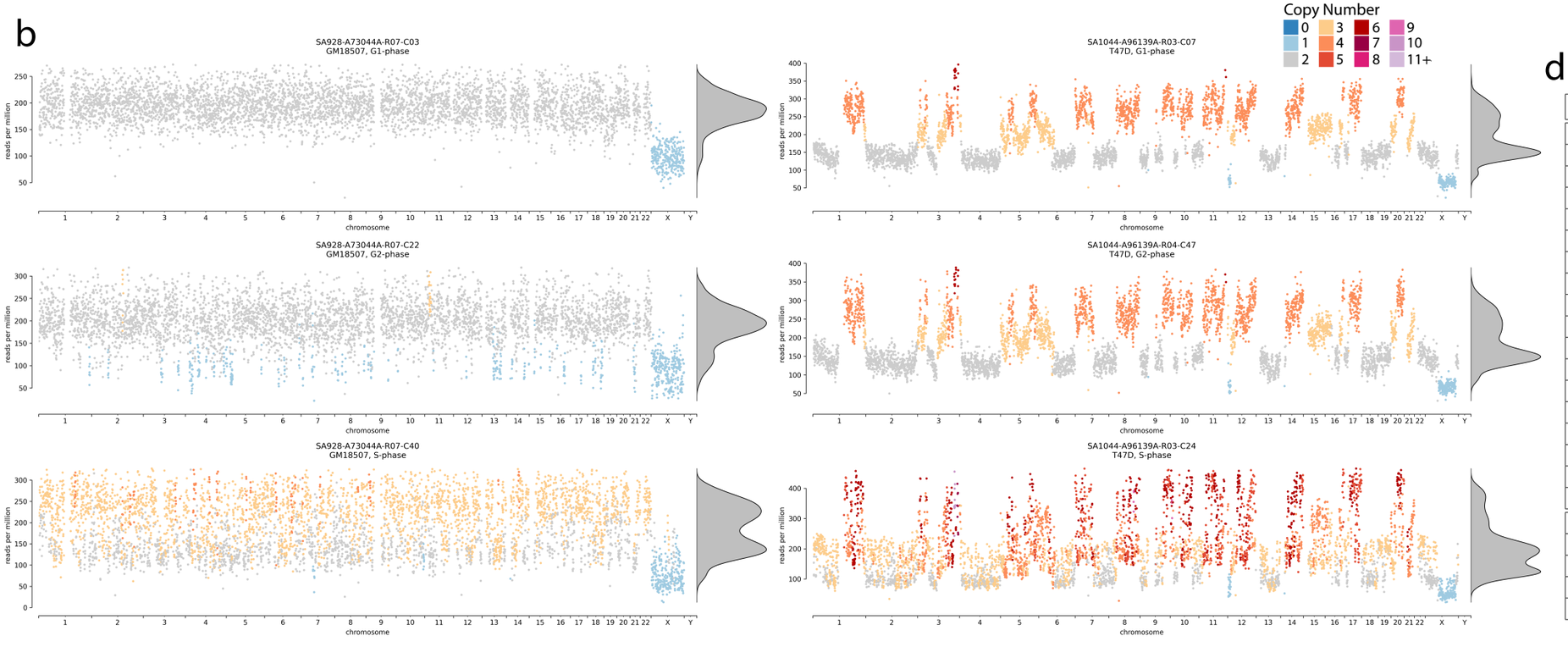
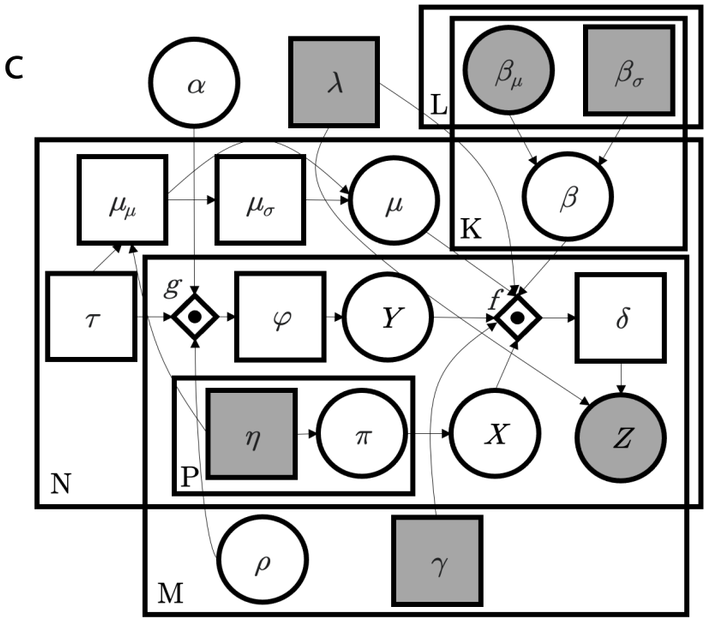
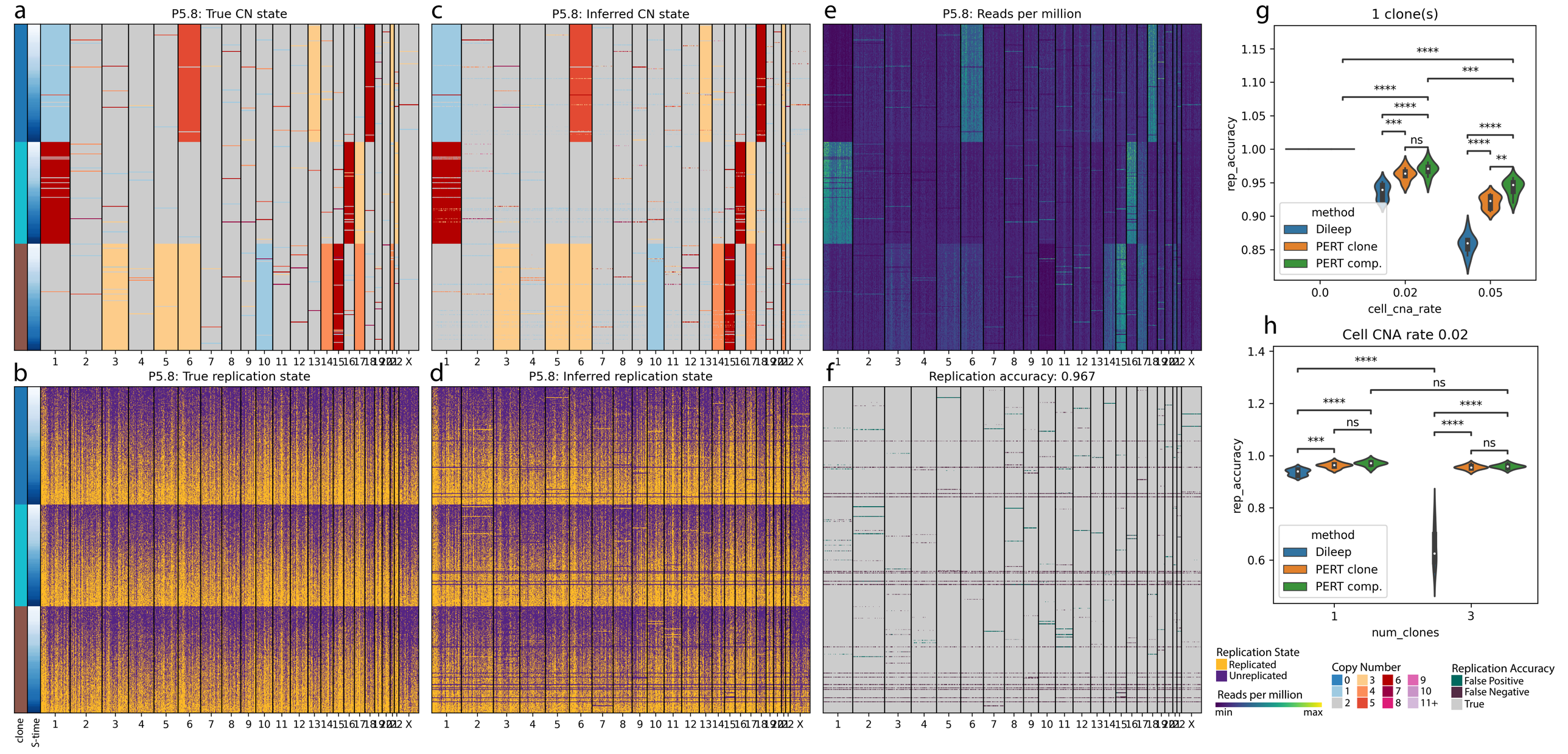






d

Name	Domain/Distribution	Description
λ	$(0, 1)$	NB event success probability (overdispersion)
δ	$[1, \infty)$	# of NB events (Eq 4.4)
γ	$[0, 1]$	GC content of locus
β_μ	$\sim \mathrm{N}(0, 1)$	GC bias polynomial coefficient means
β_σ	$(0, \infty)$	GC bias polynomial coefficient stdevs
β	$\sim \mathrm{N}(\beta_\mu, \beta_\sigma)$	GC bias polynomial coefficients
μ_μ	$(0, \infty)$	coverage/ploidy mean (Eq 4.8)
μ_σ	$(0, \infty)$	coverage/ploidy stdev (Eq 4.9)
μ	$\sim \mathrm{N}(\mu_\mu, \mu_\sigma)$	coverage/ploidy scaling term
τ	$[0, 1]$	time in S-phase
ρ	$\sim \mathrm{Beta}(1, 1)$	replication timing
α	$\sim \Gamma(2, 0.2)$	replication stochasticity term
ϕ	$(0, 1)$	replication probabilities (Eq 4.5)
Y	$\sim \mathrm{Bernoulli}(\phi)$	replication status
η	$[0, 1]$	copy number prior concentration
π	$\sim \mathrm{Dir}(\eta)$	copy number probabilities
X	$\sim \mathrm{Cat}(\pi)$	copy number state
Z	$\sim \mathrm{NB}(\delta, \lambda)$	read depth
K		GC bias polynomial degree
L		# libraries
M		# genomic loci
N		# cells
P		# copy number states


a
P5.8: True CN state
c
P5.8: Inferred CN state
e
P5.8: Reads per million
b
P5.8: True replication state
d
P5.8: Inferred replication state
f
Replication accuracy: 0.967
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X
clone
S-time
g
1 clone(s)
rep_accuracy
cell_cna_rate
0.0
0.02
0.05
method
Dileep
PERT clone
PERT comp.
****
***
**
ns
h
Cell CNA rate 0.02
num_clones
1
3
Replication State
Replicated
Unreplicated
Reads per million
min
max
Copy Number
0 1 2 3 4 5 6 7 8 9 10 11+
Replication Accuracy
False Positive
False Negative
True

a

HMMcopy states

b

Inferred CN states

c

Inferred replication states

clone
S-time

Copy Number
0 1 2 3 4 5 6 7 8 9 10 11+

Replication State
Replicated
Unreplicated

d

Reads per million UMAP

flow phase
G1
S
G2

embedding_1
embedding_0

e

Reads per million UMAP

cell line
T47D
GM18507

embedding_1
embedding_0

f

RT Diff
<--GM18507 earlier | T47D earlier -->

chromosome

g

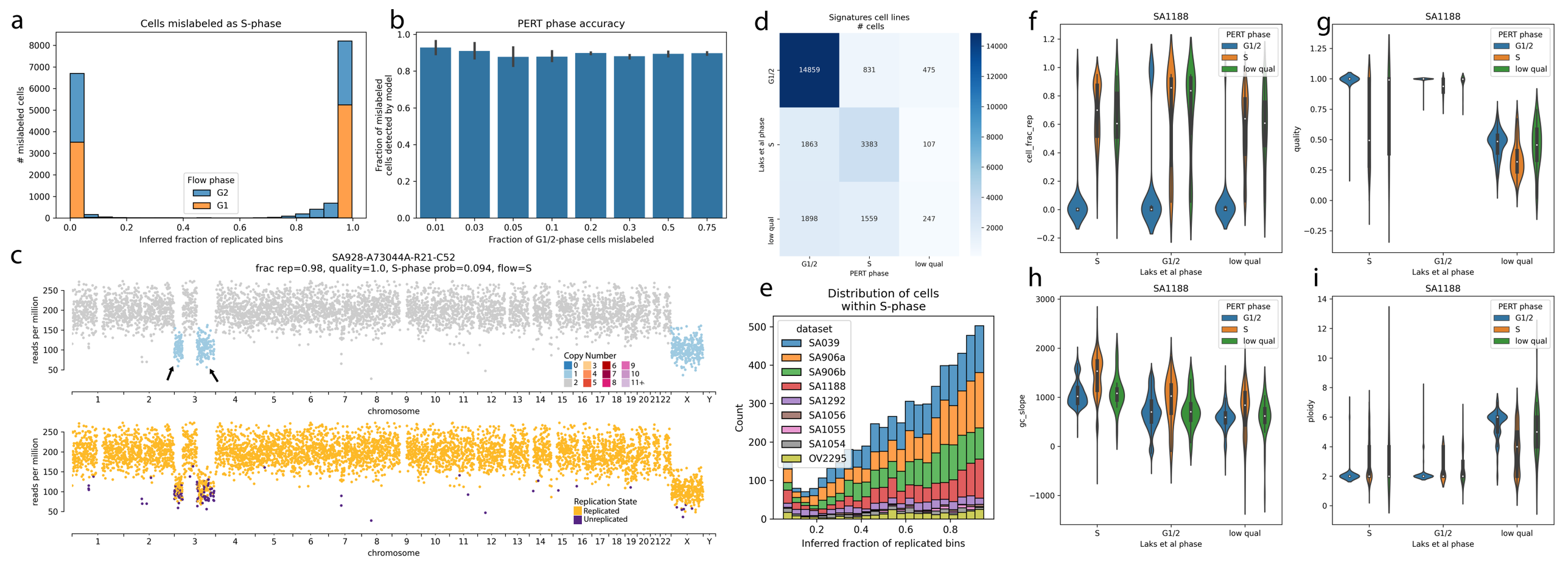
Pseudobulk RT correlations
Flow sorted data passed into PERT joint vs split by cell line

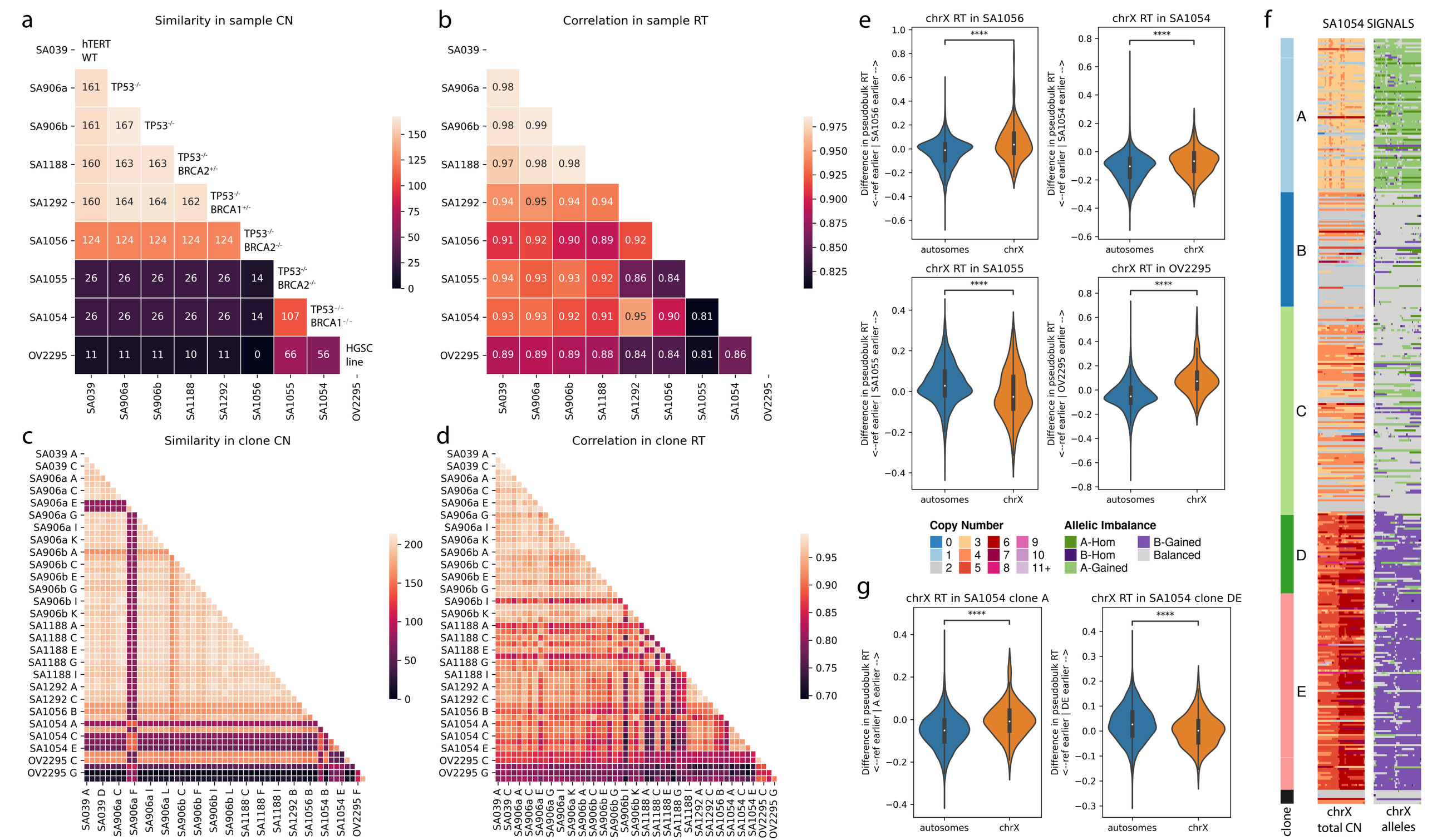
gc
T47D joint
T47D split
GM18507 joint
GM18507 split

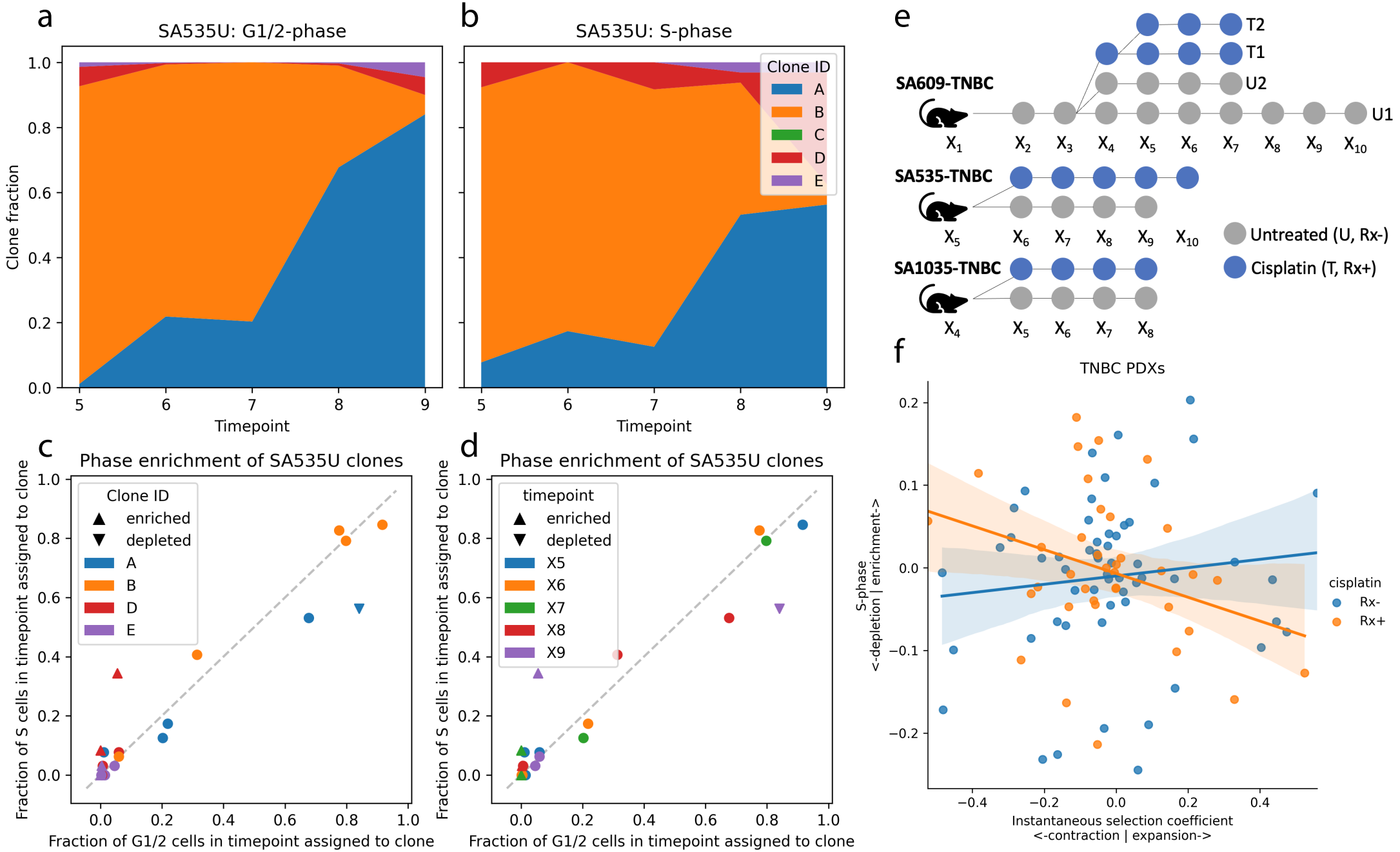
h

Pseudobulk RT correlations
Simulated datasets P10 and P11 with clone-specific RT

gm06990 P10A inferred
gm06990 P10A true
gm12801 P10B inferred
gm12801 P10B true
gm12812 P10C inferred
gm12812 P10C true
gm12813 P10D inferred
gm12813 P10D true
bj P11A inferred
bj P11A true
mcf7 P11B inferred
mcf7 P11B true
hepg2 P11C inferred
hepg2 P11C true
gm12813 P11D inferred
gm12813 P11D true


a
Cells mislabeled as S-phase
mislabeled cells
Inferred fraction of replicated bins
Flow phase
G2
G1
b
PERT phase accuracy
Fraction of mislabeled cells detected by model
Fraction of G1/2-phase cells mislabeled
c
SA928-A73044A-R21-C52
frac rep=0.98, quality=1.0, S-phase prob=0.094, flow=S
reads per million
chromosome
Copy Number
Replication State
Replicated
Unreplicated
d
Signatures cell lines
cells
Laks et al phase
PERT phase
e
Distribution of cells within S-phase
dataset
SA039
SA906a
SA906b
SA1188
SA1292
SA1056
SA1055
SA1054
OV2295
Count
Inferred fraction of replicated bins
f
SA1188
cell_frac_rep
PERT phase
G1/2
S
low qual
Laks et al phase
g
SA1188
quality
h
SA1188
gc_slope
i
SA1188
ploidy


a
Similarity in sample CN
SA039 - hTERT WT
SA906a - 161 TP53-/-
SA906b - 161 167 TP53-/-
SA1188 - 160 163 163 TP53-/- BRCA2+/-
SA1292 - 160 164 164 162 TP53-/- BRCA1+/-
SA1056 - 124 124 124 124 124 TP53-/- BRCA2-/-
SA1055 - 26 26 26 26 26 14 TP53-/- BRCA2-/-
SA1054 - 26 26 26 26 26 14 107 TP53-/- BRCA1-/-
OV2295 - 11 11 11 10 11 0 66 56 HGSC line
SA039 SA906a SA906b SA1188 SA1292 SA1056 SA1055 SA1054 OV2295
150 125 100 75 50 25 0
b
Correlation in sample RT
SA039 -
SA906a - 0.98
SA906b - 0.98 0.99
SA1188 - 0.97 0.98 0.98
SA1292 - 0.94 0.95 0.94 0.94
SA1056 - 0.91 0.92 0.90 0.89 0.92
SA1055 - 0.94 0.93 0.93 0.92 0.86 0.84
SA1054 - 0.93 0.93 0.92 0.91 0.95 0.90 0.81
OV2295 - 0.89 0.89 0.89 0.88 0.84 0.84 0.81 0.86
SA039 SA906a SA906b SA1188 SA1292 SA1056 SA1055 SA1054 OV2295
0.975 0.950 0.925 0.900 0.875 0.850 0.825
c
Similarity in clone CN
SA039 A SA039 C SA906a A SA906a C SA906a E SA906a G SA906a I SA906a K SA906b A SA906b C SA906b E SA906b G SA906b I SA906b K SA1188 A SA1188 C SA1188 E SA1188 G SA1188 I SA1292 A SA1292 C SA1056 B SA1054 A SA1054 C SA1054 E OV2295 C OV2295 G
SA039 A SA039 D SA906a C SA906a F SA906a I SA906a L SA906b C SA906b F SA906b I SA906b L SA1188 C SA1188 F SA1188 I SA1292 B SA1056 B SA1054 B SA1054 E SA1054 E OV2295 F
200 150 100 50 0
d
Correlation in clone RT
SA039 A SA039 C SA906a A SA906a C SA906a E SA906a G SA906a I SA906a K SA906b A SA906b C SA906b E SA906b G SA906b I SA906b K SA1188 A SA1188 C SA1188 E SA1188 G SA1188 I SA1292 A SA1292 C SA1056 B SA1054 A SA1054 C SA1054 E OV2295 C OV2295 G
SA039 A SA039 C SA906a A SA906a C SA906a E SA906a G SA906a I SA906a K SA906b A SA906b C SA906b E SA906b G SA906b I SA906b K SA1188 A SA1188 C SA1188 E SA1188 G SA1188 I SA1292 A SA1292 C SA1056 B SA1054 A SA1054 C SA1054 E OV2295 C OV2295 G
0.95 0.90 0.85 0.80 0.75 0.70
e
chrX RT in SA1056
chrX RT in SA1054
chrX RT in SA1055
chrX RT in OV2295
Difference in pseudobulk RT <--ref earlier | SA1056 earlier -->
Difference in pseudobulk RT <--ref earlier | SA1054 earlier -->
Difference in pseudobulk RT <--ref earlier | SA1055 earlier -->
Difference in pseudobulk RT <--ref earlier | OV2295 earlier -->
****
autosomes chrX
Copy Number
0 1 2 3 4 5 6 7 8 9 10 11+
Allelic Imbalance
A-Hom B-Hom A-Gained B-Gained Balanced
g
chrX RT in SA1054 clone A
chrX RT in SA1054 clone DE
Difference in pseudobulk RT <--ref earlier | A earlier -->
Difference in pseudobulk RT <--ref earlier | DE earlier -->
f
SA1054 SIGNALS
A B C D E
clone
chrX total CN
chrX alleles


a
SA535U: G1/2-phase
Clone fraction
Timepoint
b
SA535U: S-phase
Clone ID
A
B
C
D
E
Timepoint
e
SA609-TNBC
T2
T1
U2
U1
X1 X2 X3 X4 X5 X6 X7 X8 X9 X10
SA535-TNBC
X5 X6 X7 X8 X9 X10
SA1035-TNBC
X4 X5 X6 X7 X8
Untreated (U, Rx-)
Cisplatin (T, Rx+)
c
Phase enrichment of SA535U clones
Clone ID
enriched
depleted
A
B
D
E
Fraction of S cells in timepoint assigned to clone
Fraction of G1/2 cells in timepoint assigned to clone
d
Phase enrichment of SA535U clones
timepoint
enriched
depleted
X5
X6
X7
X8
X9
Fraction of S cells in timepoint assigned to clone
Fraction of G1/2 cells in timepoint assigned to clone
f
TNBC PDXs
S-phase
<-depletion | enrichment->
Instantaneous selection coefficient
<-contraction | expansion->
cisplatin
Rx-
Rx+