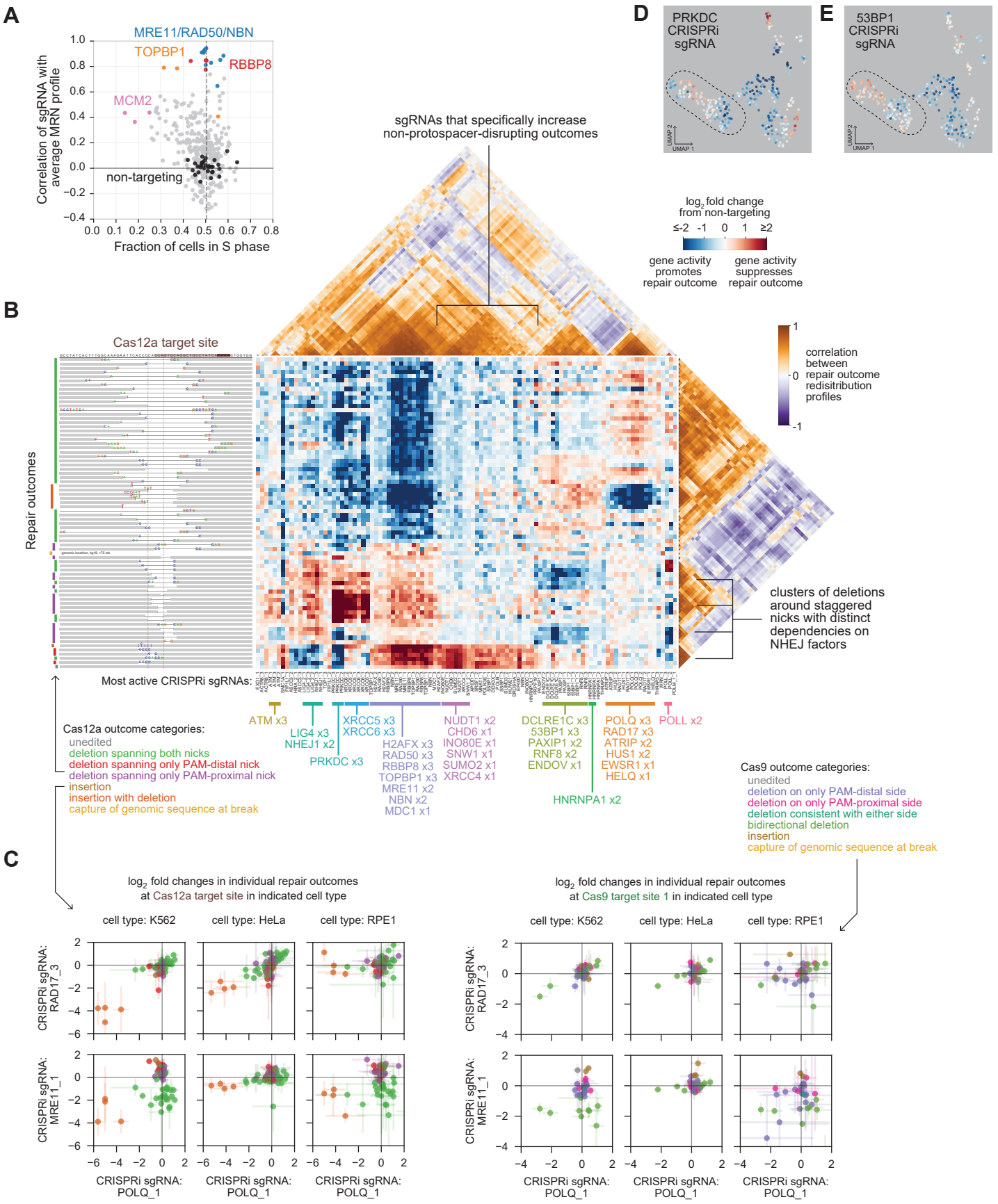
A
MRE11/RAD50/NBN
TOPBP1
RBBP8
MCM2
non-targeting
Correlation of sgRNA with average MRN profile
Fraction of cells in S phase
D
PRKDC CRISPRi sgRNA
E
53BP1 CRISPRi sgRNA
UMAP 1
UMAP 2
log2 fold change from non-targeting
≤-2 -1 0 1 ≥2
gene activity promotes repair outcome
gene activity suppresses repair outcome
sgRNAs that specifically increase non-protospacer-disrupting outcomes
B
Cas12a target site
Repair outcomes
correlation between repair outcome redisitribution profiles
clusters of deletions around staggered nicks with distinct dependencies on NHEJ factors
Most active CRISPRi sgRNAs:
ATM x3
LIG4 x3
NHEJ1 x2
PRKDC x3
XRCC5 x3
XRCC6 x3
H2AFX x3
RAD50 x3
RBBP8 x3
TOPBP1 x3
MRE11 x2
NBN x2
MDC1 x1
NUDT1 x2
CHD6 x1
INO80E x1
SNW1 x1
SUMO2 x1
XRCC4 x1
DCLRE1C x3
53BP1 x3
PAXIP1 x2
RNF8 x2
ENDOV x1
HNRNPA1 x2
POLQ x3
RAD17 x3
ATRIP x2
HUS1 x2
EWSR1 x1
HELQ x1
POLL x2
Cas12a outcome categories:
unedited
deletion spanning both nicks
deletion spanning only PAM-distal nick
deletion spanning only PAM-proximal nick
insertion
insertion with deletion
capture of genomic sequence at break
Cas9 outcome categories:
unedited
deletion on only PAM-distal side
deletion on only PAM-proximal side
deletion consistent with either side
bidirectional deletion
insertion
capture of genomic sequence at break
C
log2 fold changes in individual repair outcomes at Cas12a target site in indicated cell type
cell type: K562
cell type: HeLa
cell type: RPE1
CRISPRi sgRNA: RAD17_3
CRISPRi sgRNA: MRE11_1
CRISPRi sgRNA: POLQ_1
log2 fold changes in individual repair outcomes at Cas9 target site 1 in indicated cell type