A

```
Human 549 EEGLFSQKSFLVLGFSNENESNIANIIKENAGKIMSLLSRTVADYAVVPLLGCEVEATVG  608
Mouse 552 EEGLFSQKSFLVLGFSVENKCNIVDIIREHAGKIVSLPSRIVADYAVVPLLGCEVDVTVG  611
                  β1        α1                          β2
Human 609 EVVTNTWLVTCIDYQTLFDPKSNPLFTPVPVMTGMTPLEDCVISFSQCAGAEKESLTFLA  668
Mouse 612 EVVTNTWLVTCIDNQTLVDPKSNPLFTPVSVMSGVTPLEDCVISFSQCVGAERDSLVFLA  671
            β3        α2          αL                  β1'       α1'
Human 669 NLLGASVQEYFVRKSNAKKGMFASTHLILKERGGSKYEAAKKWNLPAVTIAWLLETARTG  728
Mouse 672 NHLGASVQEFFVRKANAKKGMLASTHLIVKEPTGSKYEAAKKWSLPAVNISWLLETARIG  731
            β2'               β3          α2'       α3'
Human 729 KRADESHFLIENSTKEER  746
Mouse 732 KRADENHFLVDNAPKQEQ  749
            α4'
```

B

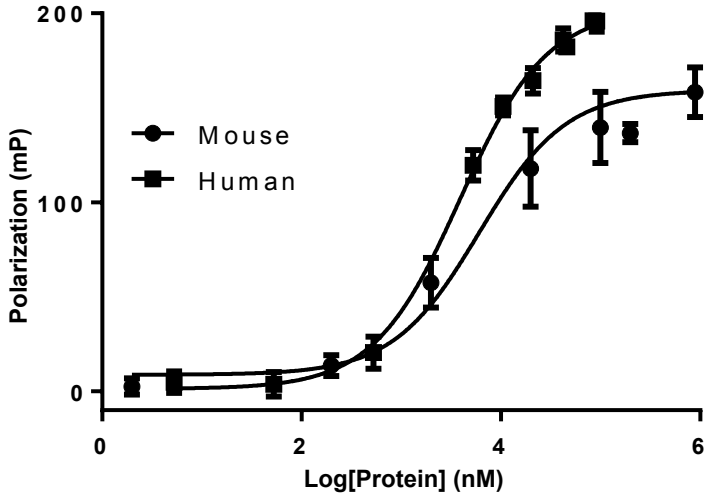

Figure S1. Related to Figure 1. Comparison of human versus mouse TopBP1 BLM interactions.

A. Sequence alignment of mouse versus human proteins with secondary structure by PROMALS3D. Residues forming the BRCT-BRCT interface are colored green, residues from the peptide binding surface are colored blue (charged loop), purple (phosphate binding pocket), and orange (hydrophobic groove).

B. Comparison of BLM interaction with mouse versus human TopBP1 BRCT4/5 by FP assay.

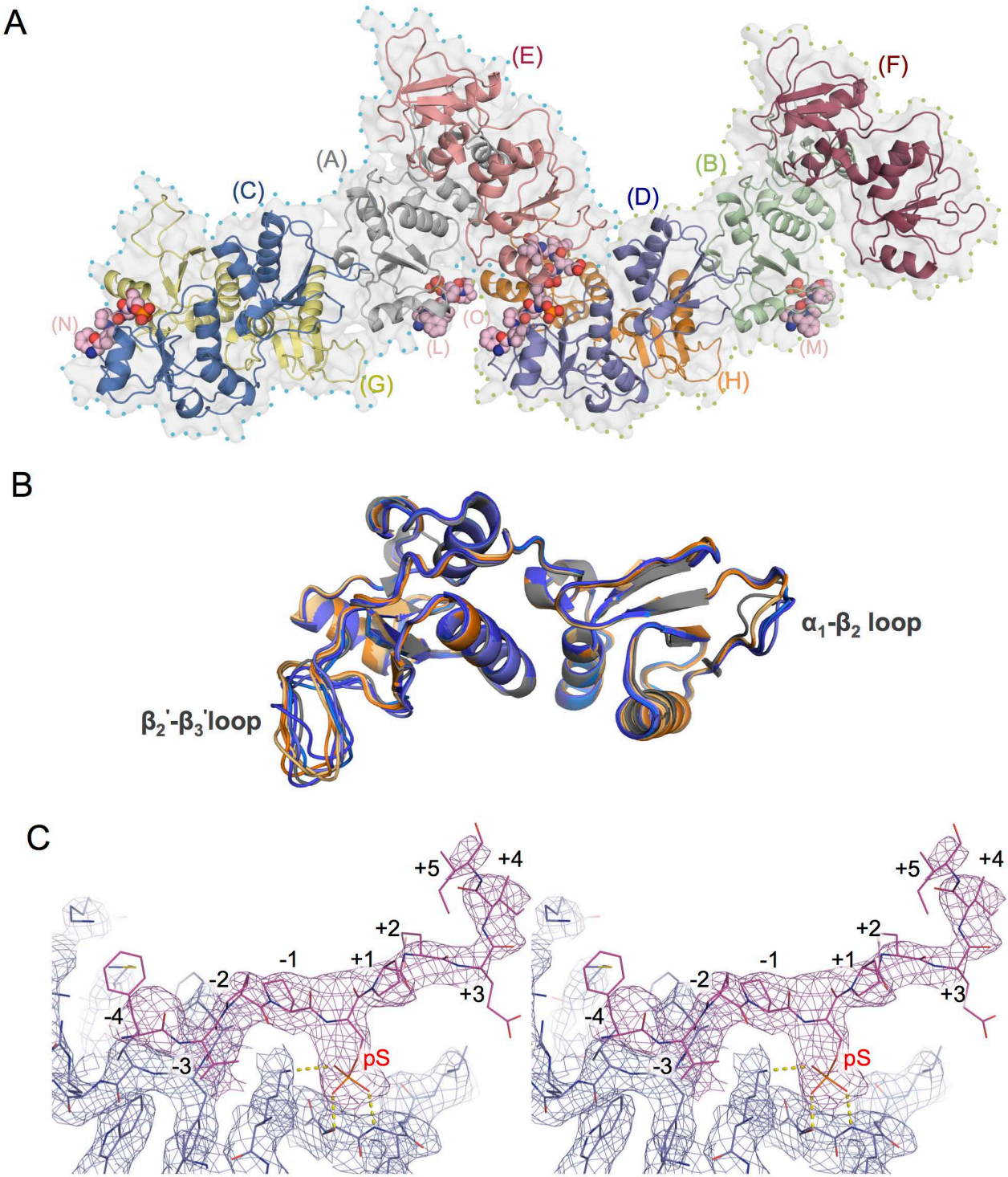

Figure S2. Related to Figure 1. X-ray crystal structure of TopBP1 BRCT4/5 with BLM.
A. Overview of the crystallographic asymmetric unit. All BLM peptide chains (L, M, N, O) are in space filling representation (pink). The two groups of protomers that are related by translational symmetry are highlighted with blue and green dotted lines.
B. Overlay of all protomers on the structure of human TopBP1 BRCT4/5 (3UEN) in light grey. Peptide bound protomers are in orange hues, apo protomers are in blue hues.
C. Representative bias-reduced density map of TopBP1 BRCT4/5 bound to BLM peptide. The stereoview is directed into the peptide-BRCT interface between protomer D and peptide O. Density maps of the peptide (pink) and the BRCT4/5 (blue) are both contoured at 1.0 sigma. The electron density map was calculated using the interact-build omit method.

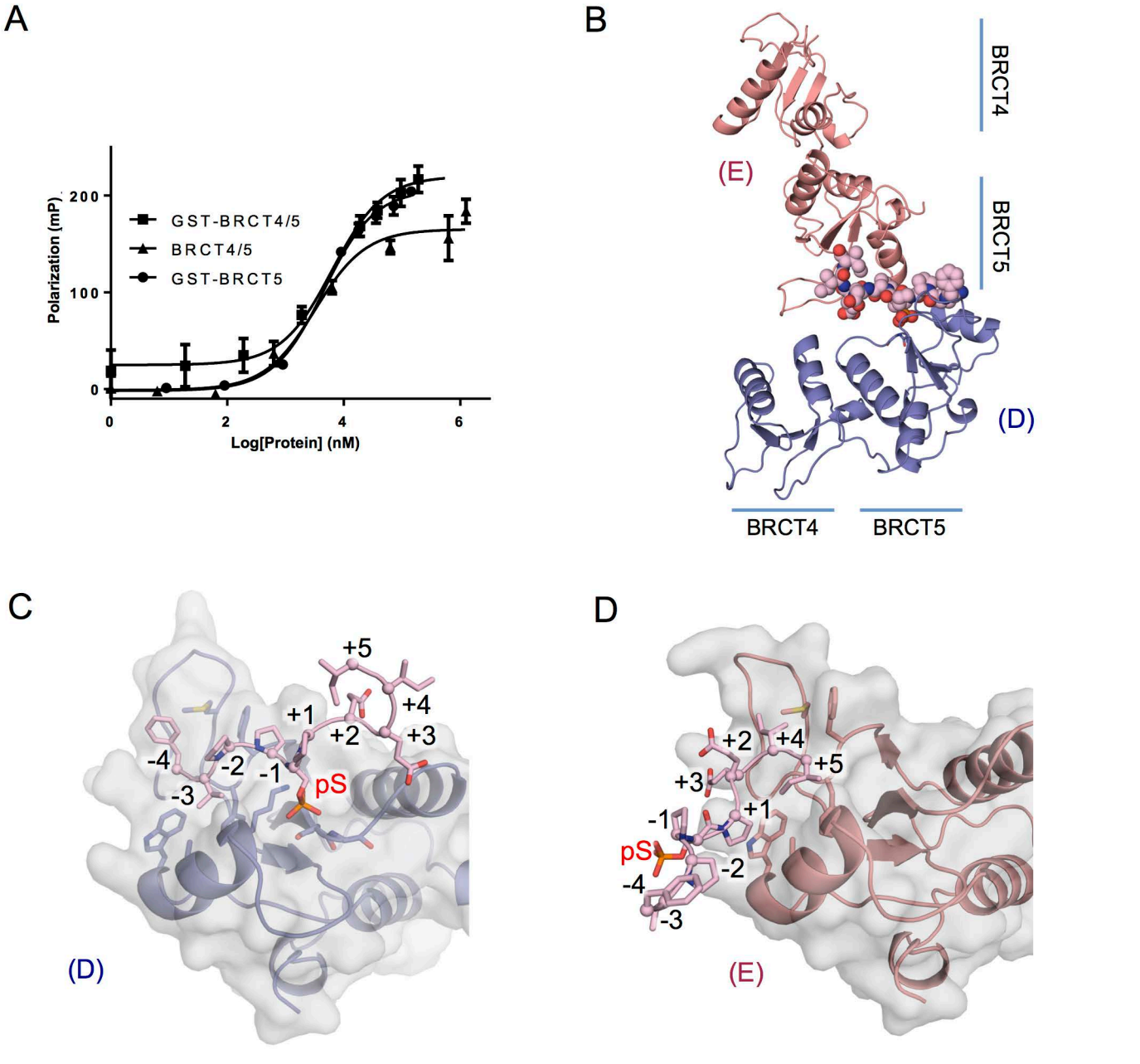

Figure S3. Related to Figure 1. Crystal packing-induced dimer of TopBP1 BRCT4/5 with BLM.

A. Interactions of various GST-tagged and non-tagged TopBP1 BRCT constructs with BLM phosphopeptide as assessed by FP.

B. Overview of protomer E (salmon) and D (slate) dimerized through peptide O (pink).

C. Conserved interaction of BLM with protomer D.

D. Packing enforced interaction of BLM with protomer E.

Table S1: Data Collection, Phasing and Refinement Statistics, Related to Star Methods

	TopBP1 BRCT4/5- BLM Complex
Space group	P 21
Unit cell dimensions	
a, b, c (Å)	98.16, 96.82, 127.05
α, β, γ (º)	90, 94.25, 90
Resolution range (Å)[a]	47.87-2.60 (2.63-2.60)
No. of unique reflections	71934
Completeness (%)	98.8
Overall I/sigma (I)	11.08 (2.65)
R_{meas}[b]	0.136 (0.920)
$CC_{1/2}$	0.970 (0.896)
R_{free}/ R_{work} (%)[c]	25.61/21.93
Number of atoms	11899
Wilson B factor (Å^2)	54.87
Ramachandran Plot (%)	
Most favoured	96.7
Outlier	0.5
Clashscore	4.17
R.M.S. Deviation	
Bonds (Å)	0.003
Angles (º)	0.546

[a]Values in parentheses are from the highest resolution shell.

[b] $$R_{meas} = \frac{\sum_{hkl}\sum_{i=1}^{n}|I_i(hkl) - \bar{I}(hkl)|}{\sum_{hkl}\sum_{i=1}^{n} I_i\,(hkl)}$$

[c] $$R_{work/free} = \frac{\sum_{hkl}|F_{obs}(hkl) - F_{calc}(hkl)|}{\sum_{hkl} F_{obs}(hkl)}$$