

Supporting Information

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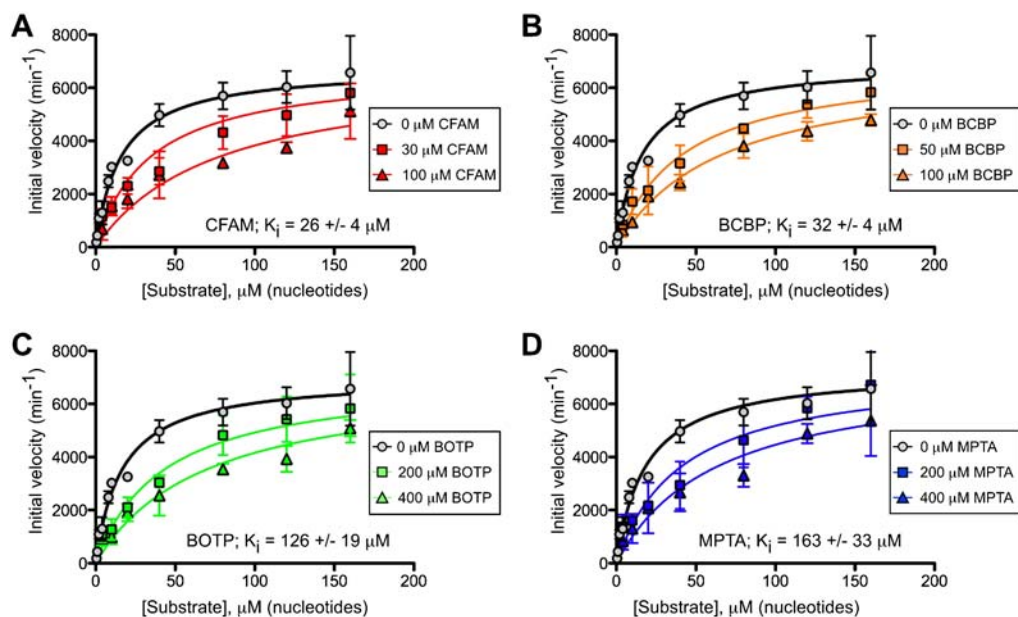


Fig. S1. Saturation kinetic data of ExoI nuclease activity on a SSB/ssDNA substrate in the presence of indicated concentrations of (A) CFAM, (B) BCBP, (C) BOTP, or (D) MPTA. Data points are the mean of three independent measurements with error bars as one standard deviation of the mean. In some instances, error bars are obscured by the symbols. Lines depict a global fit of the data to a competitive inhibition model.

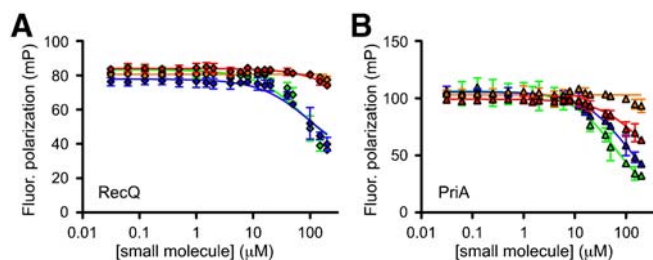


Fig. S2. Small-molecule inhibitors disrupt RecQ/ and PriA/F-SSB-Ct complexes. Inhibitors [CFAM (red), BCBP (orange), BOTP (green), and MPTA (blue)] were incubated at indicated concentrations with (A) RecQ/F-SSB-Ct or (B) PriA/F-SSB-Ct complexes. Decreases in FP are attributed to inhibitor-mediated displacement of the F-SSB-Ct peptide. FP values are presented as the mean of three measurements with error bars depicting one standard deviation. In some instances, error bars are sufficiently small to be obscured by the symbols.

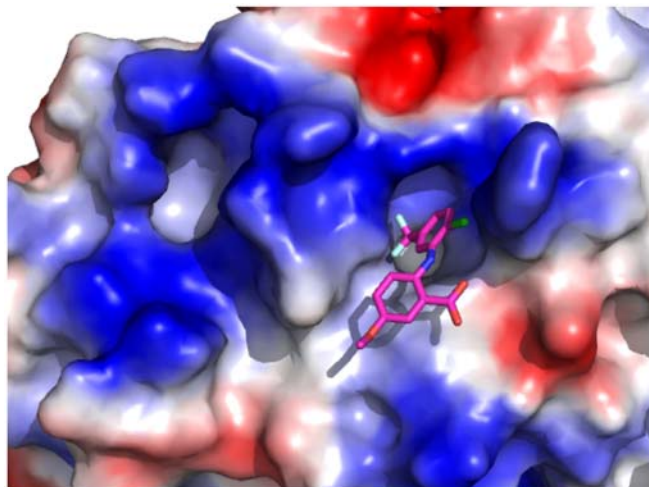
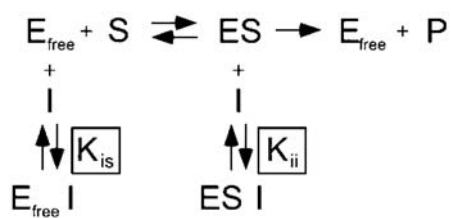


Fig. S3. Model of CFAM bound to the A site in Exol. CFAM was modeled in the A site of Exol by applying a positional transformation derived from a least-squares fit of the B-site peptide onto the A-site peptide (both peptides are shown in Fig. 3A).

Table S1. Fits of the inhibitor kinetic data to a mixed inhibition model



Compound	K_{is} (μM)	K_{ii} (μM)
CFAM	33.9 ± 11.4	973 ± 154
BCBP	38.6 ± 9.5	1832 ± 346
BOTP	147.8 ± 41.8	9445 ± 2740
MPTA	144.9 ± 53.0	$\sim 3 \times 10^9$

Table S2. X-ray data collection and refinement statistics

Data collection	CFAM-bound Exol	BCBP-bound Exol
Space group	P2 ₁ 2 ₁ 2 ₁	P2 ₁ 2 ₁ 2 ₁
Unit cell parameters (a, b, c (Å)) (α, β, γ (°))	52.67, 91.94, 103.1, 90, 90, 90	53.82, 91.97, 106.2, 90, 90, 90
Resolution range (High resolution) (Å)	50-1.60 (1.66-1.60)	50-1.55 (1.61-1.55)
R _{sym} (%) [*]	5.9 (35.0)	6.4 (36.5)
Completeness (%)	89.9 (93.2)	93.0 (85.9)
Redundancy	5.2 (3.3)	5.7 (2.1)
$\langle I/\sigma \rangle$	33.6 (2.5)	34.4 (2.7)
Refinement [†]		
Resolution (Å)	18.8–1.60	26.9–1.55
R _{work} /R _{free} (%) [‡]	20.6/23.1	17.2/20.7
Number of protein atoms [§]	3774	3761
Number of solvent atoms [¶]	472	521
$\langle B$ factor \rangle protein	15.4	23.8
$\langle B$ factor \rangle inhibitor	31.7	27.2
$\langle B$ factor \rangle solvent	28.2	35.7
RMSD bond lengths (Å)	0.009	0.009
RMSD bond angles (°)	0.84	1.36
Ramachandran statistics, % core	98.3	98.3
% allowed	1.7	1.7
% generously allowed	0	0
% disallowed	0	0

^{*}R_{sym} = $\sum_j |I_j - \langle I \rangle| / \sum_j I_j$, where I_j is the intensity measurement for reflection j and $\langle I \rangle$ is the mean intensity for multiply recorded reflections.

[†]CFAM-bound structure refinement was isotropic; BCBP-bound structure refinement was anisotropic.

[‡]R_{work,free} = $\sum ||F_{obs}| - |F_{calc}|| / |F_{obs}|$, where the working and free R factors are calculated by using the working and free reflection sets, respectively. The free R reflections (5% of the total) were held aside throughout refinement.

[§]Several side-chains were modeled in multiple rotamers/conformations; in cases where atoms have been modeled in multiple conformations, each modeled position is counted in the number of protein atoms (i.e., if a given atom is modeled in two positions it is counted as two protein atoms).

[¶]Includes water, DMSO, and ethylene glycol.