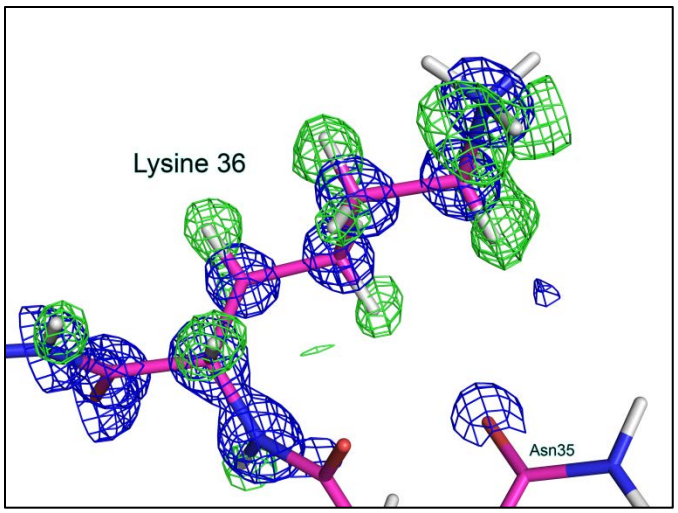
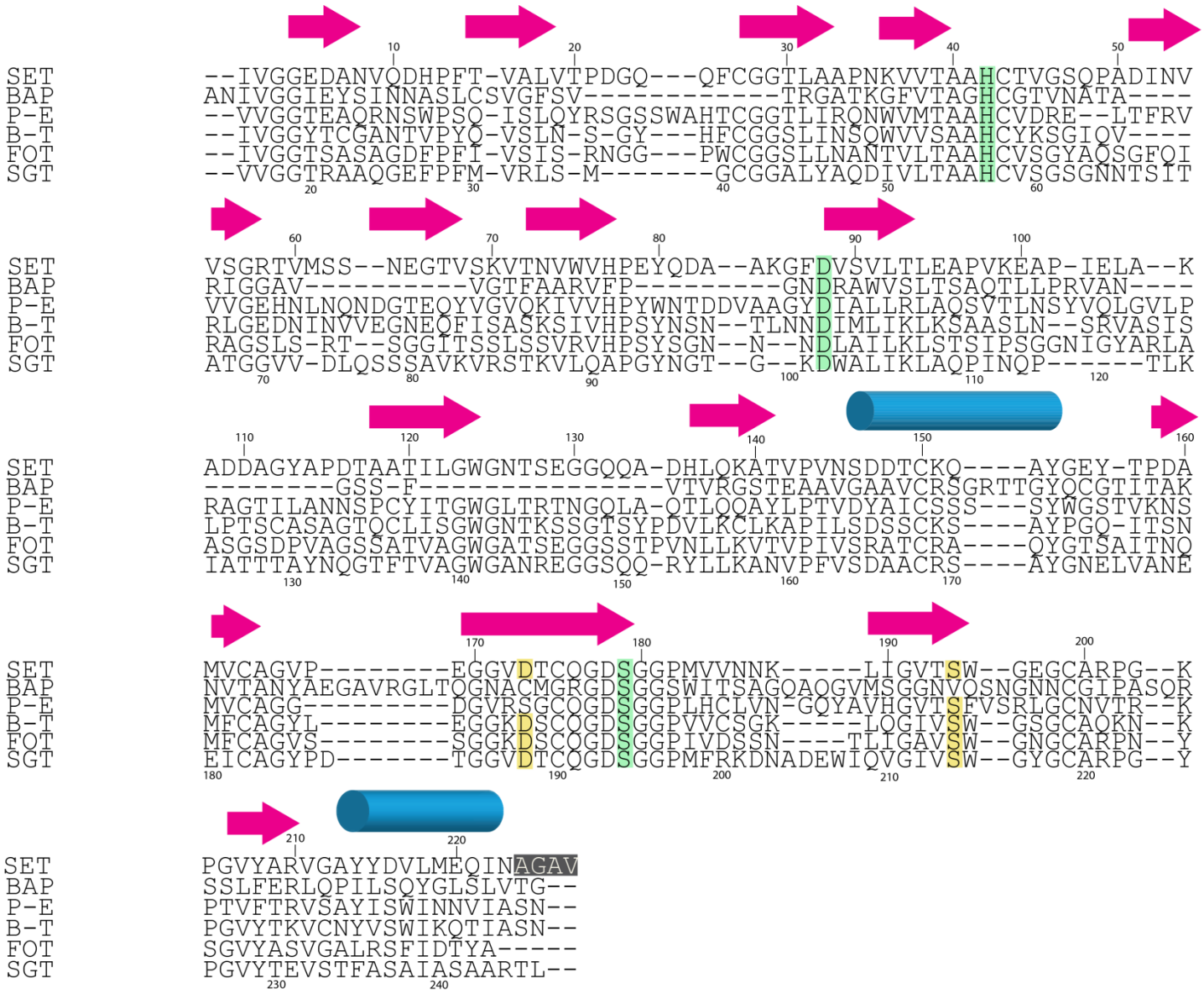
Supporting Table 1 R.M.S.D. comparisons (Å) of SET and other representative serine proteases. Rigid body alignments of α-carbon positions were calculated to allow for comparison of overall fold organization between the structures of SET, *Bacillus sp*. KSM-KP43 alkaline serine protease (PDB ID:1WMD), *A. lyticus* protease I (PDB ID:1ARB), bacterial lipase from *Bacillus sp*. H257 (PDB ID:3RM3), *S. Aureus* SplA (PDB ID:2W7S), bacterial alpha-lytic protease (PDB ID:1SSX), *F. oxysporum* trypsin (PDB ID:1XVO), bovine trypsin (PDB IDs:3UNR and 4I8H), porcine elastase (PDB ID:1QNJ), and *S. griseus* trypsin (PDB ID: 1OS8). Alignments were performed using the RAPIDO server (http://webapps.embl-hamburg.de/rapido/) (Mosca et al., 2008).

	4I8H	1OS8	1WMD	3RM3	2W7S	1ARB	1SSX	1XVO	3UNR	1QNJ	SET
SET	1.43	1.42	1.47	3.65	2.21	3.13	1.48	1.42	1.42	1.47	
1QNJ	1.37	1.78	14.10	10.10	2.35	3.18	3.42	1.48	1.37		
3UNR	0.17	1.51	9.79	5.89	2.40	3.14	3.79	1.50			
1XVO	1.50	1.68	6.99	6.71	2.11	2.74	4.06				
1SSX	3.78	3.99	7.06	8.87	3.41	3.10					
1ARB	3.19	3.03	8.86	11.12	3.05						
2W7S	2.13	2.23	13.16	1.13							
3RM3	5.86	9.61	12.59								
1WMD	6.13	10.51									
1OS8	1.52										
4I8H											



Supporting Figure S1. Representative density for hydrogen atoms. When hydrogen atoms are excluded from map calculations, F_o-F_c maps clearly show the positions of the majority of amide and non-exchangable hydrogens. Both $2F_oF_c$ map (blue) and F_o-F_c map (green) are shown contoured at 2.0σ.



Supporting Figure S2 Sequence alignment of SET and other serine proteases illustrates corresponding residues. Aligned sequences include bacterial alpha-lytic protease (BAP; PDB ID:1SSX), *F. oxysporum* trypsin (FOT; PDB ID:1XVO), bovine trypsin (B-T; PDB ID:3UNR,4I8H), porcine elastase (P-E; PDB ID:1QNJ) and *S. griseus trypsin* (SGT; PDB ID:1OS8) Alignments performed using the Omega Clustal (Sievers *et al.*, 2011) server, and aligned sequences are shown here with cartoon representations of secondary structures (beta sheets as magenta arrows, helices as cyan cylinders). Catalytic residues are highlighted in green, and other highly conserved interacting residues are highlighted in tan. Residue numbers above the sequence reflect SET residue numbers, while residue numbering below sequences reflects classical chymotrypsin numbering scheme. SET residues highlighted in black were disordered and thus not observed in the final model.