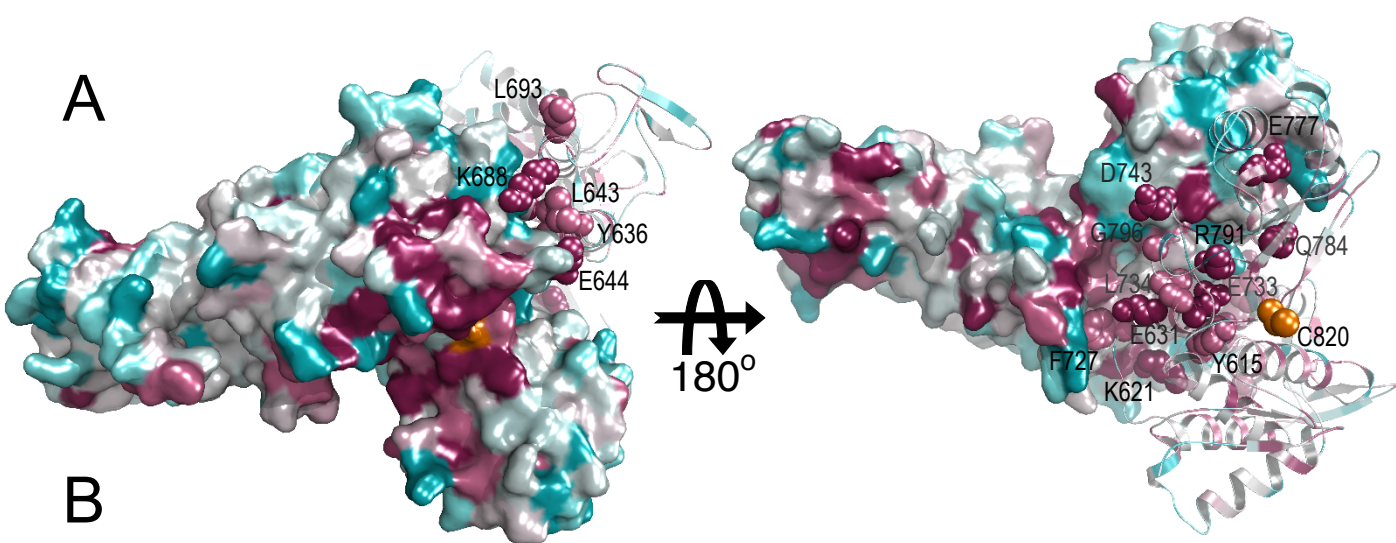
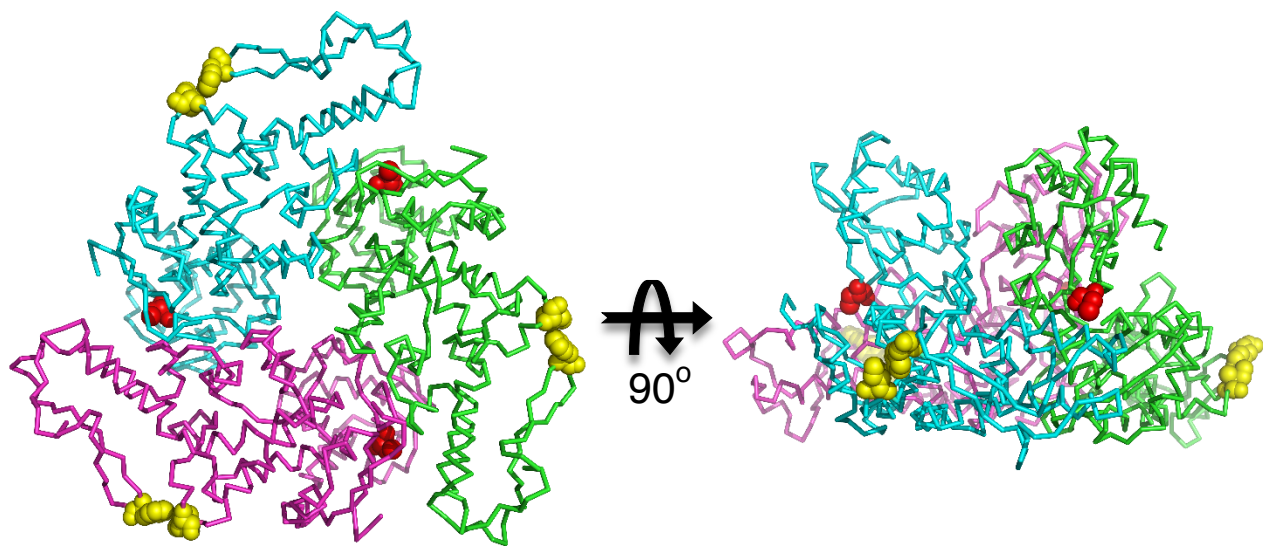


Appendix Figure S1. Clashing of the $\alpha 1$ helices at the interface of the trimeric model of Rsp5-HECT domains.



RSP5	P	G	Q	C	H	I	K	V	R	R	K	N	I	F	E	D	A	Y	Q	--	E	I	M	R	Q	T	P	E	D	-	L	K	K	R	L	M	I	K	F	D	G	E	E	--	--	--	--	492			
E6AP	N	P	Y	L	R	L	K	V	R	R	D	H	I	I	D	D	A	L	V	R	L	E	M	I	A	M	E	N	P	A	D	L	K	K	Q	L	Y	V	E	F	E	G	E	Q	Q	V	D	E	G	G	546
NEDD4	P	N	K	F	E	M	K	L	R	R	A	T	V	L	E	D	S	Y	R	--	R	I	M	G	V	K	R	A	D	F	L	K	A	R	L	W	I	E	F	D	G	E	K	G	L	D	Y	G	G	587	
RSP5	--	R	E	F	F	F	L	S	H	E	M	F	N	P	F	Y	C	L	F	E	Y	S	A	Y	D	N	Y	T	I	Q	I	N	P	N	S	G	I	N	-	P	E	H	L	N	Y	F	K	F	547		
E6AP	V	S	K	E	F	F	Q	L	V	V	E	E	I	F	N	P	D	I	G	M	F	T	Y	D	E	S	T	K	L	F	W	F	N	P	S	S	--	--	--	--	F	E	T	E	G	Q	F	T	L	591	
NEDD4	V	A	R	E	W	F	F	L	I	S	K	E	M	F	N	P	Y	Y	G	L	F	E	Y	S	A	T	D	N	Y	T	I	Q	I	N	P	N	S	G	L	C	N	E	D	H	L	S	Y	F	K	F	637
RSP5	I	G	R	V	V	G	L	G	V	F	H	R	R	F	L	D	A	F	F	V	G	A	L	Y	K	M	M	L	R	K	K	V	V	L	Q	D	M	E	G	V	D	A	E	V	Y	N	S	L	N	W	597
E6AP	I	G	I	V	L	G	L	A	I	Y	N	N	C	I	L	D	V	H	F	P	M	V	Y	R	K	L	M	G	K	K	G	T	F	R	D	L	G	D	S	H	P	V	L	Y	Q	S	L	K	D	641	
NEDD4	I	G	R	V	A	G	M	A	V	Y	H	G	K	L	L	D	G	F	F	I	R	P	F	Y	K	M	M	L	H	K	P	I	T	L	H	D	M	E	S	V	D	S	E	Y	Y	N	S	L	R	W	687
RSP5	M	L	E	N	S	I	D	G	V	L	D	L	T	F	S	A	D	D	--	E	R	F	G	E	V	V	T	V	D	L	K	P	D	G	R	N	I	E	V	T	D	G	N	K	K	E	Y	V	644		
E6AP	L	L	E	Y	E	G	N	V	E	D	D	M	M	I	T	F	Q	I	S	Q	T	D	L	F	G	N	P	M	M	Y	D	L	K	E	N	G	D	K	I	P	I	T	N	E	N	R	K	E	F	V	691
NEDD4	I	L	E	N	D	P	T	-	E	L	D	L	R	F	I	I	D	E	--	E	L	F	G	Q	T	H	Q	H	E	L	K	N	G	S	R	I	V	V	T	N	K	N	K	K	E	Y	I	733			
RSP5	E	L	Y	T	Q	W	R	I	V	D	R	V	Q	E	Q	F	K	A	F	M	D	G	F	N	E	L	I	P	E	D	-	L	V	T	V	F	D	E	R	E	L	E	L	I	G	G	I	A	E	693	
E6AP	N	L	Y	S	D	Y	I	L	N	K	S	V	E	K	Q	F	K	A	F	R	R	G	F	H	M	V	T	N	E	S	P	L	K	Y	L	F	R	P	E	E	I	E	L	L	I	C	G	S	R	N	741
NEDD4	Y	L	V	I	Q	W	R	E	V	N	R	I	Q	K	Q	M	A	A	F	K	E	G	F	E	E	L	I	P	Q	D	-	L	I	K	I	F	D	E	N	E	L	E	L	M	C	G	L	G	D	782	
RSP5	I	D	I	E	D	W	K	K	H	T	D	Y	R	-	G	Y	Q	E	S	D	E	V	I	Q	W	F	W	K	C	V	S	E	W	D	N	E	Q	R	A	R	L	L	Q	F	T	T	G	T	S	R	742
E6AP	L	D	F	Q	A	L	E	E	T	T	E	Y	D	G	Y	T	R	D	S	V	L	I	R	E	F	W	E	I	V	H	S	F	T	D	E	Q	K	R	L	F	L	Q	F	T	T	G	T	D	R	791	
NEDD4	V	D	V	N	D	W	R	E	H	T	K	Y	K	N	G	Y	S	A	N	H	Q	V	I	Q	W	F	W	K	A	V	L	M	M	D	S	E	K	R	I	R	L	L	Q	F	V	T	G	T	S	R	832
RSP5	I	P	V	N	G	F	K	D	L	Q	G	S	D	G	P	R	R	F	T	I	E	K	A	G	E	V	Q	Q	L	P	K	S	H	T	C	F	N	R	V	D	L	P	Q	Y	V	D	Y	D	S	M	792
E6AP	A	P	V	G	L	L	G	K	L	K	--	--	--	--	M	I	I	A	K	N	G	P	D	T	E	R	L	P	T	S	H	T	C	F	N	V	L	L	L	P	E	Y	S	S	K	E	K	L	835		
NEDD4	V	P	M	N	G	F	A	E	L	Y	G	S	N	G	P	Q	S	F	T	V	E	Q	W	G	T	P	E	K	L	P	R	A	H	T	C	F	N	R	L	D	L	P	F	Y	E	S	F	E	L	882	
RSP5	K	Q	K	L	T	L	A	V	E	E	T	I	804																																						
E6AP	K	E	R	L	L	K	A	I	T	Y	A	-	846																																						
NEDD4	W	D	K	L	Q	M	A	I	E	N	T	Q	893																																						

Appendix Figure S2. Conservation of E6AP interface residues. (A) Two out of three protomers (surface and cartoon representation) illustrate surface residue conservation of the trimeric structure, in two angles rotated around the X axis. We submitted E6AP structure (PDB 1C4Z) to the ConSurf server (Landau et al. 2005). Residues are coloured by conservation scale ranging from unconserved (blue) too highly conserved (bourdeaux). Catalytic cysteines are shown in orange, and interface residues are depicted as spheres. (B) Corresponding sequence alignment.



Appendix Figure S3 . Representation of E2 binding (yellow) residues and catalytic cysteines (red) in the Rsp5 trimeric model.