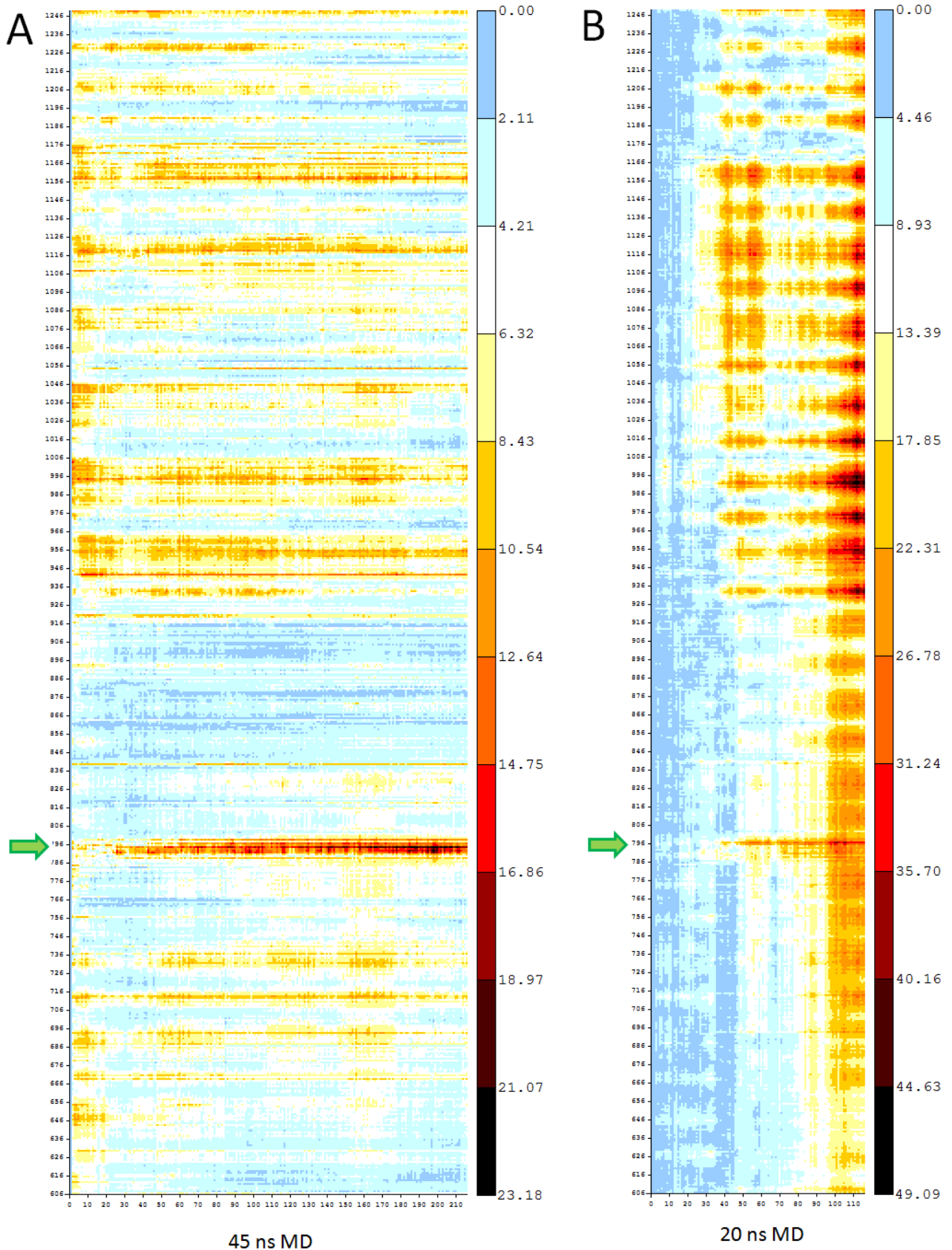


# Supplementary material

to the paper by D.N. Shalaeva, D.V. Dibrova, M.Y. Galperin, and A.Y. Mulkidjanian  
"Modeling of interaction between cytochrome c and the WD-domains of Apaf-1:  
bifurcated salt bridges underlying apoptosome assembly"



**Figure S1. Backbone coordinates RMSD heat maps for WD domains of Apaf-1 in complex with cytochrome c during MD simulation. A, The final model structure (model PatchDock'); B, ClusPro predicted structure. The green arrow indicates residues 785-805 that form a mobile loop. Created with VMD tools.**

APAF\_HUMAN 612 RPHTDAVYHACFSQDQRIASCGADKTLQVFKAETGEKLL**E**IKAH**EDE**VLCCA-FST**DD**RFIATCS**VD**KKVKIWNSTGELVHT-YDE**HS** 699  
APAF\_MOUSE 612 RPHTDAVYHACFSQDQRIASCGADKTLQVFKAETGEKLL**D**IKAH**EDE**VLCCA-FSS**DD**SYIATCS**AD**KKVKIWDSATGKLVHT-YDE**HS** 699  
APAF\_DANRE 614 HPHQGAVYYACFSKDGSKIASCASKALRVFKSTSKEKLL**E**LQAH**EED**VLCCA-FSP**DD**RHIATCAS**DR**KKVCLWNVERGVLIREFEVE**HE** 702  
XP\_011682983 616 TPHSGVTMCAQFNAAGDHVLSVCGE**D**GYVFWSSSESGKQAFSIEAHNNVWNWCE-ISP**DG**QTMVTCSS-SNVKWLWRIPNGGYPLHQAMIRK 703  
H2DL11\_SCHMD 825 -----**DDL**FC AARNNIYKNR-----ELILT-IE--- 846  
XP\_001639696 604 KVHCGAVYCCKFSSSDSSKVVSCGT**D**NHVKVWDSQSGRQLLSISGH**G**DVVNCCA-FSH**DD**SRIISCS**AD**QTVKIWDASSGEGVLC-FVGH**T** 691  
XP\_002117644 610 RIHKASAACCSFSPDGSQVSSSWNGDIQIWDAFSGASVAKFDGH**G**DE**V**VCCCCFSK**D**GR-IASAS**L**DETVKVNIANESLELV-YDKH**D** 697  
XP\_002167203 609 KLHGDAVNYCSSLHNTTTLAVSCSR**D**GMVKVWDYLTGAEKISFSGH**D**ND**V**KWCE-FS**F****DD**ENIISCS**TD**KTIKVVNMRSSEEEIC-LR**G**H**T** 696

APAF\_HUMAN 700 **E**QVNCCHFTNSSHLLLLATGSS**DC**--FLKLWDLN**Q**KECRNTMF**G**H**T**NSVNHCRFS**P**DD**K**LLASCS**AD**GTLK**L**WDATSAN**E**RKSINVK**Q**FF 787  
APAF\_MOUSE 700 **E**QVNCCHFTNKS**N**HLLLLATGS**ND**F--FLKLWDLN**Q**KECRNTMF**G**H**T**NSVNHCRFS**P**DE**L**LASCS**AD**GTLR**L**WDVRSAN**E**RKSINVK**R**FF 787  
APAF\_DANRE 703 **E**QINHCQFTNTGRRVLLATCS**ND**KFTN**T**RLWNP**N**KKTSQNTMF**G**H**M**EPVNHCCFS**P**ND**L**YLATSS**S**DGSL**K**LFEVSSAN**E**WKSIDVDS**F**F 792  
XP\_011682983 704 IPGDWLR**A**IFSHDGT**K**IAMCS**L**D**G**--LIEILD**L**TEDRR**K**MIRASDSVIRALC-Y**T**L**DD**RYIISCS**DD**TKV**K**VRRDRD**T**R**V**FDASS----- 785  
H2DL11\_SCHMD 847 **N**DVYIVKISISDN**Q**TLLALCL**T**NN--SVQVWY**N**Y**Q**TLLYSLNDS**Q**FTDVY--FL**H**D**S**DFLL**T**TGP-TSAAKWDLK**N**ISLANNNNN**N**SE- 930  
XP\_001639696 692 **Q**EVFSCSFSPDDTKAV--SCS**AD**R--TVK**V**WDSKT**G**VCYHVYMA**H**TDIVRWCCFS**P**DGGK**V**ASCS**DD**NT**V**RIWEASS**G**EDL----- 768  
XP\_002117644 698 **A**DVLWCQFS**P**DQANIV--SC**G**AD**R**--LVK**L**WNSRTGEDYATFY**G**HLDIV**R**QCAF**S**ND**G**Q**K**IVSCS**DD**TY**V**KVWDT**Q**SGDIRK**D**LL----- 778  
XP\_002167203 697 **D**EVLCCRYSK**N**KKWIA--ST**S**MD**K**--SLKI**W**EGIS**G**KLYIS**F**ND**H**TDV**N**CCS**F**S**N**CS**N**LVVCS**ND**CT**T**RV**V**NI**K**E**K**N----- 771

792

APAF\_HUMAN 788 **L**N**L**ED**P**Q**ED**ME--VIVKCCS**W**S**AD**GARIMVAA**K**NKI**F**LF**D**I**H**T**S**G**L**L**G**E**I**H**T**G**H**H**S**T**I**Q**Y**C**D**F**S**P**Q**N**H**L**A**V**V**A**L**S**Q**Y**C**V**E**L**W**N**T**D**S**R**S**K**V** 875  
APAF\_MOUSE 788 **L**SS**ED**PP**ED**VE--VIVKCCS**W**S**AD**GDKI**V**AA**K**N**K**V**L**LL**F**D**I**H**T**S**G**L**L**A**E**I**H**T**G**H**H**S**T**I**Q**Y**C**D**F**S**P**Y**D**H**L**A**V**I**A**L**S**Q**Y**C**V**E**L**W**N**I**D**S**R**L**K**V 875  
APAF\_DANRE 793 **P**ES**DE**---**E**IK--AM**V**K**C**ST**W**S**AD**GS**Q**I**I**CA**A**R**N**T**V**F**V**F**D**V**E**TS**D**LL**L**K**L**K**T**S**R**L**S**T**I**Q**F**CH**A**C**P**NS**S**L**L**A**V**A**L**S**H**Y**T**V**E**L**W**N**F**ES**S**K**K**K 877  
XP\_011682983 786 **A**MS**D**P**V**MS**Y**T**G**H**T**TS**V**IN**A**SP**S**P**D**G**Q**Y**V**AT**T**G**S**SD**V**H**V**W**T**I**V**D**G**A**L**V**G**K**C**M**S**--E**A**N**M**V**L**C**C**E**F**C**P**K**G**D**I**A**G**G**L**S**S**Y**E**I**V**W**E**T**R**R**Y**K**P**V 874  
H2DL11\_SCHMD 931 **L**NS**N**S**L**S**L**Y**Q**G**H**F**G**M**Q**N**Q**---S**Q**V**S**F**L**L**V**L**Q**S**V**N**N**N**I**E**F**F**S**Y**T**N**E**I**L**NS**K**V**I**K**E**S**S**E**M**S**C**F**Y**F**Y**--E**N**I**I**F**I**G**F**K**R**L**E**S**I**K**V**Y**D**L**T**T**Y**E**E**I 1016  
XP\_001639696 769 **C**L**L****DD****H**T-----SS**V**S**F**CC**F**M**Q**GES**V**V**T**VC**S**NC**I**K**V**W**S**C--SS**G**E**Q**T**W**V**Y**NS--S**T**C**L**S**L**A**F**S**P**DD**S**I**V**A**M**G**F**S**D**T**T**V**Q**L**W**N**S**K**T**F**A**R**L** 850  
XP\_002117644 779 **L**AL**T**H**H**D**E**-----G**V**SS**C**A**F**F**N**D**T**M**I**ISS**S**GR**N**V**I**T**S**S**V**K**D**G**S**K**L**A**S**F**R**C**F**---G**V**L**C**C**N**V**S**S**S**G**L**Y**F**A**A**G**L**T**T**S**A**L**Q**M**W**H**I**Q**D**R**Q**T**V** 860  
XP\_002167203 772 **M**T**L**V**C**SS**G**-----D**F**CT**S**C**I**F**S****L**D**Q**F**I**F**T**S**C**Q**R**F**V**L**K**CS**S**K**D**G**L**L**E**K**I**E**T**A--S**D**I**L**S**M**A**L**S**Y**N**G**K**H**M**G**L**S**H**Q**N**C**A**S**V**M**D**L**S**K**S**E**V**F** 854

877

903

925

APAF\_HUMAN 876 **A**DC**R**GHLS**W**VH**G**V**M**F**S**P**D**GSS**F**L**T**S---S**DD**Q**T**IR**L**W**E**T**K**K**V**C--K**N**S**A**V**M**L**K**Q**E**V**D**V**V**F**Q**E**N**E**V**---M**V**L**A**V**D**H**I**R**R**L**Q**L**I**N**G**R**T**G**Q**I**D**Y 958  
APAF\_MOUSE 876 **A**DC**R**GHLS**W**VH**G**V**M**F**S**P**D**GSS**F**L**T**A---S**DD**Q**T**IR**V**W**E**T**K**K**V**C--K**N**S**A**I**V**L**K**Q**E**I**D**V**V**F**Q**E**N**E**T**---M**V**L**A**V**D**N**I**R**G**L**Q**L**I**A**G**K**T**G**Q**I**D**Y 958  
APAF\_DANRE 878 **A**EC**S**GHLS**W**VH**C**V**Q**F**S**P**D**G**S**LL**S**S---S**DD**Q**T**IR**L**W**E**T**D**R**V**H--T**S**S**A**V**A**L**K**R**D****T**D**V**LS**S**H**S**D**A**---T**I**I**A**P**D**S**S**N**R**L**Q**V**L**S**G**S**T**G**A**V**V**L 960  
XP\_011682983 875 **A**V**F**K**G**H**T**S**W**V**M**S**V**K**F**D**V**K**G**E**R**L**V**S**A**---S**DD**E**T**V**R**T**W**K**V**E**Y**G**H**--T**D**L**N**S**V**W**K**R**D****F**T**A**C**F**C**D**G**K**R**L**K**F**V**V**A**G**D**N**K**N**R**C**L**V**D**T**D**G**R**N**V**D**Q**T**F 960  
H2DL11\_SCHMD 1017 **T**K**I**S**D**F**V**D**V**Q**E**I**Y**A**H**K**T**K**T**K**N**I**L**E**I**L**V**H**H**S**R**N**K**I**R**I**L**H**L**-----N**Q**V**S**L-- 1060  
XP\_001639696 851 **G**V**Y**K**G**H**K**G**W**A**H**S**V**G**I**S**K**D**S**S**K**L**V**S**G**---S**E**D**E**T**V**K**I**W**T**I**D**R**D**A--A**K**D**A**A**K**L**R**R**V**F**D**A**H**F**G**E**D**S**L**---G**V**A**V**A**D**S**S**D**R**L**L**I**F**Q**G**Q**D**G**V**L**T**A 933  
XP\_002117644 861 **A**V**Y**K**G**H**N**G**W**I**Q**S**V**S**Y**A**P**D**S**R**L**L**S**S---A**S**D**E**T**V**K**F**W**S**S**N**P**T**E**D**K**F**A**R**V**K**L**R**I**F**F**T**C**S**F**Q**D**E**P---T**I**Y**A**P**D**M**Q**E**S**L**L**V**Y**H**G**L**N**S**K**F**V**E 944  
XP\_002167203 855 **N**N**Y**Y**G**H**S**S**W**V**N**S**I**N**F**S**R**D**G**S**R**I**I**T**A**---S**AD**G**A**C**K**V**W**S**V**K**D**N**M**--D**V**E**E**K**L**I**P**V--**F**D**V**S**F**E**S**G**F**Y---I**V**V**G**T**N**Q--K**R**I**K**V**I**N**E**C**N**Y**A**H**S**A 935

981

1023

APAF\_HUMAN 959 **L**T**E**A**Q**V**S**---C**C**C**L**S**P**H**L**Q**Y**I**A**F**G**D**E****N**G**A**I**E**I**L**E**L**V**N**N**R**I**F**Q**S**R**F**Q**H**K**K**T**V**W**H**I**Q**F**T**A**D**E**K**T**L**I--S**S**S**DD**A**E**I**Q**V**W**N**W**Q**L**D**K**C**I**F--L**R**G**H** 1043  
APAF\_MOUSE 959 **L**P**E**A**Q**V**S**---C**C**C**L**S**P**H**L**E**Y**V**A**F**G**D**E****D**G**A**I**K**I**E**L**P**N**N**R**V**F**S**S**G**V**G**H**K**K**A**V**R**H**I**Q**F**T**A**D**G**K**T**L**I**--S**S**S**ED**S**V**I**Q**V**W**N**W**Q**T**G**D**Y**V**F--L**Q**A**H** 1043  
APAF\_DANRE 961 **E**S**E**E**L**S**S**R**I**R**C**S**C**I**S**R**N**A**A**F**V**A**L**G**S**E**D**G**T**V**Q**V**I**E**V**P**S**S**K**A**S**V**K**L**S**G**H**T**K**T**V**H**H**C**Q**F**T**D**D**C**E**I**L**I--T**S**S**ED**S**T**I**R**V**K**W**R**T**G**E**C**M**V**--L**Q**G**H** 1048  
XP\_011682983 961 **V**V**S**E**S**R**R**I**R**A**F**A**L**T**S**D**N**T**K**V**A**Y**G**S**D**G**G**V**V**K**V**A**N**V**E**T**H**A**V**E**R**S**L**E**A**H**T**M**D**V**R**Q**C**L**F**T**K**E**G**D**T**L**V**--T**C**S**S**D**G**L**I**K**I**W**E**P**E**G--G**E**V**I**E--C**R**G**H** 1047  
H2DL11\_SCHMD 1061 -----L**K**V**K**D**S**T**C**E**L**P**G**N**S**I**N**C**K**F**F**K**Y**E**G**D**I**V**K**F**V**S**I**C**D**I**Q**C**Y**L**C**D**V**N**E**I**K**P**I**H**T**Y**N**L 1114  
XP\_001639696 934 **E**G**E**A**M**D**S**K**I**H**S**V**T**F**S**P**R**G**E**A**I**A**V**G**C**E**S**G**T**I**S**I**Q**D**R**--S**C**K**V**L**Q**S**F**S**E**H**K**G**A**V**R**R**C**Y**F**S**Q**D**G**Q**L**L**L**--S**A**S**DD**K**T**A**K**V**F**N**L**Q**E**A**R**V**M**Y**T**L**A**G**H** 1021  
XP\_002117644 945 **E**Y**S**E**G**R**S**K**I**R**C**C**L**S**K**D**E**T**L**L**S**S**R**E**N**G**E**V**M**I**L**S**S**I**D**G**R**L**L**Q**E**L**N**G**H**K**D**T**I**I**F**I**R**I**G**D**R**K**R**L**L**--S**C**A**R**D**N**T**A**K**V**F**N**E**N**M**T**V**S**M**Y**----- 1028  
XP\_002167203 936 **S**S**L**Q**E**Q**F**L**D**L**S**W**G**H**P**----- 950

		<b>1045</b>		
APAF_HUMAN	1044	Q <b>E</b> TVKDFRLLKNSR---LLSWS <b>F</b> D----GTVKVWNIITGNK--EKDFVCHQGTVLSC-----DISH <b>D</b> ATKF-SSTSADKTAKIWSFD--LL	1117	
APAF_MOUSE	1044	Q <b>E</b> TVKDFRLLQDSR---LLSWS <b>F</b> D----GTVKVWNVITGRI--ERDFVCHQGTVLSC-----AISS <b>D</b> ATKF-SSTSADKTAKIWSFD--LL	1117	
APAF_DANRE	1049	M <b>E</b> PVRKFHLLSSSSSPHLFSWS <b>F</b> D----GTVKVWDLTRGQM--LQDLVCHGAVLSC-----DVSS <b>D</b> GRLF-ATTSANRTAKVWSSA--SW	1125	
XP_011682983	1048	TKAVTQCQLYQNDAK--ILSS <b>S</b> RD----ATLKIWELSTGHC--LATIEAHSDWIFMC-----AIS <b>P</b> DHSMV-ASVSVDKTAKVWDLQ--SH	1122	
H2DL11_SCHMD	1115	ENNVLDVDIDDNCQY--LCAISNN---GEIKVWEIGTELSCVNEEESLIGNILRKCKFRPKMSPNNWNVAVINDNAIISLFYFRGIEQ	1198	
XP_001639696	1022	TNKLRRCMFFNNDTR--ILTAS <b>L</b> D----GSLKVWDAKTGNL--EFT-CCHSSTDYVLTC--DVSH <b>S</b> QRL-ISASADCFAKVWDAS--TG	1097	
XP_002117644	1029	---KIDRLLQLFVAK--VILYSFVYMHLLLGILWDSATGNM--LYD-YSHSGHLTDC-----SIMP <b>D</b> QQSF-ITTSVDAIAKLWSCE--DG	1103	
XP_002167203	950	-----	950	
		<b>1147</b>		
APAF_HUMAN	1118	LPLHELGRHGNCV----RCSAFS <b>V</b> DSTLLAT <b>G</b> <b>D</b> DNGEIRIWNVNSGELLHLCAPLS-EEGAATHGGWVT <b>D</b> LCFSPDGKMLISAGGYIKWW	1202	
APAF_MOUSE	1118	SPLHELKGHGNCV----RCSAFS <b>L</b> DGILLAT <b>G</b> <b>D</b> DNGEIRIWNVSDGQLLHSCAPISVEEGTATHGGWVT <b>D</b> VCFSPDSKTLVSAGGYLKWW	1203	
APAF_DANRE	1126	KMLFLLLEGHKDCV----RSCRFS <b>W</b> DNKRLAT <b>G</b> <b>D</b> DNGEIRLWSMLDGALLKICPRDTKDSMNSYHAGWVT <b>D</b> LHFSPDNRVLVSTAGYIKWW	1211	
XP_011682983	1123	KLRKVLNHDSDV---RRCRFS <b>P</b> DSTLLAT <b>G</b> <b>D</b> DNGEIRIWNISSGDEVGEC-----HKHKSWVT <b>D</b> IKFSPDAKIVMTAGENVKWW	1199	
H2DL11_SCHMD	1199	KLKILIDPYETVATQIPNFIKWS <b>I</b> DGNYVLV <b>G</b> DYN--IRKWKVPEPLKDE-----NKLPLTILQTYF-----	1260	
XP_001639696	1098	ELLLSLGRHPDVV---RSISFS <b>P</b> DNMI-CTGC <b>D</b> DGIVRIWDSVSGKEVTSCKK-----NETWIA <b>D</b> CHFTRDGRNIVSVSDNIQWW	1173	
XP_002117644	1104	RLIRSYTAHEDCV----RSCRIS <b>N</b> DGKLLAVG <b>C</b> DNGSIKIWDIHSKGELMTL-----RGHNVWVNCCKFSKDGNYLVTVSDTLIWW	1180	
XP_002167203	950	-----	950	
APAF_HUMAN	1203	NVVTGESSQTFYTGNTNLKKIHVS <b>P</b> DFKTYVT <b>V</b> DNLGILYILQ <b>T</b> L	1248	
APAF_MOUSE	1204	NVATGDSSQTFYTGNTNLKKIHVS <b>P</b> DFRTYVT <b>V</b> DNLGILYILQ <b>V</b> L	1249	
APAF_DANRE	1212	SVESGEALQTFYTMGGNLKKIHVS <b>P</b> DFSTFIT <b>V</b> DSIGILYILK <b>R</b> L	1257	
XP_011682983	1200	Q-LDGTLTLLQTFHVRGTFIRVQVQASPSFQTFV <b>T</b> IDSAGILYLMCR <b>V</b> K	1244	
H2DL11_SCHMD	1261	-----GGIQNISLNEKFICT <b>V</b> DQQGFFYILK <b>K</b> ID	1289	
XP_001639696	1174	S-KSGQLIQEFFIKGGFAKDVKCS <b>S</b> DFKTFVT <b>V</b> DDTSTLYILN <b>Q</b> I-	1217	
XP_002117644	1181	DLRNGKKLQEIIRLFGRYADDIFFNG <b>D</b> FTHFVT <b>I</b> DSESIYIILK <b>R</b> L	1226	
XP_002167203	950	-----	950	

**Figure S2. Conservation of the negatively charged residues in the WD domains of Apaf-1 homologs.**

Multiple alignment of the WD domains of Apaf-1 homologs from human (APAF\_HUMAN, RefSeq accession NP\_863651), mouse (APAF\_MOUSE, NP\_033814), zebrafish (APAF\_DANRE, NP\_571683), sea urchin *Strongylocentrotus purpuratus* (XP\_011682983), planarian flatworm *Schmidtea mediterranea* (H2DL11\_SCHMD, no RefSeq entry), sea anemone *Nematostella vectensis* (A7RLM8\_NEMVE, XP\_001639696), placozoan *Trichoplax adhaerens* (B3SBJ1\_TRIAD, XP\_002117644), and the hydrozoan *Hydra vulgaris* (XP\_002167203) was generated from BLAST outputs. Conserved acidic residues are shown in bold red font. The residues that are involved in cytochrome c binding in the PatchDock' model (Table 3) are shaded yellow and their positions in human Apaf-1 are indicated above those residues.