

CARDs from PFAM

Name	Uniprot	NCBI	PFAM Residue Boundaries	Extended Boundaries (PFAM +/- 10 residues)	Structure Used for Comparison
APAF1	APAF_HUMAN	O14727	NP_863651.1	6 90	1 100 1CY5
ASC	ASC_HUMAN	Q9ULZ3	NP_037390.2	112 195	102 195 2KN6
Bcl10	BCL10_HUMAN	O95999	NP_003912.1	17 100	7 110 2MB9
CARD6	CARD6_HUMAN	Q9BX69	NP_115976.2	9 92	1 102 N/A
CARD8	CARD8_HUMAN	Q9Y2G2	NP_001171829.1	452 535	442 537 4IKM
CARD9	CARD9_HUMAN	Q9H257	NP_434700.2	11 97	1 107 N/A
CARD10	CAR10_HUMAN	Q9BWT7	NP_055365.2	28 114	18 124 N/A
CARD11	CAR11_HUMAN	Q9BXL7	NP_115791.3	23 109	13 119 4LWD
CARD14	CAR14_HUMAN	Q9BXL6	NP_077015.2	20 106	10 116 N/A
CARD16	CAR16_HUMAN	Q5EG05	NP_001017534 .1	3 90	1 100 N/A
CARD17	CAR17_HUMAN	Q5XLA6	NP_001007233.1	3 90	1 100 N/A
CARD18	CAR18_HUMAN	P57730	NP_067546.1	6 87	1 90 1DGN
CASP1	CASP1_HUMAN	P29466	NP_150634.1	3 90	1 100 N/A
CASP2	CASP2_HUMAN	P42575	NP_116764.2	37 118	27 128 N/A
CASP4	CASP4_HUMAN	P49662	NP_001216.1	5 89	1 99 N/A
CASP5	CASP5_HUMAN	P51878	NP_004338.3	61 147	51 157 N/A
CASP9	CASP9_HUMAN	P55211	NP_001220.2	17 90	7 100 4RHW
CASP12	CASPC_HUMAN	Q6UXS9	NP_001177945.2	12 91	2 101 N/A
cIAP1	BIRC2_HUMAN	Q13490	NP_001157.1	458 542	448 552 3T6P
cIAP2	BIRC3_HUMAN	Q13489	NP_001156.1	441 530	431 540 N/A
MDA5_CARD2	IFIH1_HUMAN	Q9BYX4	NP_071451.2	115 200	105 210 N/A
NLRC4	NLRC4_HUMAN	Q9NPP4	NP_067032.3	2 87	1 97 N/A
NLRP1	NALP1_HUMAN	Q9C000	NP_127497.1	1379 1460	1369 1470 4IFP
NOD1	NOD1_HUMAN	Q9Y239	NP_006083.1	21 92	11 102 2DBD
NOD2_CARD1	NOD2_HUMAN	Q9HC29	NP_071445.1	31 121	21 131 N/A
NOD2_CARD2	NOD2_HUMAN	Q9HC29	NP_071445.1	132 215	122 225 N/A
NOL3	NOL3_HUMAN	O60936	NP_003937.1	10 95	1 105 4UZO
RAIDD	CRADD_HUMAN	P78560	NP_003796.1	6 78	1 88 3CRD
RIP2	RIPK2_HUMAN	O43353	NP_003812.1	437 524	427 534 2N7Z

CARDS Added by BLASTp, PSIBLAST and JACKHMMer

BINCA	CAR19_HUMAN	Q96LW7	NP_115686.3	10	95	1	105	4DWN
CIITA			XP_006720943.2	26	87	16	97	N/A
DLG5	DLG5_HUMAN	Q8TDM6	NP_004738.3	7	88	1	98	N/A
MAVS	MAVS_HUMAN	Q7Z434	NP_065797.2	3	93	1	103	2VGQ
MDA5 CARD1	IFIH1_HUMAN	Q9BYX4	NP_071451.2	8	99	1	109	N/A
RIG-I 1	DDX58_HUMAN	O95786	NP_055129.2	2	92	1	102	4P4H
RIG-I 2	DDX58_HUMAN	O95786	NP_055129.2	100	189	90	199	4P4H

Atypical CARDS

NLRC3	NLRC3_HUMAN	Q7RTR2	NP_849172.2	1	60	1	60	N/A
NLRC5	NLRC5_HUMAN	Q86WI3	NP_115582.4	1	96	1	96	2MJM
Glutamine-rich protein	QRIC1_HUMAN	Q2TAL8	NP_060200.2	6	74	1	84	N/A
Tumour Necrosis Factor Superfamily Member 21	TNR21_HUMAN	O75509	NP_055267.1	564	655	564	655	2DBH

Novel CARDS

E3 Ubiquitin Ligase TTC3	TTC3_HUMAN	P53804	NP_003307.3	816	903	806	913	N/A
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Supplementary Table 1

Structural Alignment:

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          1      2      3      45  6      7      8      910      11 12      13 14
APAF-1 (1CY5)  ----MDAKARNCLLQHREALLEK--DLEK---TSYIMDHMLIS--DGFLITISEEEKVRNEPTQQ---QRAAMLTKMILKKN--DSYVSYFYNALLHEG--YKDLAALLHDGIP---
ASC (2KN6)    -----GLHFDQHRAALIA--RVTN--VEWLLDALYG---KVLTDQEQYQAVRAEPTNP---SKMRKLFSTPAWNW--TKCDLLQALRES---QSYLVEDLERS-----
Bcl-10 (2MB9) -----KKDALLENLRVYLCE--KII---AERHFDHLRA--KKILSREDTREISCRSSR---KRAKLLDYLQENP--KGLDTLVESIRREK-TQNFLIQKITDEVLKLKLR
CARD11 (4LWD) -----ALWENVECNRHMLSR--YIN---PAKLTPLYLRQ--CKVIDEQDEEVLNAPMLPSKINRAGRLLDILHTKGQ--RGYVVFLESLEFY---YPELYKLVGTGKE----
NLRP1 (4IFP)  -----LHFVDQYREQLIA--RVTS--VEVVLDKLHG---QVLSQEQYERVLAENTRP---SQMRKLFSLSQSWDR--KCKDGLYQALKET---HPHLMELWEK-----
BINCA (4DWN)  -----DQTYCDRLVQDTPFLTGHGRLESEQQVDRIILQLNRYYPQILTNKEAEKFRNPKASLR--VRLCDLLSHLQSRGE--RDCQEFYRALYIH---AQPLHSRLPSRH----
CARD8 (4IKM)  -----DAAFVKENHRQLQA--RMGD--LKGVLDDLDQD--NEVLTENEKELVEQEKTRQ---SKNEALLSMVEKKGD--LALDVLFRSISER---DPYLVSYLRQQNL----
CARD18 (1DGN) -----ADQLLRKKRRIFIH--SVGAGTINALLDLLE--DEVISQEDMNKVRDENDTVM--DKARVLIDLVTGKGP--KSCCKFIKHLCEE---DPQLASKMGLH-----
CIAP1 (3T6P)  -----SDDLSELRKNRMALFQ--QLTC--VLPILLDNLLK--ANVINKQEHDIKQKTQIP---LQARELIDTILVKGN--AAANIFKNCLKEI---DSTLYKNLF-----
RAIDD (3CRD)  ----MEARDKQVLRSLRLELGAE--VLV---EGLVLQYLYQ--EGILTENHIQEIQAQTGL---RKTMLLLDILPSRGP--KAFDTFLDSLQEF---PWVREKLLKKAREEAM
RIG-I_CARD1 (4P4H) ---MTTEQRRSLQAFQDYIRK--TLD---PTYILSYMA----PWFREEEVQYIQAENKNGPMEATFLFKFLELQEEGWFRGFLDALDHAG--YSGLYEATIESWDF---
RIG-I_CARD2 (4P4H) KKIEKLEEYRLLKRLQPEFKT--RII---PTDIIISDLS---ECLINQECEELQICSTKGMGAEKLEVECLLRSKDNWPKTLKLALEKE---RNKFSSELWIV-----
MAVS (2VGQ)   ---FAEDKTYKYICRNFSNFC--NVD---VVEILPYL-----PCLTARDQDRIRATCTLSGNRDTLWHLFNTLQRRP--GWVEYFIAALRGCE--LVDLADEVASVYQ---
Caspase-9 (4RHW) ---MDEADRRLLRRCRLRLVE--ELQ---VDQLWDALLS--RELFPHMIEDIQRAGSGS--RRDQARQLIIDLETRGS--QALPLFISCLEDTG--QDMLASFLRTRNRQA--
NOD1 (2DBD)   -----HPHIQLKSNRELLVT--HIRN--TQCLVDNLLK--NDYFSAEDAETVCACPTQP---DKVRKILLDLVQSKGE--EVSEFFLYLLQQLADAYVDLRPWLEIGF---
RIPK2 (2N7Z)  -----GIAQQWIQSKREDIVN--QMTACLNQSLDALLS--RDLIMKEDYELVSTKPTRT---SKVRQLDITTDIQGE--EFAKVIVQKLDKN-----KQMGLPYPEIIL---
NOL3 (4UZ0)   -----QERPSETIDREKRLVE--TLQAD--SGLLLDALLA--RGVLTGPEYEALDALPDAE---RRVRRLLLLLVQKGE--AACQELLRCAQRTAGA-----
          1111111111  bb      222222      tt333333333      44444444      555555555      66666

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Supplementary Figure 1: Final alignment of the 17 CARD structures available from the PDB. PDB identifiers for each structure are provided in brackets. Hydrophobic residues are highlighted yellow and numbered above the alignment. Helix position as per the Apaf-1 structure, PDB 1CY5, are marked by numbers below the alignment.