

Supplementary Table 1. Putative caspase-8 substrates with PoPS score >24.

Putative caspase-8 substrate	Score	Recognition Sequence (P10-P10')	Experimental evidence
Fanconi anemia, complementation group C (NM_00136)	25	MFRCALLET ₃₀₆ -GALEIIATIQ	Cleaved at Asp ₃₀₆ by an unidentified caspase in response to intrinsic apoptosis pathways (1)
DNA directed RNA polymerase II polypeptide A (NM_000937)	25	ALQEWILETD ₁₃₃₉ -GVSLMRVLSE	Cleaved by recombinant caspase-3 and 8 <i>in vitro</i> ; cleaved by an unknown caspases during apoptosis (2)
Histone deacetylase 7 splice variant 3 (AY321367)	25	IPSAEDLETD ₃₇₅ -GGGPGQVVDD	Cleaved by recombinant caspases and endogenous caspase-8 in response to extrinsic apoptosis pathways (this publication)
Nucleobindin 1 (NM_006184)	25	QEVIDVLETD ₆₅ -GHFREKLQAA	ND
Euchromatic histone methyltransferase 1 (NM_024757)	25	ANGPDVLETD ₄₈₁ -GLQEVPLCSC	ND
hypothetical protein MGC16353 (NM_138774)	25	QYLLTLLETD ₈₆ -GGLPGLEDGD	ND
Pleckstrin and Sec7 domain containing 4 (NM_012455)	25	ASQSSLETD ₄₉₆ -GEQPSSLKKK	ND
Phosphoinositide-3-kinase, regulatory subunit 5, p101 (NM_014308)	25	EEVEEDLETD ₃₃₇ -GHCAERDSSL	ND
Tripartite motif-containing 3 (TRIM3); brain expressed ring finger (BERP) (NM_006458)	24.07	AQLELVLEVD ₃₀₃ -GLRRSVLNLG	Not cleaved by recombinant caspase-8 (this publication, data not shown)
RAB9A (NM_004251)	24.07	EFLNKDLEVD ₅₂ -GHFVTMQIWD	Not cleaved by recombinant caspase-8 (this publication, data not shown); cleavage site is in a tight turn between two beta strands (PDB 1S8F)
RAB9B (NM_01630)	24.07	EFLNRDLEVD ₅₂ -GRFVTLQIWD	ND; predicted to have a similar structure to RAB9A
Prostaglandin-D synthase; hematopoietic prostaglandin D2 synthase (NM_014485)	24.07	FGKIPILEVD ₅₇ -GLTLHQSLAI	ND; cleavage site is in a tight turn between two beta strands (PDB 1IYH)
c-FLIP (NM_003879)	24.07	LENSLLEVD ₃₇₆ -GPAMKNVEFK	c-FLIP-L cleaved by recombinant caspase-8 (3)
AT-hook transcription factor (NM_030767)	24.07	EGGGDSLEVD ₇₉₉ -GVAATPGKAE	ND
guanylate binding protein 2, interferon-inducible (NP_004111)	24.07	RDFTLELEVD ₁₉₀ -GEPITADDYL	ND; based on identity with guanylate binding protein 1 (PDB 1F5N) this site is predicted to be accessible
Known and proposed caspase-8 substrates			
Bid (NM_001196)	20.63	WEGYDELQTD ₆₀ -GNRSSHSLRG	Caspase-8 cleaves recombinant and endogenous Bid in response to extrinsic apoptosis pathways (4,5)
Procaspase-3 (NM_004346)	20.56	TELDCGIETD ₁₇₅ -SGVDDDMACH	Caspase-8 cleaves recombinant and endogenous procaspase-3 (6)
Procaspase-7 (NM_001227)	12.72	TELDDGIQAD ₁₉₈ -SGPINDTDAN	Caspase-8 cleaves recombinant procaspase-7 (7)
RIP (NM_003804)	11.09	VKRMQSLQLD ₃₂₄ -CVAVPSSRSN	Caspase-8 cleaves RIP in extrinsic apoptosis (8)
Rat plectin (X59601)	8.31	AENRALILRD ₂₃₉₈ -KDNTQRFLEE	A fragment of rat plectin can be cleaved by caspase-8 <i>in vitro</i> ; not confirmed <i>in vivo</i> (9)
ND, not determined			

1. Brodeur, I., Goulet, I., Tremblay, C. S., Charbonneau, C., Delisle, M. C., Godin, C., Huard, C., Khandjian, E. W., Buchwald, M., Levesque, G., and Carreau, M. (2004) *J Biol Chem* **279**, 4713-4720
2. Lu, Y., Luo, Z., and Bregman, D. B. (2002) *Biochem Biophys Res Commun* **296**, 954-961
3. Boatright, K. M., Deis, C., Denault, J. B., Sutherlin, D. P., and Salvesen, G. S. (2004) *Biochem J* **382**, 651-657
4. Li, H., Zhu, H., Xu, C. J., and Yuan, J. (1998) *Cell* **94**, 491-501
5. Luo, X., Budihardjo, I., Zou, H., Slaughter, C., and Wang, X. (1998) *Cell* **94**, 481-490
6. Stennicke, H. R., Jurgensmeier, J. M., Shin, H., Deveraux, Q., Wolf, B. B., Yang, X., Zhou, Q., Ellerby, H. M., Ellerby, L. M., Bredesen, D., Green, D. R., Reed, J. C., Froelich, C. J., and Salvesen, G. S. (1998) *J Biol Chem* **273**, 27084-27090
7. Denault, J. B., and Salvesen, G. S. (2003) *J Biol Chem* **278**, 34042-34050
8. Lin, Y., Devin, A., Rodriguez, Y., and Liu, Z. G. (1999) *Genes Dev* **13**, 2514-2526
9. Stegh, A. H., Herrmann, H., Lampel, S., Weisenberger, D., Andra, K., Seper, M., Wiche, G., Krammer, P. H., and Peter, M. E. (2000) *Mol Cell Biol* **20**, 5665-5679