Caspases (E.C. 3.4.22.-)

Overview: Caspases, which derive their name from Cysteine ASPartate-specific proteASES, include at least two families; initiator caspases (caspases 2, 8, 9 and 10), which are able to hydrolyse and activate a second family of effector caspases (caspases 3, 6 and 7), which themselves are able to hydrolyse further cellular proteins to bring about programmed cell death. Caspases are heterotetrameric, being made up of two pairs of subunits, generated by a single gene product, which is proteolysed to form the mature protein. Members of the mammalian inhibitors of apoptosis proteins (IAP) are able to bind the procaspases, thereby preventing maturation to active proteinases.

Nomenclature	Caspase 1	Caspase 2	Caspase 3	Caspase 4
Other names	CASP1, interleukin-1β convertase, IL-1BC, interleukin-1 β-converting enzyme, IL-1 β-converting enzyme, ICE, p45	CASP2, ICH-1 protease, neural precursor cell expressed developmentally down-regulated protein 2, NEDD-2	CASP3, apopain, cysteine protease CPP32, Yama protein, SREBP cleavage activity 1, SCA-1	CASP4, ICH-2 protease, TX protease, ICE(rel)-II,
Subunits	Caspase-1 subunit p20; Caspase-1 subunit p10	Caspase-2 subunit p18; Caspase-2 subunit p13; Caspase-2 subunit p12	Caspase-3 subunit p17; Caspase-3 subunit p12	Caspase-4 subunit 1; Caspase-4 subunit 2
EC	3.4.22.36	3.4.22.55	3.4.22.56	3.4.22.57
Ensembl ID	ENSG00000137752	ENSG00000106144	ENSG00000164305	ENSG00000196954
Substrates	Pro-caspase 4, pro-interleukin-1β, D4-GD1, parkin		Pro-caspase 7, caspase 3, PARP, ICAD, Rb, PKCδ, Huntingtin	Pro-caspase 1
Endogenous activators			Caspase 8, caspase 9, caspase 10, GrB	
Activators			PAC1 (Putt *et al.*, 2006), PETCM (Jiang *et al.*, 2003)	
Selective inhibitors	Z-YVAD-FMK (Avivi-Green *et al.*, 2002)	Z-VDVAD-FMK (Gamen *et al.*, 2000)	AZ10417808 (Scott *et al.*, 2003), Z-DEVD-FMK (Brockstedt *et al.*, 1998), Z-DQMD-FMK (Izban *et al.*, 2001)	

CARD16 (Caspase recruitment domain-containing protein 16, caspase-1 inhibitor COP, CARD only domain-containing protein 1, pseudo interleukin-1β converting enzyme, pseudo-ICE, ENSG00000204397) shares sequence similarity with some of the caspases.

Nomenclature	Caspase 5	Caspase 6	Caspase 7	Caspase 8
Other names	CASP5, ICH-3 protease, TY protease, ICE(rel)-III	CASP6, apoptotic protease Mch-2	CASP7, ICE-like apoptotic protease 3, ICE-LAP3, apoptotic protease Mch-3, CMH-1	CASP8, CE-like apoptotic protease 5, MORT1-associated CED-3 homolog, MACH, FADD-homologous ICE/ CED-3-like protease, FADD-like ICE, FLICE, apoptotic cysteine protease, apoptotic protease Mch-5, CAP4
Subunits	Caspase-5 subunit p20; Caspase-5 subunit p10	Caspase-6 subunit p18; Caspase-6 subunit p11	Caspase-7 subunit p20; Caspase-7 subunit p11	Caspase-8 subunit p18; Caspase-8 subunit p10
EC	3.4.22.58	3.4.22.59	3.4.22.60	3.4.22.61
Ensembl ID	ENSG00000137757	ENSG00000138794	ENSG00000165806	ENSG00000064012
Substrates			Pro-caspase 7, caspase 3, PARP, ICAD, Rb, PKCδ, Huntingtin	Pro-caspase 3, pro-caspase 7, caspase 8, Bid, FLIP, pro-caspase 6
Endogenous activators		Caspase 8, caspase 9, caspase 10, GrB	Caspase 8, caspase 9, caspase 10, GrB	DISC
Selective inhibitors	Z-WEHD-FMK (Naito *et al.*, 2002)	Z-VEID-FMK (Ruchaud *et al.*, 2002)		Z-IETD-FMK (Gregoli and Bondurant, 1999)

Nomenclature	Caspase 9	Caspase 10	Caspase 14
Other names	ICE-like apoptotic protease 6, ICE-LAP6, apoptotic protease Mch-6, apoptotic protease-activating factor 3, APAF-3	CASP10, ICE-like apoptotic protease 4, apoptotic protease Mch-4, FAS-associated death domain protein interleukin-1B-converting enzyme 2, FLICE2	CASP14
Subunits	Caspase-9 subunit p35; Caspase-9 subunit p10	Caspase-10 subunit p23/17; Caspase-10 subunit p12	Caspase-14 subunit p19; Caspase-14 subunit p10
EC	3.4.22.62	3.4.22.63	3.4.22.-
Ensembl ID	ENSG00000132906	ENSG00000003400	ENSG00000105141
Substrates	Pro-caspase 3, pro-caspase 7, caspase 9, pro-caspase 6, PARP	Pro-caspase 3, pro-caspase 7, caspase 10, pro-caspase 6	
Endogenous activators		DISC	
Selective inhibitors	Z-LEHD-FMK (Mocanu *et al.*, 2000)		

Abbreviations: **AZ10417808**, 2-([3,4-dichlorophenyl]amino)-1,4-dihydro-6-nitro-4-oxo-*N*-2-propenyl-8-quinazolinecarboxamide; **PAC1**, 4-(phenylmethyl)-1-piperazineacetic acid ([2-hydroxy-3-{2-propenyl}phenyl]methylene)hydrazide; **PETCM**, 1-(trichloromethyl)-2-(4-pyridine)ethanol; **Z-DEVD-FMK**, benzyloxycarbonyl-Asp(OMe)-Glu(OMe)-Val-Asp(OMe)-fluoromethylketone; **Z-DQMD-FMK**, benzyloxycarbonyl-Asp(OMe)-Gln-Met-Asp(OMe)-fluoromethylketone; **Z-LEHD-FMK**, benzyloxycarbonyl-Leu-Glu(OMe)-His-Asp(OMe)-fluoromethylketone; **Z-VDVAD-FMK**, benzyloxycarbonyl-Val-Asp(OMe)-Val-Ala-Asp(OMe)-fluoromethylketone; **Z-VEID-FMK**, benzyloxycarbonyl-Val-Glu(OMe)-Ile-Asp(OMe)-fluoromethylketone; **Z-VYAD-FMK**, benzyloxycarbonyl-Tyr-Val-Ala-Asp(OMe)-fluoromethylketone; **Z-WEHD-FMK**, benzyloxycarbonyl-Trp-Glu(OMe)-His-Asp(OMe)-fluoromethylketone

Further Reading

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