Caspase-7 3.4.22.60

1 Nomenclature

EC number
3.4.22.60

Recommended name
caspase-7

Synonyms
C14.004 (Merops-ID)
CMH-1
ICE-LAP3
ICE-like apoptotic protease 3
LICE2 cysteine protease
SCA-2
SREBP cleavage activity 2
apoptotic protease Mch-3
caspase 7 <2> [28]

CAS registry number
189258-14-8

2 Source Organism

<1> *Mus musculus* (no sequence specified) [22, 32]
<2> *Homo sapiens* (no sequence specified) [3, 4, 5, 6, 9, 10, 11, 12, 13, 18, 19, 20, 23, 24, 25, 27, 28, 29, 30, 31, 32, 33, 34, 35]
<3> *Rattus norvegicus* (no sequence specified) [26]
<4> *Xenopus laevis* (no sequence specified) [2, 21, 29]
<5> *Homo sapiens* (UNIPROT accession number: P55210) [1,7,14,15,16]
<6> *Mus musculus* (UNIPROT accession number: P97864) [1,8,16]
<7> *Mesocricetus auratus* (UNIPROT accession number: P55214) [17]

3 Reaction and Specificity

Catalyzed reaction
strict requirement for an Asp residue at position P1 and has a preferred cleavage sequence of Asp-Glu-Val-Asp-/-

Reaction type

hydrolysis of peptide bond

Natural substrates and products

S epidermal growth factor receptor + H_2O <2> (<2> cleavage during apoptosis [12]) (Reversibility: ?) [12]
P ?
S kinectin + H_2O <2> (<2> kinectin is cleaved by caspase 7 during apoptosis induced by different stimuli. Kinectin functions as a membrane anchor for kinesin and may be relevant to the disruption of vesicle trafficking during apoptosis [18]) (Reversibility: ?) [18]
P ?
S poly(ADP-ribose) polymerase + H_2O <2, 5> (<2> whereas caspase-7 can cleave poly(ADP-ribose) polymerase in vivo, a collaborating caspase facilitates access to poly(ADP-ribose) polymerase, possibly by enhancing nuclear entry [23]; <5> the cleavage of poly(ADP-ribose) polymerase observed during apoptosis cannot solely be attributed to CPP32 but can als be an activity of Mch2α [15]) (Reversibility: ?) [11, 15, 23]
P ?
S pro-endothelial monocyte-activating polypeptide II + H_2O <1> (<1> caspase-7-mediated generation and release of mature endothelial monocyte-activating polypeptide II may provide a mechanism for leukocyte recruitment to sites of programmed cell death, and thus may link apoptosis to inflammation [22]) (Reversibility: ?) [22]
P ?
S viral nucleocapsid protein of transmissible gastroenteritis coronovirus + H_2O <2> (<2> cleavage site VVPD359-/-. Destruction of viral protein by the host cell death machinery [9]) (Reversibility: ?) [9]
P ?
S Additional information <2, 6> (<6> overexpression induces apoptosis [8]; <2> caspase-7 is the most downstream caspase, overexpression does not lead to the activation of other caspases [23]; <2> the enzyme is activated during Fas- and tumor necrosis factor-induced apoptosis [23,24]) (Reversibility: ?) [8, 23, 24]
P ?

Substrates and products

S Ac-DEVD-7-amido-4-methylcoumarin + H_2O <1, 2> (Reversibility: ?) [27, 29, 30, 32]
P Ac-DEVD + 7-amino-4-methylcoumarin
S Ac-DEVD-*p*-nitroanilide + H_2O <2> (Reversibility: ?) [34]
P *p*-nitroaniline + Ac-DEVD
S Ac-DQTD-7-amido-4-methylcoumarin + H_2O <2> (Reversibility: ?) [27]
P Ac-DQTD + 7-amino-4-methylcoumarin
S Ac-DVAD-*p*-nitroanilide + H_2O <2> (Reversibility: ?) [31]
P *p*-nitroaniline + Ac-DVAD
S Ac-LDVAD-*p*-nitroanilide + H_2O <2> (Reversibility: ?) [31]
P *p*-nitroaniline + Ac-LDVAD

S Ac-VDVAD-*p*-nitroanilide + H_2O <2> (Reversibility: ?) [31]
P *p*-nitroaniline + Ac-VDVAD
S DEVD-7-amido-4-methylcoumarin + H_2O <5> (Reversibility: ?) [15]
P DEVD + 7-amino-4-methylcoumarin
S DEVD-7-amido-4-trifluoromethylcoumarin + H_2O <2> (Reversibility: ?) [25]
P DEVD + 7-amino-4-methylcoumarin
S PARP + H_2O <2> (<2> cleaved by caspase-7 during the initiation of apoptosis, cleavage at a single aspartate residue into a large N-terminal fragment and a smaller C-terminal fragment that contains different functional domains [29]) (Reversibility: ?) [25, 29]
P ?
S acetyl-ASTD-7-amido-4-methylcoumarin + H_2O <1> (Reversibility: ?) [22]
P acetyl-ASTD + 7-amino-4-methylcoumarin
S acetyl-Asp-Glu-Val-Asp-7-amido-4-methylcoumarin <3> (Reversibility: ?) [26]
P acetyl-Asp-Glu-Val-Asp + 7-amino-4-methylcoumarin
S acetyl-DEVD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10, 23]
P acetyl-DEVD + 4-nitroaniline
S acetyl-DEVD-7-amido-4-fluoromethylcoumarin + H_2O <2> (Reversibility: ?) [23]
P acetyl-DEVD + 7-amino-4-fluoromethylcoumarin
S acetyl-DEVD-7-amido-4-methylcoumarin + H_2O <1, 2> (<2> iDEVD s the optimal tetrapeptide recognition motif [4]) (Reversibility: ?) [4, 22]
P acetyl-DEVD + 7-amino-4-methylcoumarin
S acetyl-DQMD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-DQMD + 4-nitroaniline
S acetyl-VDQQD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-VDQQD + 4-nitroaniline
S acetyl-VDQVDGW-amide + H_2O <2> (<2> preferred peptide substrate [10]) (Reversibility: ?) [10]
P ?
S acetyl-VDVAD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-VAVAD + 4-nitroaniline
S acetyl-VEID-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-VEID + 4-nitroaniline
S acetyl-VQVD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-VQVD + 4-nitroaniline
S acetyl-VQVDGW-amide + H_2O <2> (<2> preferred peptide substrate [4]) (Reversibility: ?) [4]
P ?
S acetyl-YEVD-4-nitroanilide + H_2O <2> (Reversibility: ?) [10]
P acetyl-YEVD + 4-nitroaniline
S claspin + H_2O <2, 4> (<2,4> cleaved by caspase-7 during the initiation of apoptosis, cleavage at a single aspartate residue into a large N-terminal

fragment and a smaller C-terminal fragment that contain different functional domains [29]) (Reversibility: ?) [29]
P ?
S epidermal growth factor receptor + H_2O <2> (<2> cleavage during apoptosis [12]) (Reversibility: ?) [12]
P ?
S inhibitor of caspase-actived DNase + H_2O <1, 2> (<2> human caspase-7 is less efficient than caspase-3 at cleaving [32]; <1> mouse caspase-7 and caspase-3 are equally efficient at cleaving [32]) (Reversibility: ?) [32]
P ?
S kinectin + H_2O <2> (<2> proteolytic cleavage of the 160000 Da enzyme form to a 120000 Da fragment [18]; <2> kinectin is cleaved by caspase 7 during apoptosis induced by different stimuli. Kinectin functions as a membrane anchor for kinesin and may be relevant to the disruption of vesicle trafficking during apoptosis [18]) (Reversibility: ?) [18]
P ?
S poly(ADP-ribose) polymerase + H_2O <2, 5, 7> (<2> whereas caspase-7 can cleave poly(ADP-ribose) polymerase in vivo, a collaborating caspase facilitates access to poly(ADP-ribose) polymerase, possibly by enhancing nucear entry [23]; <2> whereas caspase-7 can cleave poly(ADP-ribose) polymerase in vivo, a collaborating caspase facilitates access to poly(-ADP-ribose) polymerase, possibly by enhancing nuclear entry [23]; <5> the cleavage of poly(ADP-ribose) polymerase observed during apoptosis cannot solely by attributed to CPP32 but can als be an activity of Mch2α [15]) (Reversibility: ?) [11, 14, 15, 17, 23]
P ?
S pro-endothelial monocyte-activating polypeptide II + H_2O <1> (<1> caspase-7-mediated generation and release of mature endothelial monocyte-activating polypeptide II may provide a mechanism for leukocyte recruitment to sites of programmed cell death, and thus may link apoptosis to inflammation [22]) (Reversibility: ?) [22]
P ?
S pro-endothelial monocyte-activating polypeptide II + H_2O <1> (<1> pro-endothelial monocyte-activating polypeptide II in which the ASTD cleavage site is changed to the sequence ASTA, is not processed by caspase-7 [22]) (Reversibility: ?) [22]
P endothelial monocyte-activating polypeptide II + ?
S sterol regulatory element binding protein-2 + H_2O <7> (<7> SREBP-2 is sterol regulatory element binding protein-2 [17]) (Reversibility: ?) [17]
P ?
S tumor necrosis factor receptor-I + H_2O <2> (<2> mutation E260Q of tumor necrosis factor receptor-I is sufficient to prevent cleavage [19]) (Reversibility: ?) [19]
P ?
S viral nucleocapsid protein of transmissible gastroenteritis coronovirus + H_2O <2> (<2> cleavage site VVPD359-/- [9]; <2> cleavage site

VVPD359-/-. Destruction of viral protein by the host cell death machinery [9]) (Reversibility: ?) [9]

P ?

S Additional information <2, 5, 6> (<2> the preferred cleavage sequence is DEVD-/- [5,6]; <5> no cleavage of YVAD-7-amido-4-methylcoumarin [15]; <5> no cleavage of interleukin 1β precursor [14]; <6> overexpression induces apoptosis [8]; <2> caspase-7 is the most downstream caspase, overexpression does not lead to the activation of other caspases [23]; <2> the enzyme is activated during Fas- and tumor necrosis factor-induced apoptosis [23,24]) (Reversibility: ?) [5, 6, 8, 14, 15, 23, 24]

P ?

Inhibitors

AC-DEVD-aldehyde inhibitor <2> [34]
AC-DQTD-CHO <2> [27]
Ac-DEVD-CHO <2, 4> [27, 29]
Ac-Z-Val-Ala-Asp-fluoromethylketone <2> [27]
DEVD-CHO <2> [25]
DEVD-aldehyde <5> (<5> potent inhibitor [15]) [15]
DEVD-fluoromethylketone <2> (<2> more specific than YVAD-cmk [12]) [12]
X-linked inhibitor of apoptosis <2> [30]
YVAD-aldehyde <5> (<5> weak inhibitor [15]) [15]
YVAD-chloromethylketone <2> [12]
Z-Val-Ala-Asp-fluoromethylketone <2, 3> (<2> inhibits Enterovirus 70-induced apoptosis and virus release, but not intracellular viral production [35]) [26, 29, 30, 35]
acetyl-AEVD-aldehyde <2> [3]
acetyl-Ala-Pro-Nle-Asp-aldehyde <2> [13]
acetyl-DEVD-aldehyde <2> [3, 11]
acetyl-IETD-aldehyde <2> [3]
benzyloxycarbonyl-ASTD-fluoromethylketone <1> (<1> 0.01 mM, complete inhibition of cleavage of pro-endothelial monocyte-activating polypeptide II [22]) [22]
benzyloxycarbonyl-DEVD-chloromethylketone <1> (<1> 0.01 mM, complete inhibition [22]) [22]
benzyloxycarbonyl-Pro-Nle-Asp-aldehyde <2> [13]
benzyloxycarbonyl-VAD-[(2,6-dichlorobenzoyl)-oxy]methyl ketone <2> [11]
benzyloxycarbonyl-VAD-fluoromethylketone <2> (<2> $t_{1/2}$ at 0.001 mM is 98 s [3]) [3]
cowpox seroin CrmA <5> (<5> very weak inhibitor [15]) [15]
ketonic peptides <2> (<2> in the straight-chain aliphatic series, increasing inhibition with increasing chain length, for the unsubstituted aromatic P1 inhibitors increasing potency with decreasing linker length [34]) [34]
Additional information <2> (<2> K_i-values higher than 0.01 mM are determined for acetyl-WEHD-aldehyde and acetyl-YVAD-aldehyde and cowpox serin CrmA [3]) [3]

Activating compounds

ceramide <2> [33]
FSH <3> (<3> antiapoptotic effect on granulosa cells and a proapoptotic effect on theca-interstitial cells [26]) [26]
LH <3> (<3> antiapoptotic effect on granulosa cells and a proapoptotic effect on theca-interstitial cells [26]) [26]
apoptosome complex <2> [30]
cytolethal distending toxin <2> (<2> from Actinobacillus actinomycetemcomitans [27]) [27]
gonadotropins <3> (<3> increases caspase-7 activity in both theca-interstitial cells and granulosa cells [26]) [26]
hypoxia <2> [33]
nitric oxide <2> [33]
topoisomerase II inhibitor etoposide <2> (<2> procaspase-7 cleavage (= activation of caspase-7), which is abrogated in cells with ectopically expressed p53 [25]) [25]
topoisomerase II poison etopside <2> [29]
Additional information <3> (<3> caspase-7 activity not increased by IGF-I [26]) [26]

Turnover number (min^{-1})

1.26 <2> (Ac-VDVAD-*p*-nitroanilide) [31]
5.5 <2> (acetyl-DEVD-7-amido-4-methylcoumarin, <2> pH 7.0 [4]) [4]
6.08 <2> (Ac-DVAD-*p*-nitroanilide) [31]
6.08 <2> (Ac-LDVAD-*p*-nitroanilide) [31]
6.3 <2> (acetyl-DEVD-7-amido-4-methylcoumarin, <2> pH 7.5 [4]) [4]
6.9 <2> (acetyl-DEVD-7-amido-4-fluoromethylcoumarin, <2> pH 7.2, 37°C [23]) [23]
10.3 <2> (acetyl-DEVD-*p*-nitroanilide, <2> pH 7.2, 37°C [23]) [23]
Additional information <2> [10]

K_m-Value (mM)

0.012 <2> (acetyl-DEVD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]
0.015 <2> (acetyl-DEVD-7-amido-4-methylcoumarin, <2> pH 7.0 [4]) [4]
0.0605 <2> (acetyl-DEVD-7-amido-4-fluoromethylcoumarin, <2> pH 7.2, 37°C [23]) [23]
0.0646 <2> (acetyl-DEVD-4-nitroanilide, <2> pH 7.2, 37°C [23]) [23]
0.1 <2> (acetyl-DEVD-7-amido-4-methylcoumarin, <2> pH 7.5 [4]) [4]
0.125 <2> (acetyl-VDQVDGW-amide, <2> pH 7.5, 30°C [10]) [10]
0.13 <2> (acetyl-DQMD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]
0.13 <2> (acetyl-VQVDGW-amide, <2> pH 7.5, 30°C [4]) [4]
0.2 <2> (acetyl-VDVAD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]
0.2193 <2> (Ac-DVAD-*p*-nitroanilide) [31]
0.3149 <2> (Ac-VDVAD-*p*-nitroanilide) [31]
0.3239 <2> (Ac-LDVAD-*p*-nitroanilide) [31]
0.49 <2> (acetyl-YEVD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]
0.57 <2> (acetyl-YEID-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]

2.1 <2> (acetyl-YQVD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]
3.1 <2> (acetyl-VDQQD-4-nitroanilide, <2> pH 7.5, 30°C [10]) [10]

K_i-Value (mM)

1.6e-006 <2> (acetyl-DEVD-aldehyde, <2> pH 7.5, 25°C [3]) [3]
1.8e-006 <5> (DEVD-aldehyde, <5> pH 7.5, 37°C [15]) [15]
3.5e-005 <2> (acetyl-DEVD-aldehyde, <2> pH 7.5 [10]) [10]
0.000425 <2> (acetyl-AEVD-aldehyde, <2> pH 7.5, 25°C [3]) [3]
0.00328 <2> (acetyl-IETD-aldehyde, <2> pH 7.5, 25°C [3]) [3]
0.126 <2> (benzyloxycarbonyl-Pro-Nle-Asp-aldehyde, <2> pH 7.5, 25°C [13]) [13]
0.133 <2> (acetyl-Ala-Pro-Nle-Asp-aldehyde, <2> pH 7.5 [13]) [13]

pH-Optimum

6.5 <7> (<7> cleavage of sterol regulatory element binding protein [17]) [17]
7 <2> (<2> reaction with acetyl-DEVD-7-amido-4-methylcoumarin [4]) [4]

pH-Range

6-7 <7> (<7> pH 6.0: about 35% of maximal activity, pH 7.0: about 15% of maximal activity, cleavage of sterol regulatory element binding protein [17]) [17]

4 Enzyme Structure

Molecular weight

26000 <2> (<2> active form of caspase-7, Western blot analysis [35]) [35]
32000 <2> (<2> procaspase-7, Western blot analysis [35]) [35]
60000 <2> (<2> procaspase-7, immunoblotting [30]) [30]
200000 <2> (<2> X-linked inhibitor of apoptosis-caspase-7 complex, immunoblotting [30]) [30]
250000 <2> (<2> Western blot analysis [29]) [29]

Subunits

tetramer <2> [30]
Additional information <2, 5> (<2> 2 * 35000, procaspase-7 C285A mutant, in the homodimeric procaspase-7 each monomer is organized in two structured subdomains connected by partially flexible linkers, which asymmetrically occupy and block the central cavity, SDS-PAGE [20]; <5> it is proposed that the 22000 Da peptide and the 12000 Da peptide are two subunits of the enzyme [14,15]) [14, 15, 20]

Posttranslational modification

proteolytic modification <2, 5, 7> (<2> viral nucleocapsid protein of transmissible gastroenteritis coronavirus triggers the processing of procaspase 6 in human rectal tumor cell line HRT18jap1 [9]; <5> Mch3α is made of two subunits derived from a precursor ProMch3α. Asp23 and Asp198 are the most likely processing sites. Bacterially expressed Mch3 has intrinsic autocatalytic and autoactivation activity [15]; <7> enzyme is synthesized as an inactive 30000-35000 Da precursor and is thought to be cleaved during apopto-

sis to generate active fragments of 20000 Da and 10000 Da [17]; <2> the N-peptide of caspase-7 must be removed, probably be caspase-3, before efficient activation of the zymogen can occur in vivo. The N-peptide serves to physically sequester the caspase-7 zymogen in a cytosolic location that prevents access by upstream activators, caspase-8, caspase-9 and caspase-10 [23]; <5> both Mch4 and the serine protease granzyme B cleave proMch3 at a conserved IXXD-S sequence to produce the large and small subunits of the active protease. Mch3 is a target of mature protease in apoptotic cells [7]; <2> activation site is IQAD (P4,P3,P2,P1) [6]; <2> the 12000 Da and the 11000 Da polypeptides are generated by processing of the CMH-1 protein at Asp198-Ser199 and to a lesser extent at Asp206-Ala207 [23]; <5> CPP32 can efficiently cleave proMch3α [15]) [6, 7, 9, 14, 15, 17, 23]

5 Isolation/Preparation/Mutation/Application

Source/tissue

Chang cell <2> (<2> conjunctival cell [35]) [35]
HEK-293 cell <2> [33]
HRT-18 cell <2> [9]
HeLa cell <2> [18, 28, 29]
JURKAT cell <2> [18, 19, 24, 27, 29]
MCF-7 cell <2> [30]
MOLT-4 cell <2> [27]
NCI-H1299 cell <2> [25]
SH-SY5Y cell <2> [33]
T-cell <5> [15]
T-lymphocyte <2> [27]
brain <1, 6> (<6> low activity [8]) [8, 32]
egg <4> [29]
granulosa cell <3> [26]
heart <6> [8]
kidney <1, 6> [8, 32]
liver <1, 6, 7> [8, 17, 32]
lung <5, 6> (<5> fetal lung [16]) [8, 16]
neuron <2> [33]
skeletal muscle <6> [8, 16]
skin <5> [1]
spleen <1, 5, 6> (<5> getal spleen [16]) [8, 14, 16, 32]
stomach <1> [32]
tadpole <4> (<4> stage 62 tadpole tail [2]) [2]
tail <4> (<4> stage 62 tadpole tail [2]) [2]
telencephalon <1> (<1> precursor neurons [32]) [32]
testis <6> [8]
Additional information <2, 3> (<2> NCI-H358 cell [25]; <3> theca-interstitial cells, preovulatory follicles [26]; <2> U3A cell, 2fTGH cell, G8 cell, 1CC cell, 1C5 cell [28]) [25, 26, 28]

Localization

cytoplasm <2> [33]
cytosol <1, 2, 7> [17, 18, 29, 32]
nucleus <2, 4> (<4> caspase-7 is activated and accumulates in the nucleus. A prodomain of caspase-7, 31 amino acid residues, inhibits both the apoptosis-inducing activity and the nuclear localization, removal of the prodomain induces both the nuclear import of the catalytic protease and the cell killing activity [21]) [21, 29, 33]
plasma membrane <7> (<7> juxtamembrane structures [17]) [17]
Additional information <2> (<2> human caspase-7 is not a nuclear caspase removal of the N-peptide does not allow an active transport or accumulation of human caspase-7 in the nuclei [23]) [23]

Purification

<1> [32]
<2> [32, 34]
<2> (by nickel affinity chromatography, anion exchange chromatography and gel filtration) [31]
<2> (partially purified X-linked inhibitor of apoptosis-caspase-7 complex by gel filtration and immunopurification, SDS-PAGE) [30]
<5> [14]
<7> [17]

Crystallization

<2> (2.9 A crystal structure of recombinant C285A procaspase, sitting drop vapor diffusion method) [20]

Cloning

<1> (cloned into the NcoI site of the pET11d vector and expression in Escherichia coli BL21codon+) [32]
<2> [3, 24, 25, 31, 32]
<2> (expression in CG1945 yeast strain) [33]
<2> (expression in Escherichia coli) [34]
<2> (expression in Escherichia coli BL21 (DE3) transformed with a pET-21b plasmid expression vector) [30]
<4> [2]
<5> (bacterially expressed Mch3 has intrinsic autocatalytic and autoactivation activity) [15]
<5> (overexpression in COS cells) [14]
<6> [8]
<7> [17]

Engineering

C285A <2> (<2> mutant procaspase-7 shows no autoactivation [20]) [20]

Application

medicine <1, 2, 4> (<2> Actinobacillus actinomycetemcomitans cytolethal distending toxin acts as an immunosuppressive factor, it possesses the ability to induce human T-cell apoptosis through activation of caspase-7 [27]; <2>

acute hemorrhagic conjunctivitis, Enterovirus 70 infection induces caspase-7-mediated apoptosis [35]; <2,4> cleavage of claspin by caspase-7 inactivates the Chk1 signaling pathway, this mechanism may regulate the balance between cell cycle arrest and induction of apoptosis during response of genotoxic stress [29]; <2> hydrophobic P5 residue has a favorable contribution to the recognition and hydrolysis of substrates but not by caspase-7, this information helps to design specific inhibitors for each caspase [31]; <2> low-dosage topoisomerase II inhibitor etoposide effectively inhibits proliferation rate [25]; <2> strong correlation between caspase-7 activity, normal brain development, and apoptotic DNA fragmenation in Casp3-/-mice [32]; <1> strong correlation between caspase-7 activity, normal brain development, and apoptotic DNA fragmenation in Casp3-/-mice, caspase-7 is a caspase-3 surrogate in Casp3-/-mice [32]; <2> substitution in the P1 position could be used in synergy with other elements to obtain highly potent and isozyme-selective caspase inhibitors [34]; <2> SUMO-1 modification in caspase-7 may contribute to the cleavage of nuclear substrates during neuronal apoptosis [33]) [25, 27, 29, 31, 32, 33, 34, 35]
Additional information <2> (<2> apoptosis is preceded by proteolytic cleavage of e.g. caspase 7, prolonged nuclear localization of activated signal transducer and activator of transcription 1 results in apoptosis involving specific regulation of caspase pathway [28]) [28]

References

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