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(54) **CASPASE HOMOLOGUE**

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(56) **References Cited**

**U.S. PATENT DOCUMENTS**

6,340,740 B1 1/2002 Alnemri et al.  
6,376,226 B1 4/2002 Alnemri  
6,432,628 B1 8/2002 Alnemri et al.  
2002/0081705 A1 6/2002 Mankovich  
2002/0146804 A1 10/2002 Alnemri

**FOREIGN PATENT DOCUMENTS**

WO WO 91/03551 3/1991  
WO WO 96/20276 4/1996  
WO WO 96/13603 5/1996  
WO WO 99/10504 3/1999  
WO WO 00/04169 1/2000

**OTHER PUBLICATIONS**

Poyet et al. Accession P31944. Jul. 1, 1993 (Alignment No. 1).\*

Attwood et al. Which craft is best in bioinformatics? Comput. Chem. 2001, vol. 25(4), pp. 329-339.\*

Ponting, C.P. Issues in predicting protein function from sequence. Brief. Bioinform. Mar. 2001, vol. 2(1), pp. 19-29.\*

Abstract XP-002085023.

Abstract XP-002085024.

Abstract XP-002085055.

Abstract XP-002092996.

Fernandes-Alnemri et al., "CPP32, a Novel Human Apoptotic Protein with Homology to *Caenorhabditis elegans* Cell Death Protein Ced-3 and Mammalian Interleukin-1  $\beta$ -converting Enzyme", *The Journal of Biological Chemistry*, vol. 269, No. 49, pp. 30761-30764, Dec. 9, 1994.

Hu et al., "Caspase-14 Is a Novel Developmentally Regulated Protease", *The Journal of Biological Chemistry*, vol. 273, No. 45, pp. 29648-29653, Nov. 6, 1998.

Juan et al., "Identification and Mapping of Casp7, a Cysteine Protease Resembling CPP32 $\beta$ , Interleukin-1 $\beta$  Converting Enzyme, and CED-3", *Genomics*, 40, pp. 86-93, 1997.

PCT International Preliminary Examination Report, PCT/EP99/04939, dated Sep. 19, 2000.

PCT International Search Report, PCT/EP99/04939, dated Aug. 24, 1999, 7 pages.

Van de Craen et al., "Identification of a new caspase homologue: caspase-14", *Cell Death and Differentiation*, 5, pp. 838-846, 1998.

Cohen, Caspases: the executioners of apoptosis, *Biochem J.*, 1997, pp. 1-16, vol. 326.

#Rendl et al., Caspase-14 Expression by Epidermal Keratinocytes is Regulated by Retinoids in a Differentiation-associated Manner, *The Journal of Investigative Dermatology*, 2002, pp. 1150-1155, vol. 119, No. 5.

#Haake et al., Apoptosis: A Role in Skin Aging? *J. Investig. Dermatol. Symp. Proc.*, Aug. 1998, pp. 28-35, vol. 3, No. 1.

\* cited by examiner

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**ABSTRACT**

Caspases are cysteinyl aspartate-specific proteinases, many of which play a central role in apoptosis. This invention relates to the identification of a new murine caspase and its human homologue. The new molecules are most related to human/murine caspase-2 and human caspase-9 and possess all the typical amino acid residues of the caspases involved in catalysis, including the QACRG box, and contains no or only a very short prodomain. Northern blot analysis revealed that mRNA expression of the new caspase is predominant in skin.

**2 Claims, 12 Drawing Sheets**