Atlas of Genetics and Cytogenetics in Oncology and Haematology

OPEN ACCESS JOURNAL AT INIST-CNRS

Gene Section
Mini Review

XPE (xeroderma pigmentosum, complementation group E)

Anne Stary, Alain Sarasin

Laboratory of Genetic Instability and Cancer, UPR2169 CNRS, Institut de Recherches sur le Cancer, 7, rue guy Moquet, BP 8, 94801 Villejuif, France (AS, AS)

Published in Atlas Database: September 2001

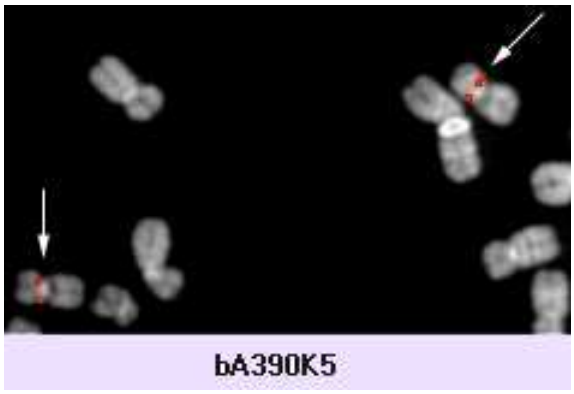
Online updated version : http://AtlasGeneticsOncology.org/Genes/XPEID298.html
DOI: 10.4267/2042/37808

Identity

Other names: XPE (xeroderma pigmentosum, complementation group E); UV-DDB; DDB2

HGNC (Hugo): DDB2

Location: 11p12-11p11



XPE (11p11) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Transcription

4193 bp.

Protein

Description

DDB1: 1140 amino acids, 127 kDa; DDB2: 427 amino acids, 48 kDa; DDB1 (p127) and DDB2 (p48) form a stable heterodimer UV-DDB.

Function

The damage-specific DNA binding (UV-DDB) activity purified as a heterodimer (p127 and p48) is expected to play a role in damage recognition prior to the Nucleotide Excision Repair (NER) because the DDB protein is reported to recognize many types of DNA lesions and is inducible by treatment with DNA-damaging agents. After UV irradiation, dynamic nuclear accumulation of DDB1 from the cytoplasm was found after 24 h. The function of the gene product is not completely clarified yet. Band shift assays suggested that the XPE gene product acts as a damaged DNA binding protein (DDB), with high affinity to UV-induced 6-4Pyrimidine-Pyrimidone photoproducts. However, defective DDB binding activity is not a common feature of XPE mutant cell lines and in fact two (or even more) proteins may be involved in the binding activity: p48 and p125. In cells from several XPE patient mutations in p48 have been found but so far no mutations have been found in the p125 gene. XPE patients show mild dermatological symptoms and cells from these patients have a relatively high repair capacity. XPE cells are not necessarily defective in repair: p125 is proposed to play a role in opening up chromatin to make CPD accessible to the NER machinery, but is not required for repair of 6-4PP. Interestingly, cell lines and primary tissues from rodents are fully deficient in the expression of the p48 protein. This explains the absence of GGR of CPD in these cells. Exogenous expression of p48 in hamster cells confers enhanced removal of CPD from genomic DNA and nontranscribed strand of active genes. The p48 protein is upregulated by p53.

Mutations

Germinal

Three single base substitutions only in DDB2 (p48) gene.

Implicated in

Xeroderma pigmentosum, XP group E

Oncogenesis

Early skin tumours.

References

Protić M, Hirschfeld S, Tsang AP, Wagner M, Dixon K, Levine AS. Induction of a novel damage-specific DNA binding protein correlates with enhanced DNA repair in primate cells. Mol Toxicol. 1989 Oct-Dec;2(4):255-70

Abramić M, Levine AS, Protić M. Purification of an ultraviolet-inducible, damage-specific DNA-binding protein from primate cells. J Biol Chem. 1991 Nov 25;266(33):22493-500

Reardon JT, Nichols AF, Keeney S, Smith CA, Taylor JS, Linn S, Sancar A. Comparative analysis of binding of human damaged DNA-binding protein (XPE) and Escherichia coli damage recognition protein (UvrA) to the major ultraviolet photoproducts: T[c,s]T, T[t,s]T, T[6-4]T, and T[Dewar]T. J Biol Chem. 1993 Oct 5;268(28):21301-8

Takao M, Abramic M, Moos M Jr, Otrin VR, Wootton JC, McLenigan M, Levine AS, Protic M. A 127 kDa component of a UV-damaged DNA-binding complex, which is defective in some xeroderma pigmentosum group E patients, is homologous to a slime mold protein. Nucleic Acids Res. 1993 Aug 25;21(17):4111-8

Aboussekhra A, Biggerstaff M, Shivji MK, Vilpo JA, Moncollin V, Podust VN, Protić M, Hübscher U, Egly JM, Wood RD. Mammalian DNA nucleotide excision repair reconstituted with purified protein components. Cell. 1995 Mar 24;80(6):859-68

Dualan R, Brody T, Keeney S, Nichols AF, Admon A, Linn S. Chromosomal localization and cDNA cloning of the genes (DDB1 and DDB2) for the p127 and p48 subunits of a human damage-specific DNA binding protein. Genomics. 1995 Sep 1;29(1):62-9

Hwang BJ, Liao JC, Chu G. Isolation of a cDNA encoding a UV-damaged DNA binding factor defective in xeroderma pigmentosum group E cells. Mutat Res. 1996 Jan 2;362(1):105-17

Kazantsev A, Mu D, Nichols AF, Zhao X, Linn S, Sancar A. Functional complementation of xeroderma pigmentosum complementation group E by replication protein A in an in vitro system. Proc Natl Acad Sci U S A. 1996 May 14;93(10):5014-8

Nichols AF, Ong P, Linn S. Mutations specific to the xeroderma pigmentosum group E Ddb- phenotype. J Biol Chem. 1996 Oct 4;271(40):24317-20

Otrin VR, McLenigan M, Takao M, Levine AS, Protić M. Translocation of a UV-damaged DNA binding protein into a tight association with chromatin after treatment of mammalian cells with UV light. J Cell Sci. 1997 May;110 (Pt 10):1159-68

Hayes S, Shiyanov P, Chen X, Raychaudhuri P. DDB, a putative DNA repair protein, can function as a transcriptional partner of E2F1. Mol Cell Biol. 1998 Jan;18(1):240-9

Lin GY, Paterson RG, Richardson CD, Lamb RA. The V protein of the paramyxovirus SV5 interacts with damage-specific DNA binding protein. Virology. 1998 Sep 15;249(1):189-200

Rapić Otrin V, Kuraoka I, Nardo T, McLenigan M, Eker AP, Stefanini M, Levine AS, Wood RD. Relationship of the xeroderma pigmentosum group E DNA repair defect to the chromatin and DNA binding proteins UV-DDB and replication protein A. Mol Cell Biol. 1998 Jun;18(6):3182-90

Stöhr H, Marquardt A, Rivera A, Kellner U, Weber BH. Refined mapping of the gene encoding the p127 kDa UV-damaged DNA-binding protein (DDB1) within 11q12-q13.1 and its exclusion in Best's vitelliform macular dystrophy. Eur J Hum Genet. 1998 Jul-Aug;6(4):400-5

Cleaver JE, Thompson LH, Richardson AS, States JC. A summary of mutations in the UV-sensitive disorders: xeroderma pigmentosum, Cockayne syndrome, and trichothiodystrophy. Hum Mutat. 1999;14(1):9-22

Fujiwara Y, Masutani C, Mizukoshi T, Kondo J, Hanaoka F, Iwai S. Characterization of DNA recognition by the human UV-damaged DNA-binding protein. J Biol Chem. 1999 Jul 9;274(28):20027-33

Hwang BJ, Ford JM, Hanawalt PC, Chu G. Expression of the p48 xeroderma pigmentosum gene is p53-dependent and is involved in global genomic repair. Proc Natl Acad Sci U S A. 1999 Jan 19;96(2):424-8

Itoh T, Mori T, Ohkubo H, Yamaizumi M. A newly identified patient with clinical xeroderma pigmentosum phenotype has a non-sense mutation in the DDB2 gene and incomplete repair in (6-4) photoproducts. J Invest Dermatol. 1999 Aug;113(2):251-7

Mizukoshi T, Fujiwara Y, Iwai S. DNA structures recognized by the human UV-DDB protein. Nucleic Acids Symp Ser. 1999;(42):265-6

Shiyanov P, Hayes SA, Donepudi M, Nichols AF, Linn S, Slagle BL, Raychaudhuri P. The naturally occurring mutants of DDB are impaired in stimulating nuclear import of the p125 subunit and E2F1-activated transcription. Mol Cell Biol. 1999 Jul;19(7):4935-43

Shiyanov P, Nag A, Raychaudhuri P. Cullin 4A associates with the UV-damaged DNA-binding protein DDB. J Biol Chem. 1999 Dec 10;274(50):35309-12

Tornaletti S, Hanawalt PC. Effect of DNA lesions on transcription elongation. Biochimie. 1999 Jan-Feb;81(1-2):139-46

Watanabe T, Sukegawa J, Sukegawa I, Tomita S, Iijima K, Oguchi S, Suzuki T, Nairn AC, Greengard P. A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the Alzheimer's amyloid precursor protein. J Neurochem. 1999 Feb;72(2):549-56

Itoh T, Linn S, Ono T, Yamaizumi M. Reinvestigation of the classification of five cell strains of xeroderma pigmentosum group E with reclassification of three of them. J Invest Dermatol. 2000 May;114(5):1022-9

Liu W, Nichols AF, Graham JA, Dualan R, Abbas A, Linn S. Nuclear transport of human DDB protein induced by ultraviolet light. J Biol Chem. 2000 Jul 14;275(28):21429-34

Nichols AF, Itoh T, Graham JA, Liu W, Yamaizumi M, Linn S. Human damage-specific DNA-binding protein p48. Characterization of XPE mutations and regulation following UV irradiation. J Biol Chem. 2000 Jul 14;275(28):21422-8

Sitterlin D, Bergametti F, Tiollais P, Tennant BC, Transy C. Correct binding of viral X protein to UVDDB-p127 cellular protein is critical for efficient infection by hepatitis B viruses. Oncogene. 2000 Sep 7;19(38):4427-31

Sitterlin D, Bergametti F, Transy C. UVDDB p127-binding modulates activities and intracellular distribution of hepatitis B virus X protein. Oncogene. 2000 Sep 7;19(38):4417-26

Tang JY, Hwang BJ, Ford JM, Hanawalt PC, Chu G. Xeroderma pigmentosum p48 gene enhances global genomic repair and suppresses UV-induced mutagenesis. Mol Cell. 2000 Apr;5(4):737-44

Acquati F, Morelli C, Cinquetti R, Bianchi MG, Porrini D, Varesco L, Gismondi V, Rocchetti R, Talevi S, Possati L, Magnanini C, Tibiletti MG, Bernasconi B, Daidone MG, Shridhar V, Smith DI, Negrini M, Barbanti-Brodano G, Taramelli R. Cloning and characterization of a senescence inducing and class II tumor suppressor gene in ovarian carcinoma at chromosome region 6q27. Oncogene. 2001 Feb 22;20(8):980-8

Datta A, Bagchi S, Nag A, Shiyanov P, Adami GR, Yoon T, Raychaudhuri P. The p48 subunit of the damaged-DNA binding protein DDB associates with the CBP/p300 family of histone acetyltransferase. Mutat Res. 2001 Jul 12;486(2):89-97

Hahn H. Genetically determined susceptibility markers in skin cancer and their application to chemoprevention. IARC Sci Publ. 2001;154:93-100

Hanawalt PC. Controlling the efficiency of excision repair. Mutat Res. 2001 Feb 25;485(1):3-13

Ishikawa T, Ide F, Qin X, Zhang S, Takahashi Y, Sekiguchi M, Tanaka K, Nakatsuru Y. Importance of DNA repair in carcinogenesis: evidence from transgenic and gene targeting studies. Mutat Res. 2001 Jun 2;477(1-2):41-9

Wakasugi M, Shimizu M, Morioka H, Linn S, Nikaido O, Matsunaga T. Damaged DNA-binding protein DDB stimulates the excision of cyclobutane pyrimidine dimers in vitro in concert with XPA and replication protein A. J Biol Chem. 2001 May 4;276(18):15434-40

This article should be referenced as such:

Stary A, Sarasin A. XPE (xeroderma pigmentosum, complementation group E). Atlas Genet Cytogenet Oncol Haematol. 2002; 6(1):5-7.