

NEIL1 (nei endonuclease VIII-like 1 (E. coli))

Identity

Other names **FLJ22402**
FPG1
hFPG1
NEH1
NEI1

Hugo [NEIL1](#)

Location 15q24.2

DNA/RNA

Description The NEIL1 gene maps on chromosome 15q24.2 spanning 8,179bp. It contains 11 exons, and the orientation is plus strand.

Transcription The transcript of 1,828bp, expressed in Brain, Liver, Lung, Kidney, Colon, and Stomach. The NEIL1 gene is up-regulated during S-phase.

Protein



Description NEIL1 encodes 390 amino acids, theoretical molecular weight is 43684 Da, Formamidopyrimidine-DNA glycosylase N-terminal domain and Formamidopyrimidine-DNA glycosylase H2TH domain.

Localisation Nucleus, centrosome, and mitotic condensed chromosomes.

Function

- (1) Bifunctional DNA glycosylase and apurinic/aprimidinic (AP) lyase that catalyzes beta- and delta-elimination reactions at the site of damaged base.
- (2) Reported substrates: thymine glycol (Tg), 5-hydroxycytosine, 5-hydroxyuracil, 5,6-dihydrouracil, 5,6-dihydrothymine, 2,6-diamino-4-hydroxy-5-formamidopyrimidine (FapyG), 4,6-diamino-5-formamidopyrimidine (FapyA), 5-formyluracil, 5-hydroxymethyluracil, spiroiminodihydantoin (Sp), guanidinohydantoin, (Gh) and 8-hydroxyguanine.
- (3) Since NEIL1 catalyzes beta- and delta-elimination reactions, the protein generates DNA strand breaks with 3' phosphate termini. In mammalian cells, this 3' phosphate is removed by polynucleotide kinase, but not by . NEIL1 stably interacts with other BER proteins, DNA polymerase beta and DNA ligase III alpha.
- (4) In mammalian BER, DNA glycosylases generate abasic (AP) sites, which are then converted to deoxyribo-5'-phosphate (dRP) and excised by a dRP lyase (dRPase) activity of DNA polymerase beta. Since NEIL1 also has dRPase activity, NEIL1 has a role as a backup dRPase in mammalian cells.
- (5) NEIL1 has a repair activity for oxidized bases in single-strand DNA and bubble DNA, suggesting a possibility that NEIL1 is preferentially involved in repair of lesions in DNA bubbles generated during transcription and/or replication.
- (6) Proteins that associate and stimulate the repair activity of NEIL1: a) The (WRN), a member of RecQ family of DNA helicases, b) , , and as individual proteins and as the 9-1-1 complex.
- (7) The major DNA glycosylase for the excision of 8-hydroxyguanine is . In the repair of 8-ydroxyguanine by OGG1, after excising the base lesion, OGG1 remains bound to the resulting AP site and does not turn over efficiently. The APE1, which cleaves the phosphodiester bond 5' to the AP site, displaces the bound OGG1 and thus increases

its turnover. NEIL1 stimulates turnover of OGG1 in a fashion similar to that of APE1, and carries out beta/delta- elimination at the AP site.

(8) Although OGG1 has limited activity on 8-hydroxyguanine lesion located in the vicinity of the 3' end of a DNA single-strand break, NEIL1 effectively excises the 3' end proximal 8-hydroxyguanine lesion. NEIL1 also effectively excises 5-hydroxyuracil lesions located in the proximity of the 3'-end of a DNA single-strand break. (9) The NEIL1 gene is induced by reactive oxygen species.

Homology Homo sapiens: (NP_659480, 20.1%), (NP_060718, 15.0%) using the CLUSTALW software.

Implicated in

Entity Gastric cancer

Note The following is the abstract of the paper by Shinmura K. et al. (Carcinogenesis, 2004). Oxidized DNA base lesions, such as thymine glycol (Tg) and 8-hydroxyguanine, are often toxic and mutagenic and have been implicated in carcinogenesis. To clarify whether NEIL1 protein, which exhibits excision repair activity towards such base lesions, is involved in gastric carcinogenesis, we examined 71 primary gastric cancers from Japanese patients and four gastric cancer cell lines for mutations and genetic polymorphisms of the NEIL1 gene. We also examined 20 blood samples from Chinese patients for NEIL1 genetic polymorphisms. Three mutations (c.82_84delGAG:p.Glu28del, c.936G > A and c.1000A > G:p.Arg334Gly) and two genetic polymorphisms were identified. When the excision repair activity towards double-stranded oligonucleotide containing a Tg:A base pair was compared among six types of recombinant NEIL1 proteins, p.Glu28del-type NEIL1, found in a primary case, was found to exhibit an extremely low activity level. Moreover, c.936G > A, located in the last nucleotide of exon 10 and detected in the KATO-III cell line, was shown to be associated with a splicing abnormality using an in vivo splicing assay. An immunofluorescence analysis showed that the wild-type NEIL1 protein, but not the truncated protein encoded by the abnormal transcript arising from the c.936G > A mutation, was localized in the nucleus, suggesting that the truncated protein is unlikely to be capable of repairing nuclear DNA. An expression analysis revealed that NEIL1 mRNA expression was reduced in six of 13 (46%) primary gastric cancer specimens that were examined. These results suggest that low NEIL1 activities arising from mutations and reduced expression may be involved in the pathogenesis in a subset of gastric cancers.

External links

[Hugo](#)

[GDB](#)

[Entrez_Gene](#)

[Atlas](#)

[GeneCards](#)

[Ensembl](#)

[Genatlas](#)

[GeneLynx](#)

[eGenome](#)

[euGene](#)

[GoldenPath](#)

[Ensembl](#)

[NCBI](#)

Nomenclature

[NEIL1](#)

[NEIL1](#)

[NEIL1_79661](#) nei endonuclease VIII-like 1 (E. coli)

Cards

[NEIL1ID41519ch15q24](#)

[NEIL1](#)

[NEIL1](#) [Search_View] [ENSG00000140398](#) [Gene_View]

[NEIL1](#)

[NEIL1](#)

[NEIL1](#)

[79661](#)

Genomic and cartography

[NEIL1](#) - [15q24.2](#) [chr15:73426463-73434639 + 15q24.2](#) (hg18-Mar_2006)

[NEIL1 - 15q24.2 \[CytoView\]](#)

[Mapview](#)

[OMIM](#)
[HomoloGene](#)

[Genbank](#)
[Genbank](#)
[Genbank](#)
[Genbank](#)
[Genbank](#)
[RefSeq](#)
[RefSeq](#)
[RefSeq](#)
[RefSeq](#)
[RefSeq](#)
[AceView](#)

[Unigene](#)
[Fast-db](#)

[HPRD](#)

[OMIM](#)
[GENECLINICS](#)
[SNP](#)
[SNP](#)
[SNP](#)
[HAPMAP](#)
[COSMIC](#)
[HGMD](#)

[Family Browser](#)
[SOURCE](#)
[SMD](#)
[SAGE](#)

[GO](#)

[GO](#)
[GO](#)

[GO](#)

[GO](#)

[GO](#)

[GO](#)

[GO](#)

[PubGene](#)

[Disease map \[OMIM\]](#)
[NEIL1](#)
Gene and transcription
[AB079068](#) [ENTREZ]
[AK026055](#) [ENTREZ]
[AK026216](#) [ENTREZ]
[AK097008](#) [ENTREZ]
[AK128372](#) [ENTREZ]
[NM_024608](#) [SRS] [NM_024608](#) [ENTREZ]
[AC_000058](#) [SRS] [AC_000058](#) [ENTREZ]
[NC_000015](#) [SRS] [NC_000015](#) [ENTREZ]
[NT_010194](#) [SRS] [NT_010194](#) [ENTREZ]
[NW_925907](#) [SRS] [NW_925907](#) [ENTREZ]
[NEIL1](#) AceView - NCBI
[Hs.512732](#) [SRS] [Hs.512732](#) [NCBI]
[HS512732](#) [spliceNest]
[8481](#) (alternative variants)
Protein : pattern, domain, 3D structure
[17894](#)
Polymorphism : SNP, mutations, diseases
[608844](#) [map]
[608844](#)
[NEIL1](#) [dbSNP-NCBI]
[NM_024608](#) [SNP-NCI]
[NEIL1](#) [GeneSNPs - Utah] [NEIL1](#) [HGBASE - SRS]
[NEIL1](#) [HAPMAP]
[NEIL1](#) [Somatic mutation (COSMIC-CGP-Sanger)]
[NEIL1](#)
General knowledge
[NEIL1](#) [UCSC Family Browser]
[NM_024608](#)
[Hs.512732](#)
[Hs.512732](#)
[damaged DNA binding](#) [Amigo] [damaged DNA binding](#)
[nucleus](#) [Amigo] [nucleus](#)
[base-excision repair](#) [Amigo] [base-excision repair](#)
[nucleotide-excision repair](#) [Amigo] [nucleotide-excision repair](#)
[metabolic process](#) [Amigo] [metabolic process](#)
[zinc ion binding](#) [Amigo] [zinc ion binding](#)
[oxidized purine base lesion DNA N-glycosylase activity](#) [Amigo] [oxidized purine base lesion DNA N-glycosylase activity](#)
[lyase activity](#) [Amigo] [lyase activity](#)
[NEIL1](#)
Probes

[Probe](#)

[NEIL1 Related clones \(RZPD - Berlin\)](#)

[PubMed](#)

[PubMed](#)

[25 Pubmed reference\(s\) in LocusLink](#)

Bibliography

A novel human DNA glycosylase that removes oxidative DNA damage and is homologous to *Escherichia coli* endonuclease VIII.

Bandaru V, Sunkara S, Wallace SS, Bond JP.
DNA Repair (Amst) 2002; 1(7): 517-529.
Medline [12509226](#)

Identification and characterization of a human DNA glycosylase for repair of modified bases in oxidatively damaged DNA.

Hazra TK, Izumi T, Boldogh I, Imhoff B, Kow YW, Jaruga P, Dizdaroglu M, Mitra S.
Proc Natl Acad Sci U S A 2002; 99(6): 3523-3528.
Medline [11904416](#)

Identification and characterization of a novel human DNA glycosylase for repair of cytosine-derived lesions.

Hazra TK, Kow YW, Hatahet Z, Imhoff B, Boldogh I, Mokkapatil SK, Mitra S, Izumi T.
J Biol Chem 2002; 277(34): 30417-30420.
Medline [12097317](#)

Human DNA glycosylases of the bacterial Fpg/MutM superfamily: an alternative pathway for the repair of 8-oxoguanine and other oxidation products in DNA.

Morland I, Rolseth V, Luna L, Rognes T, Bjoras M, Seeberg E.
Nucleic Acids Res 2002; 30(22): 4926-4936.
Medline [12433996](#)

A back-up glycosylase in *Nth1* knock-out mice is a functional *Nei* (endonuclease VIII) homologue.

Takao M, Kanno S, Kobayashi K, Zhang QM, Yonei S, van der Horst GT, Yasui A.
J Biol Chem 2002; 277(44): 42205-42213.
Medline [12200441](#)

Repair of oxidized bases in DNA bubble structures by human DNA glycosylases NEIL1 and NEIL2.

Dou H, Mitra S, Hazra TK.
J Biol Chem 2003; 278(50): 49679-49684.
Medline [14522990](#)

Cross-linking of 2-deoxyribonolactone and its beta-elimination product by base excision repair enzymes.

Kroeger KM, Hashimoto M, Kow YW, Greenberg MM.
Biochemistry 2003; 42(8): 2449-2455.
Medline [12600212](#)

The novel DNA glycosylase, NEIL1, protects mammalian cells from radiation-mediated cell death.

Rosenquist TA, Zaika E, Fernandes AS, Zharkov DO, Miller H, Grollman AP.
DNA Repair (Amst) 2003; 2(5): 581-591.
Medline [12713815](#)

Overproduction, crystallization and preliminary crystallographic analysis of a novel human DNA-repair enzyme that recognizes oxidative DNA damage.

Bandaru V, Cooper W, Wallace SS, Doublé S.
Acta Crystallogr D Biol Crystallogr 2004; 60(Pt 6): 1142-1144.
Medline [15159582](#)

The crystal structure of human endonuclease VIII-like 1 (NEIL1) reveals a zincless finger motif

required for glycosylase activity.

Doublié S, Bandaru V, Bond JP, Wallace SS.
Proc Natl Acad Sci U S A 2004; 101(28): 10284-10289.
Medline [15232006](#)

Expression of the oxidative base excision repair enzymes is not induced in TK6 human lymphoblastoid cells after low doses of ionizing radiation.

Inoue M, Shen GP, Chaudhry MA, Galick H, Blaisdell JO, Wallace SS.
Radiat Res 2004; 161(4): 409-417.
Medline [15038771](#)

Mouse NEIL1 protein is specific for excision of 2,6-diamino-4-hydroxy-5-formamidopyrimidine and 4,6-diamino-5-formamidopyrimidine from oxidatively damaged DNA.

Jaruga P, Birincioglu M, Rosenquist TA, Dizdaroglu M.
Biochemistry 2004; 43(50): 15909-15914.
Medline [15595846](#)

Differential specificity of human and Escherichia coli endonuclease III and VIII homologues for oxidative base lesions.

Katafuchi A, Nakano T, Masaoka A, Terato H, Iwai S, Hanaoka F, Ide H.
J Biol Chem 2004; (14): 14464-14471.
Medline [14734554](#)

Stereoselective excision of thymine glycol from oxidatively damaged DNA.

Miller H, Fernandes AS, Zaika E, McTigue MM, Torres MC, Wente M, Iden CR, Grollman AP.
Nucleic Acids Res 2004; 32(1): 338-345.
Medline [14726482](#)

Stimulation of DNA glycosylase activity of OGG1 by NEIL1: functional collaboration between two human DNA glycosylases.

Mokkapati SK, Wiederhold L, Hazra TK, Mitra S.
Biochemistry 2004; 43(36): 11596-11604.
Medline [15350146](#)

Inactivating mutations of the human base excision repair gene NEIL1 in gastric cancer.

Shinmura K, Tao H, Goto M, Igarashi H, Taniguchi T, Maekawa M, Takezaki T, Sugimura H.
Carcinogenesis 2004; 25(12): 2311-2317.
Medline [15319300](#)

AP endonuclease-independent DNA base excision repair in human cells.

Wiederhold L, Leppard JB, Kedar P, Karimi-Busheri F, Rasouli-Nia A, Weinfeld M, Tomkinson AE, Izumi T, Prasad R, Wilson SH, Mitra S, Hazra TK.
Mol Cell 2004; 15(2): 209-220.
Medline [15260972](#)

Action of human endonucleases III and VIII upon DNA-containing tandem dihydrouracil.

Ali MM, Hazra TK, Hong D, Kow YW.
DNA Repair (Amst) 2005; 4(6): 679-686.
Medline [15907775](#)

Induction of the human oxidized base-specific DNA glycosylase NEIL1 by reactive oxygen species.

Das A, Hazra TK, Boldogh I, Mitra S, Bhakat KK.
J Biol Chem 2005; 280(42): 35272-35280.
Medline [16118226](#)

Recognition of the oxidized lesions spiroiminodihydroantoin and guanidinohydroantoin in DNA by the mammalian base excision repair glycosylases NEIL1 and NEIL2.

Hailer MK, Slade PG, Martin BD, Rosenquist TA, Sugden KD.
DNA Repair (Amst) 2005; 4(1): 41-50.

Medline [15533836](#)

Repair of formamidopyrimidines in DNA involves different glycosylases: role of the OGG1, NTH1, and NEIL1 enzymes.

Hu J, de Souza-Pinto NC, Haraguchi K, Hogue BA, Jaruga P, Greenberg MM, Dizdaroglu M, Bohr VA. J Biol Chem 2005; 280(49): 40544-40551.

Medline [16221681](#)

NEIL1 excises 3' end proximal oxidative DNA lesions resistant to cleavage by NTH1 and OGG1.

Parsons JL, Zharkov DO, Dianov GL. Nucleic Acids Res 2005; 33(15): 4849-4856.

Medline [16129732](#)

DNA glycosylase activities for thymine residues oxidized in the methyl group are functions of the hNEIL1 and hNTH1 enzymes in human cells.

Zhang QM, Yonekura S, Takao M, Yasui A, Sugiyama H, Yonei S. DNA Repair (Amst) 2005; 4(1): 71-79.

Medline [15533839](#)

Evaluation of NTHL1, NEIL1, NEIL2, MPG, TDG, UNG and SMUG1 genes in familial colorectal cancer predisposition.

Broderick P, Bagratuni T, Vijayakrishnan J, Lubbe S, Chandler I, Houlston RS. BMC Cancer 2006; 6: 243.

Medline [17029639](#)

Deoxyribose phosphate lyase activity of mammalian endonuclease VIII-like proteins.

Grin IR, Khodyreva SN, Nevinsky GA, Zharkov DO. FEBS Lett 2006; 580(20): 4916-4922.

Medline [16920106](#)

Purification and characterization of NEIL1 and NEIL2, members of a distinct family of mammalian DNA glycosylases for repair of oxidized bases.

Hazra TK, Mitra S. Methods Enzymol 2006; 408: 33-48.

Medline [16793361](#)

Repair of thymine glycol by hNth1 and hNeil1 is modulated by base pairing and cis-trans epimerization.

Ocampo-Hafalla MT, Altamirano A, Basu AK, Chan MK, Ocampo JE, Cummings A Jr, Boorstein RJ, Cunningham RP, Teebor GW.

DNA Repair (Amst) 2006; 5(4): 444-454.

Medline [16446124](#)

The metabolic syndrome resulting from a knockout of the NEIL1 DNA glycosylase.

Vartanian V, Lowell B, Minko IG, Wood TG, Ceci JD, George S, Ballinger SW, Corless CL, McCullough AK, Lloyd RS.

Proc Natl Acad Sci U S A 2006; 103(6): 1864-1869.

Medline [16446448](#)

Different organization of base excision repair of uracil in DNA in nuclei and mitochondria and selective upregulation of mitochondrial uracil-DNA glycosylase after oxidative stress.

Akbari M, Otterlei M, Pena-Diaz J, Krokan HE.

Neuroscience 2007; 145(4): 1201-1212.

Medline [17101234](#)

Human endonuclease VIII-like (NEIL) proteins in the giant DNA Mimivirus.

Bandaru V, Zhao X, Newton MR, Burrows CJ, Wallace SS.

DNA Repair (Amst) 2007; [Epub ahead of print]

Medline [17627905](#)

Major oxidative products of cytosine are substrates for the nucleotide incision repair pathway.
Daviet S, Couvé-Privat S, Gros L, Shinozuka K, Ide H, Saparbaev M, Ishchenko AA.
DNA Repair (Amst) 2007; 6(1): 8-18.
Medline [16978929](#)

The human werner syndrome protein stimulates repair of oxidative DNA base damage by the DNA glycosylase Neil1.
Das A, Boldogh I, Lee JW, Harrigan JA, Hegde ML, Piotrowski J, de Souza-Pinto N, Ramos W, Greenberg MM, Hazra TK, Mitra S, Bohr VA.
J Biol Chem 2007; [Epub ahead of print]
Medline [17611195](#)

The human checkpoint sensor Rad9-Rad1-Hus1 interacts with and stimulates NEIL1 glycosylase.
Guan X, Bai H, Shi G, Theriot CA, Hazra TK, Mitra S, Lu AL.
Nucleic Acids Res 2007; 35(8): 2463-2472.
Medline [17395641](#)

Human NEIL1 localizes with the centrosomes and condensed chromosomes during mitosis.
Hildrestrand GA, Rolseth V, Bjørås M, Luna L.
DNA Repair (Amst) 2007; [Epub ahead of print]
Medline [17556049](#)

Lesion specificity in the base excision repair enzyme hNeil1: modeling and dynamics studies.
Jia L, Shafirovich V, Geacintov NE, Broyde S.
Biochemistry 2007; 46(18): 5305-5314.
Medline [17432829](#)

NEIL1 is the major DNA glycosylase that processes 5-hydroxyuracil in the proximity of a DNA single-strand break.
Parsons JL, Kavli B, Slupphaug G, Dianov GL.
Biochemistry 2007; 46(13): 4158-4163.
Medline [17348689](#)

Human polymorphic variants of the NEIL1 DNA glycosylase.
Roy LM, Jaruga P, Wood TG, McCullough AK, Dizdaroglu M, Lloyd RS.
J Biol Chem 2007; 282(21): 15790-15798.
Medline [17389588](#)

[REVIEW articles](#) *automatic search in PubMed*
[Last year publications](#) *automatic search in PubMed*

[BiblioGene - INIST](#)
Search in all [EBI](#) [NCBI](#)

Contributor(s)

Written 07-2007 Masaya Suzuki, Kazuya Shinmura, Haruhiko Sugimura
Department of Pathology, Hamamatsu University School of Medicine, 1-20-1, Handayama, Hamamatsu, Shizuoka 431-3192, Japan

Citation

This paper should be referenced as such :

Suzuki M, Shinmura K, Sugimura H . NEIL1 (nei endonuclease VIII-like 1 (E. coli)). Atlas Genet Cytogenet Oncol Haematol. July 2007 .
URL : <http://AtlasGeneticsOncology.org/Genes/NEIL1ID41519ch15q24.html>

© *Atlas of Genetics and Cytogenetics in Oncology and Haematology*