

CHEK2 (CHK2 checkpoint homolog (*S. pombe*))

Identity

Other names **CHK2**
CDS1
Rad53
Hugo **CHEK2**
Location 22q12.1

DNA/RNA

Description 17 exons spanning 57 kb
Transcription Two isoforms are expressed, isoform a (2547nt) includes all 17 exons, while isoform b (2460 nt) does not include exon 12, deleting 87nt (29 codons) from the mRNA. The translation start site is in exon 4.

Protein

Description 61 kDa. Isoform a: 543 amino acids; isoform b: 514 amino acids. Contains FHA and ser/thr kinase domains. Molecular studies of Chk2 typically do not distinguish between the different isoforms.

Expression All tissues tested.

Localisation nuclear

Function Chk2 plays a role in the DNA damage signal cascade, especially in response to double-strand breaks. After detection of DNA damage, Chk2 is phosphorylated on Thr-68 by [ATM](#) and ATR. Thus activated, Chk2 targets [p53](#) for phosphorylation on Ser20, releasing p53 from its inhibitor MDM2 and allowing transcriptional activation of genes responsible for cell cycle arrest, such as [p21waf1/cip1](#), as well as initiation of apoptosis. In S phase, Chk2 phosphorylates Cdc25A on Ser123, targeting it for degradation and making it unavailable for the activation of cdk2, thus inhibiting the advance of S phase. In G2 phase, Chk2 phosphorylates Ser216 of Cdc25C, blocking entry into mitosis.

Chk2 is also involved in the regulation of BRCA1. Under normal conditions the two proteins are associated; after irradiation Chk2 phosphorylates Ser988 of BRCA1. This step is required for their dissociation, and the liberated BRCA1 participates directly in DNA repair and cell cycle arrest.

Finally, Chk2 can provoke apoptosis independently of p53, for example via phosphorylation of [PML](#).

Homology 26 % identical to the Rad53 *S. cereviscea* homolog. The FHA and kinase domains are particularly conserved.

Mutations

Germinal The northern european founder mutation "1100delC" is the most common found in [breast cancer](#) families. Other small deletions, stops, and missense mutations in the FHA or kinase domains such as Arg145Trp and Ile157Thr are rare in cancer families but not found in

controls. The 1100delC mutation appears to increase the penetrance of mutations in certain other breast cancer genes, notably BRCA2. It should be noted that the publications describing "1100delC" have used the A of the initiation codon as nucleotide 1. This mutation thus corresponds to position 1861 in the complete, isoform a mRNA.

Somatic Missense mutations in the FHA and kinase domains as well as frameshifts and nonsense mutations have been found at low frequencies in [osteosarcoma](#) and more rarely in [carcinomas of the ovary](#), [lung](#), and vulva. Reduced or missing protein expression has been observed in some cases of [non-Hodgkins lymphoma](#), although neither mutation nor silencing of the gene by methylation was detected.

Implicated in

Entity [Li-Fraumeni](#), Li-Fraumeni-like syndrome, somatic osteosarcoma and familial aggregations of [breast cancer](#) and colon cancer.

Note The importance of Chk2 mutations in hereditary cancer risk is controversial, as some studies have failed to show an excess of mutations in selected populations, such as male breast cancer and patients with multiple colorectal adenomas developing colon cancer. In addition, some studies of breast cancer families suggest that only the relatively frequent 1100delC mutation is significant.

Prognosis No known association with the clinical parameters of solid tumors. There is a possible association with more aggressive non-Hodgkins lymphomas.

External links

Nomenclature

[Hugo](#) [CHEK2](#)
[GDB](#) [CHEK2](#)
[Entrez Gene](#) [CHEK2](#) [11200](#) [CHK2](#) checkpoint homolog (S. pombe)

Cards

[Atlas](#) [CHEK2ID312](#)
[GeneCards](#) [CHEK2](#)
[Ensembl](#) [CHEK2](#)
[CancerGene](#) [CHEK2](#)
[Genatlas](#) [CHEK2](#)
[GeneLynx](#) [CHEK2](#)
[eGenome](#) [CHEK2](#)
[euGene](#) [11200](#)

Genomic and cartography

[GoldenPath](#) [CHEK2](#) - [22q12.1](#) [chr22:27408285-27462376](#) - [22q12.1](#) (hg17-May_2004)
[Ensembl](#) [CHEK2 - 22q12.1 \[CytoView\]](#)
[NCBI](#) [Genes](#) [Cyto](#) [Gene Seq](#) [Map View - NCBI]
[OMIM](#) [Disease map \[OMIM\]](#)
[HomoloGene](#) [CHEK2](#)

Gene and transcription

[Genbank](#) [AL117330](#) [SRS] [AL117330](#) [ENTREZ]
[Genbank](#) [AL121825](#) [SRS] [AL121825](#) [ENTREZ]
[Genbank](#) [AB040105](#) [SRS] [AB040105](#) [ENTREZ]
[Genbank](#) [AF086904](#) [SRS] [AF086904](#) [ENTREZ]
[Genbank](#) [AF096279](#) [SRS] [AF096279](#) [ENTREZ]

RefSeq	NM_001005735 [SRS] NM_001005735 [ENTREZ]
RefSeq	NM_007194 [SRS] NM_007194 [ENTREZ]
RefSeq	NM_145862 [SRS] NM_145862 [ENTREZ]
RefSeq	NT_086921 [SRS] NT_086921 [ENTREZ]
AceView	CHEK2 AceView - NCBI
TRASER	CHEK2 Traser - Stanford
Unigene	Hs.291363 [SRS] Hs.291363 [NCBI] HS291363 [spliceNest]
Protein : pattern, domain, 3D structure	
SwissProt	O96017 [SRS] O96017 [EXPASY] O96017 [INTERPRO]
Prosite	PS50006 FHA DOMAIN [SRS] PS50006 FHA DOMAIN [Expasy]
Prosite	PS00107 PROTEIN KINASE ATP [SRS] PS00107 PROTEIN KINASE ATP [Expasy]
Prosite	PS50011 PROTEIN KINASE DOM [SRS] PS50011 PROTEIN KINASE DOM [Expasy]
Prosite	PS00108 PROTEIN KINASE ST [SRS] PS00108 PROTEIN KINASE ST [Expasy]
Interpro	IPR000253 FHA [SRS] IPR000253 FHA [EBI]
Interpro	IPR011009 Kinase like [SRS] IPR011009 Kinase like [EBI]
Interpro	IPR000719 Prot kinase [SRS] IPR000719 Prot kinase [EBI]
Interpro	IPR008271 Ser thr pkin AS [SRS] IPR008271 Ser thr pkin AS [EBI]
Interpro	IPR002290 Ser thr pkinase [SRS] IPR002290 Ser thr pkinase [EBI]
Interpro	IPR008984 SMAD FHA [SRS] IPR008984 SMAD FHA [EBI]
CluSTr	O96017
Pfam	PF00498 FHA [SRS] PF00498 FHA [Sanger] pfam00498 [NCBI-CDD]
Pfam	PF00069 Pkinase [SRS] PF00069 Pkinase [Sanger] pfam00069 [NCBI-CDD]
Smart	SM00240 FHA [EMBL]
Smart	SM00220 S_TKc [EMBL]
Prodom	PD000001 Prot kinase [INRA-Toulouse]
Prodom	O96017 CHK2 HUMAN [Domain structure] O96017 CHK2 HUMAN [sequences sharing at least 1 domain]
Blocks	O96017
PDB	1GXC [SRS] 1GXC [PdbSum], 1GXC [IMB]
Polymorphism : SNP, mutations, diseases	
OMIM	604373 [map]
GENECLINICS	604373
SNP	CHEK2 [dbSNP-NCBI]
SNP	NM_001005735 [SNP-NCI]
SNP	NM_007194 [SNP-NCI]
SNP	NM_145862 [SNP-NCI]
SNP	CHEK2 [GeneSNPs - Utah] CHEK2 [SNP - CSHL] CHEK2 [HGBASE - SRS]
General knowledge	
Family Browser	CHEK2 [UCSC Family Browser]
SOURCE	NM_001005735
SOURCE	NM_007194
SOURCE	NM_145862
SMD	Hs.291363
SAGE	Hs.291363
Enzyme	2.7.1.37 [Enzyme-SRS] 2.7.1.37 [Brenda-SRS] 2.7.1.37 [KEGG] 2.7.1.37 [WIT]
Amigo	function ATP binding

[Amigo](#) [process|DNA damage checkpoint](#)
[Amigo](#) [process|cell cycle](#)
[Amigo](#) [function|kinase activity](#)
[Amigo](#) [component|nucleus](#)
[Amigo](#) [process|protein amino acid phosphorylation](#)
[Amigo](#) [function|protein serine/threonine kinase activity](#)
[Amigo](#) [function|protein serine/threonine kinase activity](#)
[Amigo](#) [function|protein-tyrosine kinase activity](#)
[Amigo](#) [process|response to DNA damage stimulus](#)
[Amigo](#) [function|transferase activity](#)
[BIOCARTA](#) [ATM Signaling Pathway](#)
[BIOCARTA](#) [Role of BRCA1, BRCA2 and ATR in Cancer Susceptibility](#)
[BIOCARTA](#) [Cell Cycle: G2/M Checkpoint](#)
[BIOCARTA](#) [Regulation of cell cycle progression by Plk3](#)
[PubGene](#) [CHEK2](#)

Other databases

Probes

[Probe](#) [CHEK2 Related clones \(RZPD - Berlin\)](#)

PubMed

[PubMed](#) [58 Pubmed reference\(s\) in LocusLink](#)

Bibliography

Linkage of ATM to cell cycle regulation by the Chk2 protein kinase.

Matsuoka S, Huang M, Elledge SJ.

Science 1998; 282: 1893-1897.

Medline [9836640](#)

DNA damage-induced cell cycle checkpoints and DNA strand break repair in development and tumorigenesis.

Dasika GK, Lin SC, Zhao S, Sung P, Tomkinson A, Lee EY.

Oncogene 1999; 18: 7883-7899. Review.

Medline [10630641](#)

p53, CHK2, and CHK1 genes in Finnish families with Li-Fraumeni syndrome: further evidence of CHK2 in inherited cancer predisposition.

Vahteristo P, Tamminen A, Karvinen P, Eerola H, Eklund C, Aaltonen LA, Blomqvist C, Aittomaki K, Nevanlinna H.

Cancer Res 2001; 61: 5718-5722.

Medline [11479205](#)

Mutations of the CHK2 gene are found in some osteosarcomas, but are rare in breast, lung, and ovarian tumors.

Miller CW, Ikezoe T, Krug U, Hofmann WK, Tavor S, Vegesna V, Tsukasaki K, Takeuchi S, Koeffler HP.

Genes Chromosomes Cancer 2002; 33(1): 17-21.

Medline [11746983](#)

Contribution of the CHEK2 1100delC variant to risk of multiple colorectal adenoma and carcinoma.

Lipton L, Fleischmann C, Sieber OM, Thomas HJ, Hodgson SV, Tomlinson IP, Houlston RS.

Cancer Lett 2003; 200(2): 149-152.
Medline [14568168](#)

Variants in CHEK2 other than 1100delC do not make a major contribution to breast cancer susceptibility.

Schutte M, Seal S, Barfoot R, Meijers-Heijboer H, Wasielewski M, Evans DG, Eccles D, Meijers C, Lohman F, Klijn J, van den Ouweland A, Futreal PA, Nathanson KL, Weber BL, Easton DF, Stratton MR, Rahman N; Breast Cancer Linkage Consortium. Am J Hum Genet 2003; 72: 1023-1028.
Medline [12610780](#)

CHEK2 1100delC is not a risk factor for male breast cancer population.

Syrjakoski K, Kuukasjarvi T, Auvinen A, Kallioniemi OP. Int J Cancer 2004; 108(3): 475-476.
Medline [14648717](#)

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[Citation](#)

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