NQO1 (updated: old version not available)

Identity

Other names	**DIA4** **DT-Diaphorase** **NMO1**
Hugo	**NQO1**
Location	16q22.1

NQO1 (16q22) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics. Laboratories willing to validate the probes are welcome : contact rocchi@biologia.uniba.it

DNA/RNA

Description	Spans approximately 20 kb consisting of 6 exons and 5 introns. Highly inducible protein and the 5' flanking region contains an AP2, ARE or EpRE(antioxidant or electrophile responsive element) and an XRE (xenobiotic responsive element).
Transcription	Three mRNA sizes (1.2, 1.7 and 2.7 kb) have been observed due to multiple polyadenylation sites. An alternatively spliced form of NQO1 mRNA lacking exon 4 is also possible although the corresponding truncated protein has not been detected.

Protein

Description	NQO1 is a flavoprotein which functions as a homodimer. The physiological dimer has one catalytic site per monomer. Each monomer consists of 273 amino acids. For structures of human recombinant NQO1 with quinones complexed in the active site see Structures of recombinant human and mouse NAD(P)H:quinone oxidoreductases: species comparison and structural changes with substrate binding and release (Structure Explorer - 1D4A) and. Structure-based development of antitumor quinones. Complexes of NQO1 with three potential chemotherapeutic quinones (Structure Explorer - 1H66).
Expression	NQO1 is expressed in human epithelial and endothelial tissues and at high levels throughout many human solid tumors.
Localisation	NQO1 is a mainly cytosolic enzyme (approx. 90%) although it has also been localized in smaller amounts to mitochondria, endoplasmic reticulum and nucleus.
Function	NQO1 catalyzes obligate two electron reduction of a wide variety of substrates. The most efficient substrates are quinones but the enzyme

will also reduce quinone-imines, nitro and azo compounds. The enzyme functions via a hydride transfer mechanism and requires a pyridine nucleotide cofactor. Reduction proceeds with equal facility with both NADH and NADPH. NQO1 can generate antioxidant forms of both vitamin E and ubiquinone after free radical attack. The capability to protect cells from oxidative challenge and the ability to reduce quinones via an obligate two electron mechanism, which precludes generation of reactive oxygen radicals, demonstrates that NQO1 is a chemoprotective enzyme. NQO1 knockout mice demonstrated increased susceptibility to benzo(a)pyrene and 7,12-dimethylbenz(a) anthracene induced skin carcinogenesis. NQO1 has been proposed to stabilize the tumor suppressor gene p53 and has been shown to interact with p53 in a protein-protein interaction.

Certain compounds such as antitumor quinones, however, can be bioactivated by two electron reduction and in these cases NQO1 serves as an activating enzyme. Because of the high levels of NQO1 in certain tumors, this has led to an interest in designing compounds which can be efficiently bioactivated by NQO1 as antitumor agents.

Homology: Amino acid homology across species is high (mouse/human 86%, mouse/rat -94%, human/rat 86%). NQO2 is a separate gene product demonstrating 49% and 54% similarity at the amino acid and nucleotide levels respectively.

Mutations

Germinal: Two polymorphisms have been characterized. The NQO1 *2 allele represents a C609T change in the cDNA coding for a Pro187Ser change in the enzyme. The NQO1 *3 allele is a C465T change in the cDNA coding for an Arg139Trp change. The NQO1 * 2 allele is much more frequent than the *3 allele and has profound consequences for phenotype. The NQO1 *2 protein has diminished catalytic activity and the protein is rapidly degraded by the ubiquitin-proteasomal system. As a result, cells and tissues carrying the homozygous NQO1 *2 allele have no detectable NQO1 activity and at best, trace levels of NQO1 protein. The NQO1 *2/*2 genotype is effectively a null polymorphism. NQO1 is highly inducible and although NQO1 levels can vary considerably among individuals with the same genotype, the NQO1 *2 allele has been reported to show a gene dose effect since heterozygotes (NQO1 *1/*2) contained significantly less NQO1 protein than wild type (NQO1 *1/*1) samples.

Implicated in

Entity Leukemia

Note Increased risk of leukemia has been associated with the NQO1 *2 allele and diminished NQO1 activity. Childhood leukemia (particularly with MLL fusions) , adult leukemia (ALL, AML particularly with translocations or inversions) and secondary leukemias and myelodysplasias as a result of chemotherapy have been associated with the NQO1 *2 polymorphism. Increased benzene induced myelotoxicity in occupationally exposed individuals has also been linked to the NQO1 *2 polymorphism.

Entity Solid tumors

Note Increased risk of renal and urothelial cell carcinomas and cutaneous basal cell carcinomas have also been associated with the NQO1 *2 polymorphism but conflicting results have been obtained in colon cancer and lung cancer. A number of epidemiological studies have investigated the possible link between NQO1 and cancer and have been recently summarized [6].DISEASE

External links

	Nomenclature
Hugo	NQO1
GDB	NQO1
Entrez_Gene	NQO1 1728 NAD(P)H dehydrogenase, quinone 1
	Cards
Atlas	**NQO1ID375**
GeneCards	NQO1
Ensembl	NQO1
CancerGene	NQO1
Genatlas	NQO1
GeneLynx	NQO1
eGenome	NQO1
euGene	1728
	Genomic and cartography
GoldenPath	NQO1 - 16q22.1 chr16:68300810-68317893 - 16q22.1 (hg17-May_2004)
Ensembl	NQO1 - 16q22.1 [CytoView]
NCBI	Genes Cyto Gene Seq [Map View - NCBI]
OMIM	Disease map [OMIM]
HomoloGene	NQO1
	Gene and transcription
Genbank	AY281093 [SRS] AY281093 [ENTREZ]
Genbank	M81600 [SRS] M81600 [ENTREZ]
Genbank	BC000906 [SRS] BC000906 [ENTREZ]
Genbank	BC007659 [SRS] BC007659 [ENTREZ]
Genbank	J03934 [SRS] J03934 [ENTREZ]
RefSeq	NM_000903 [SRS] NM_000903 [ENTREZ]
RefSeq	NT_086851 [SRS] NT_086851 [ENTREZ]
AceView	NQO1 AceView - NCBI
TRASER	NQO1 Traser - Stanford
Unigene	Hs.406515 [SRS] Hs.406515 [NCBI] HS406515 [spliceNest]
	Protein : pattern, domain, 3D structure
SwissProt	P15559 [SRS] P15559 [EXPASY] P15559 [INTERPRO]
Interpro	IPR003680 NADHdh_2 [SRS] IPR003680 NADHdh_2 [EBI]
CluSTr	P15559
Pfam	PF02525 Flavodoxin_2 [SRS] PF02525 Flavodoxin_2 [Sanger] pfam02525 [NCBI-CDD]
Blocks	P15559
PDB	1D4A [SRS] 1D4A [PdbSum], 1D4A [IMB]
PDB	1DXO [SRS] 1DXO [PdbSum], 1DXO [IMB]
PDB	1GG5 [SRS] 1GG5 [PdbSum], 1GG5 [IMB]
PDB	1H66 [SRS] 1H66 [PdbSum], 1H66 [IMB]

PDB	1H69 [SRS] 1H69 [PdbSum], 1H69 [IMB]
PDB	1KBO [SRS] 1KBO [PdbSum], 1KBO [IMB]
PDB	1KBQ [SRS] 1KBQ [PdbSum], 1KBQ [IMB]
PDB	1QBG [SRS] 1QBG [PdbSum], 1QBG [IMB]
	Polymorphism : SNP, mutations, diseases
OMIM	125860 [map]
GENECLINICS	125860
SNP	NQO1 [dbSNP-NCBI]
SNP	NM_000903 [SNP-NCI]
SNP	NQO1 [GeneSNPs - Utah] NQO1 [SNP - CSHL] NQO1] [HGBASE - SRS]
	General knowledge
Family Browser	NQO1 [UCSC Family Browser]
SOURCE	NM_000903
SMD	Hs.406515
SAGE	Hs.406515
Enzyme	1.6.99.2 [Enzyme-SRS] 1.6.99.2 [Brenda-SRS] 1.6.99.2 [KEGG] 1.6.99.2 [WIT]
Amigo	function|NAD(P)H dehydrogenase (quinone) activity
Amigo	function|cytochrome-b5 reductase activity
Amigo	component|cytoplasm
Amigo	process|electron transport
Amigo	process|nitric oxide biosynthesis
Amigo	function|oxidoreductase activity
Amigo	process|response to toxin
Amigo	process|synaptic transmission, cholinergic
Amigo	process|xenobiotic metabolism
BIOCARTA	Hypoxia and p53 in the Cardiovascular system
KEGG	Sterol Biosynthesis
PubGene	NQO1
	Other databases
	Probes
Probe	Cancer Cytogenetics (Bari)
Probe	NQO1 Related clones (RZPD - Berlin)
	PubMed
PubMed	**34 Pubmed reference(s) in LocusLink**

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Contributor(s)

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