

Introduction

Description

Nuclear factor erythroid-derived 2-like 2, a transcription factor that regulates ROS metabolism and inflammation, upregulated in diabetic nephropathy, and pancreas, esophageal, and endometrial carcinomas; mRNA is decreased in obstructive pulmonary disease

Gene symbol

NFE2L2

Synonyms

(NRF2); (HEBP1); Nrf-2; IMDDHH; NFE2L2; NF-E2-related factor 2; nuclear factor, erythroid 2-like 2; nuclear factor, erythroid 2 like 2; NFE2 like bZIP transcription factor 2; nuclear factor (erythroid-derived 2)-like 2; nuclear factor, erythroid derived 2, like 2

Gene Ontology [what is this?](#)

Molecular function

ligand-dependent nuclear receptor binding [E], protein heterodimerization activity [E], sequence-specific DNA binding [E]... [details](#)

Biological process

apoptotic process [E], cell growth [E], cellular response to gamma radiation [E], mitotic G1 phase [E], regulation of apoptotic process [E]... [details](#)

Cellular component

cytoplasm [E], cytosol [Y], nucleoplasm [Y], nucleus [E], plasma membrane [Y] [details](#)

Orthologs & Molecular Hierarchy [what is this?](#)

Hierarchy of orthologous relationships for this locus

[+](#) View orthologous relationships

Biomarker Associations [what is this?](#)

Diseases associated with NFE2L2 (43 entries)

Show **5** ▾ entries

Search:

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Locus Report - Human

NFE2L2 (NF-E2L2)

logout

help

Table of Contents

Carcinoma, Hepatocellular	38 associations	6 associations	32 associations			4 associations		2 associations
Colorectal Neoplasms	35 associations	1 associations	34 associations			1 associations	11 associations	
Carcinoma, Non-Small-Cell Lung	34 associations	9 associations	25 associations			7 associations	7 associations	4 associations
Colonic Neoplasms	32 associations	10 associations	22 associations			9 associations	3 associations	2 associations

Showing 1 to 5 of 43 entries

First

Previous

1

2

3

4

5

Next

Last

GENE

Mutations

Inherited NFE2L2 mutations

The [Human Gene Mutation Database \(HGMD®\) report](#) provides information on the following inherited NFE2L2 mutations (subscription required):

Mutation Type	Count	Mutation Type	Count
Missense/nonsense	8	Small indels	0
Splicing	0	Gross deletions	0
Regulatory	2	Gross insertions	0
Small deletions	0	Complex rearrangements	0
Small insertions	0	Repeat variations	0

Mutant Phenotype [what is this?](#)

Mutant phenotype of closely related homolog(s)

Mouse **Nfe2l2** (68.8% identity to Human NFE2L2 [0.0])

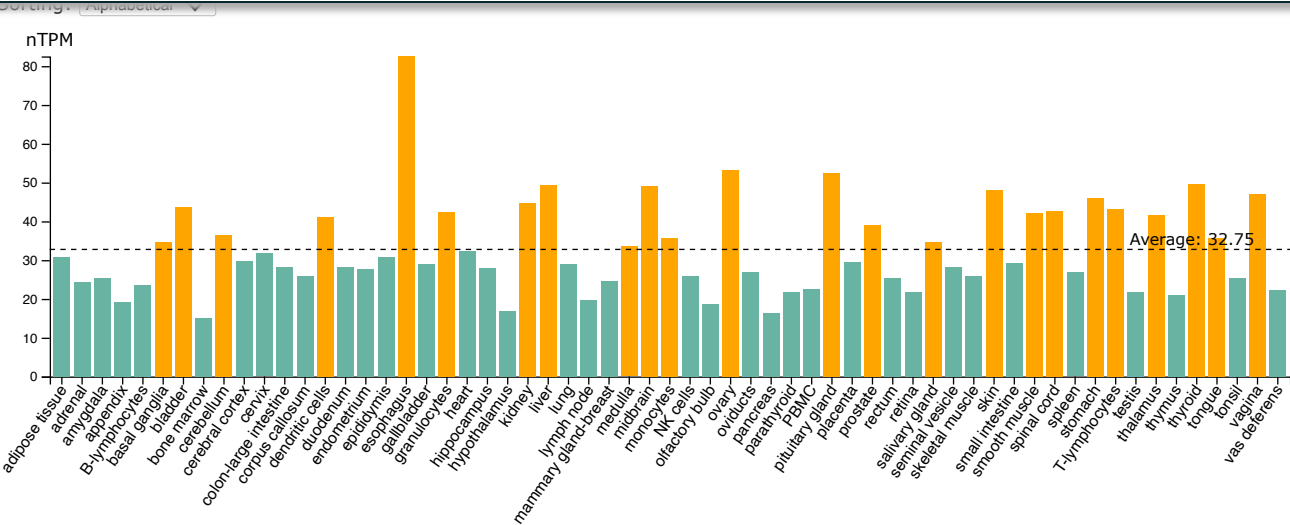
Viability effects : inviable; viable [details](#)

Anatomical effects : body; bronchi; endoderm/endoderm-derived tissues; epithelium/epithelial cells; fibroblasts; hematopoietic cells; hepatocytes; intestine; liver; lung alveoli; lung ... [details](#)

Physiological effects : cell death/apoptosis; drug response; fertile; immunity and inflammation; metabolism; regulated expression; response to injury; transcription; transport; wound healing [details](#)

Expression [what is this?](#)

Tissue expression



+ View organ or tissue, cell type, and tumor type entries in detail

Regulation of NFE2L2 expression

Proteins, complexes, or pathways that influence NFE2L2 expression (2 entries)

Show 5 entries Search:

Regulator details	Effect
ERR2	Downregulated by
HNF-4alpha	Upregulated by

Showing 1 to 2 of 2 entries

First Previous 1 Next Last

Transcriptional Regulation [what is this?](#)

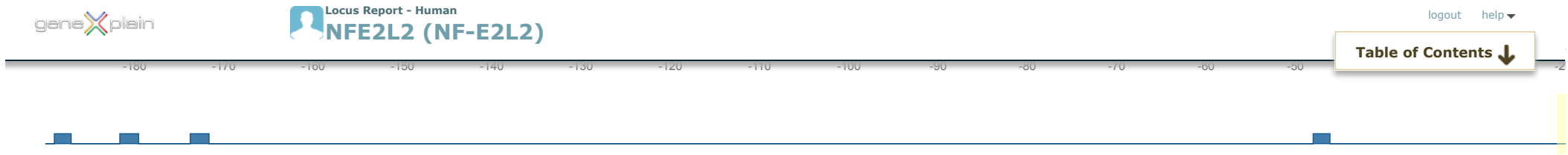
Regulation of NFE2L2 gene expression

Analyze NFE2L2 with MATCH Suite →

Predicted promoter sequences : Match →

Best supported : PM000920219

All promoters for the gene : PM000920219



Viewing nucleotides -190 to 0

* Note: Only binding sites whose location is relative to the TSS are graphically displayed. Binding sites with an asterisk (*) are not included in the graphical display.

Transcription factor binding sites within the NFE2L2 gene (4 entries)

Show 5 entries

Search:

Identifier	Relative Location	Genomic Location	Binding Factor(s)	DNA Binding Reaction	Effect
HS\$NFE2L2_01	-3394 to -3360		Runx1(h)	Runx1(h) --> NFE2L2(h)	DNA binding
HS\$NFE2L2_03	-3102 to -3068		Runx1(h)	Runx1(h) --> NFE2L2(h)	DNA binding
HS\$NFE2L2_10	around -690	Chr2 177265347 177265371 -	RBP-Jkappa(h)	RBP-Jkappa(h) --> NFE2L2(h)	DNA binding
HS\$NFE2L2_02	-3253 to -3216		Runx1(h)	Runx1(h) --> NFE2L2(h)	DNA binding

Showing 1 to 4 of 4 entries

FirstPrevious1NextLast

In vivo fragments within the promoter(s) of the NFE2L2 gene that are bound by transcription factors (3727 entries)

Show 5 entries

Search:

Promoter	Transcription Factor	Genomic Location	Cell Source	Matrix	Relative Location	CSS	MSS	Sequence	Reference
PM000920219	hHR21(h)	2:177273459..177273854	liver	V\$RAD21_01	-10114	0.833	0.689	TAACCCTCTGCTCTTGATC	ENCODE Data 22955616
PM000920219	PRDM4(h)	2:177273734..177274113	HEK293	V\$SC1_01	-10099	0.647	0.645	TTGATTAAGGCT	ENCODE Data 22955616
PM000920219	HOMEZ(h)	2:177273684..177274087	HepG2	V\$HOMEZ_03	-10078	0.804	0.754	TGTATTTGTTTT	ENCODE Data 22955616
PM000920219	HOMEZ(h)	2:177273442..177273845	HepG2	V\$HOMEZ_03	-10078	0.804	0.754	TGTATTTGTTTT	ENCODE Data 22955616
PM000920219	STAT3(h)	2:177273541..177273820	MCF10A-Er-Src + 4-hydroxytamoxifen (12h)	V\$STAT3_01	-10067	1.000	0.714	TAAGATTCCATGTATTGTT	ENCODE Data 22955616

Showing 1 to 5 of 3,727 entries

FirstPrevious12345NextLast

Predicted enhancers / silencers for NFE2L2 regulation (36 entries)

Show 5 entries

Search:

Accession	Effect	Chromosomal location	Length (bp)	Identification method	Active in tissue (cell type or line)	Reference
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NFE2L2 (NF-E2L2)

logout

help

Table of Contents

EN000032706	activation	chr2:177165435..177165792	358	promoter chromatin interaction study, pair-wise expression correlation with RefSeq promoter		FANTOM5 HACER
EN000032707	activation	chr2:177166056..177166562	507	chromatin interaction study, pair-wise expression correlation with RefSeq promoter	blood (monocytes), blood (mast cells), blood (T cells), bone marrow (mesenchymal cell)	FANTOM5 HACER
EN000032708	activation	chr2:177171544..177171825	282	chromatin interaction study, pair-wise expression correlation with RefSeq promoter	bladder (urothelial cell), gingiva (gingival epithelial cell), skin (hair follicle cell)	FANTOM5 HACER
EN000032711	activation	chr2:177239916..177240441	526	pair-wise expression correlation with RefSeq promoter, pair-wise expression correlation with robust FANTOM5 promoter	blood (B lymphocytes), blood (natural killer cells), blood (monocytes), blood (dendritic cells), blood (mast cells), blood (T cells), blood, blood vessels (blood vessel endothelial cell), bone marrow (mesenchymal cell), brain, cartilage (chondrocytes), colon/large intestine (large intestine), eye (iris pigment epithelial cell), fat (preadipocyte), fibroblasts (pulmonary artery fibroblasts), gingiva (gingival fibroblast), heart, internal male genitalia, lung (respiratory epithelial cell), lung, lymph node (endothelial cell of lymphatic vessel), lymph node, macrophages (macrophages), mammary gland/breast (mammary epithelial cell), muscle (smooth muscle), muscle (skeletal muscle), nervous tissue (astrocytes), neurons (neuronal stem cell), pancreas (acinar cell), placenta (placental epithelial cell), prostate (epithelial cell of prostate), prostate, salivary gland, skin (skin fibroblasts), small intestine (intestinal epithelial cells), spleen, stroma (stromal cells), teeth (epithelial cell of Malassez), thymus, umbilical cord, urinary system (sensory epithelial cell), uterus	FANTOM5

Showing 1 to 5 of 36 entries

First

Previous

1

2

3

4

5

Next

Last

Translational Regulation [what is this?](#)

Regulation of NFE2L2 mRNA expression

miRNA binding sites within NFE2L2 mRNA (21 entries)

Show

5

 entries

Search:

Identifier	Region	Location	Location Reference Point	Binding Factor(s)
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NFE2L2 (NF-E2L2)

logout

help

Table of Contents

HS\$NFE2L2_06	3' UTR	79 to 92	stop codon (end of coding sequence (CDS))	hsa-miR-142-5p(h)
HS\$NFE2L2_07	3' UTR	83 to 107	stop codon (end of coding sequence (CDS))	hsa-miR-153-3p(h)
HS\$NFE2L2_08	3' UTR	259 to 277	stop codon (end of coding sequence (CDS))	hsa-miR-144-3p(h)

Showing 1 to 5 of 21 entries

First

Previous

1

2

3

4

5

Next

Last

RNA Features [what is this?](#)

Overview of RNA sequence

Nucleotide Sequence : AAGCCCA...ATTAAAA (1..2746; 2746 nt) [details](#)

Sequence source : REFSEQ#NM_001145412

FASTA

PROTEIN

Drug Interactions [what is this?](#)

Drug(s) targeting NFE2L2 (39 entries)

Show 5 entries

Search:

Drug(s)	Status	Interaction Data Source	Reference(s)
(1S,6BR,9AS,11R,11BR)-9A,11B-DIMETHYL-1-[(METHYLOXY)METHYL]-3,6,9-TRIOXO-1,6,6B,7,8,9,9A,10,11,11B-DECAHYDRO-3H-FURO[4,3,2-DE]INDENO[4,5-H][2]BENZOPYRAN-11-YL ACETATE	small molecule,experimental	DGIdb	12391262 29156001
AGI-1067	small molecule,investigational	DrugBank	25619973
antroquinonol	small molecule, investigational	DrugBank	21540101
arundine	small molecule, investigational	DrugBank	31861353
Bromocriptine	small molecule,approved,investigational	DGIdb	18455424 29156001

Showing 1 to 5 of 39 entries

First

Previous

1

2

3

4

5

Next

Last

Pathways & Interactions [what is this?](#)

Show 5 entries

Search:

Name	View Supporting Reactions	View Graphic Representation	Load in PathFinder
beta-catenin network	View Supporting Reactions	View Graphic Representation	 Load in PathFinder →
Nrf2 pathway	View Supporting Reactions		 Load in PathFinder →

Showing 1 to 2 of 2 entries

First Previous 1 Next Last

Subcomponents assembled from experiments involving orthologous proteins (5 entries)

Show 5 entries

Search:

Name	View Supporting Reactions	View Graphic Representation	Load in PathFinder
Cul3 ---/ Nrf2	View Supporting Reactions		 Load in PathFinder →
E-cadherin ---/ HMOX1, NQO1	View Supporting Reactions		 Load in PathFinder →
ERK1 ---> NQO1	View Supporting Reactions		 Load in PathFinder →
Nrf2	View Supporting Reactions		 Load in PathFinder →
Nrf2 ---> HMOX1	View Supporting Reactions		 Load in PathFinder →

Showing 1 to 5 of 5 entries

First Previous 1 Next Last

Pathways from Reactome (11 entries)Provided by the [Reactome](#) database, release 78 ([ReactomePathways.gmt ↗](#)).

Show 5 entries

Search:

Name	Reactome pathway report link	Reactome pathway browser link
Cellular response to chemical stress	R-HSA-9711123 ↗	Open in Reactome Browser ↗
Cellular responses to stimuli	R-HSA-8953897 ↗	Open in Reactome Browser ↗
Cellular responses to stress	R-HSA-2262752 ↗	Open in Reactome Browser ↗
Cytoprotection by HMOX1	R-HSA-9707564 ↗	Open in Reactome Browser ↗
Disease	R-HSA-1643685 ↗	Open in Reactome Browser ↗

Showing 1 to 5 of 11 entries

First Previous 1 2 3 Next Last

Pathways from WikiPathways (23 entries)Provided by the [WikiPathways](#) database.

Show 5 entries

Search:

Name	Display below	WikiPathways external link
Antiviral and anti-inflammatory effects of Nrf2 on SARS-CoV-2 pathway	View ↗	WikiPathways ↗
Aryl hydrocarbon receptor pathway	View ↗	WikiPathways ↗

WikiPathways ↗

First	Previous	1	2	3	4	5	Next	Last
-------	----------	---	---	---	---	---	------	------



- + Proteins bound by NFE2L2 (53 partners)
- + Protein-protein associations (3 partners)

- + Proteins or complexes that inhibit NFE2L2 (1 partner)
- + Proteins or complexes that phosphorylate NFE2L2 (8 partners)
- + Proteins or complexes that affect NFE2L2 in other ways (63 partners)

Show 5 entries

Search:

Gene details	Effect
AKR7A3	Upregulated by
CAMKMT	Upregulated by
CBR3	Upregulated by
GCLC	Upregulated by
GCLM	Upregulated by

Showing 1 to 5 of 12 entries

FirstPrevious123NextLast

Transcription Factor Activity

Regulation of gene expression by NFE2L2

Transcription factor classification :

NF-E2L2 (NRF2); 1.1.1.2.3
Basic leucine zipper factors (bZIP); 1.1 (A DNA-binding basic region is followed by a leucine zipper. The leucine zipper consists of repeated leucine residues at every seventh position and mediates protein dimerization as a prerequisite for DNA-binding. The leucines are directed towards one side of an alpha-helix. The leucine side chains of two polypeptides are thought to interdigitate upon dimerization (knobs-into-holes model). The leucine zipper dictates dimerization specificity. Upon DNA-binding of the dimer, the basic regions adopt alpha-helical conformation as well. Possibly, a sharp angulation point separates two alpha-helices of the subregions A and B leading to the scissors grip model for the bZIP-DNA complex. The DNA is contacted through the major groove over a whole turn. (PROSITE motif for Fos-Jun bZIP region only!))

Genes bound by NFE2L2 (93 entries)

Show 5 entries

Search:

Gene	Location within Gene	Binding Site Identifier	DNA Binding Reaction	Effect	Quality Score
ABCB11(h)	-195 to -175	HS\$ABCB11_03	NF-E2L2(h) --> ABCB11(h)	DNA binding	4
ABCC1(h)	-502 to -486	HS\$ABCC1_16	NF-E2L2(h) --> ABCC1(h)	transactivation	3
ABCC1(h)	-69 to -53	HS\$ABCC1_17	NF-E2L2(h) --> ABCC1(h)	transactivation	3
Abcc2(m)	-101 to -79	MOUSE\$ABCC2_01	NF-E2L2(h) --> Abcc2(m)	DNA binding	3
Abcc2(m)	-1397 to -1375	MOUSE\$ABCC2_02	NF-E2L2(h) --> Abcc2(m)	DNA binding	5

Showing 1 to 5 of 93 entries

FirstPrevious12345NextLast

Artificial sites bound by NFE2L2 (2 entries)

Show 5 entries

Search:

Description	Binding Site Identifier	Quality Score
artificial sequence	AS\$NFE2_01	5
Artificial sequence	AS\$NRF2_08	4

Showing 1 to 2 of 2 entries

FirstPrevious1NextLast

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Locus Report - Human

NFE2L2 (NF-E2L2)

logout

help

Table of Contents

View Report

Human: 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22

16890

IMR-90

ENCODE Data

22955616

View Report

Human: 1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22

6742

HeLa

ENCODE Data

22955616

View Report

Human Genome

5647

A375 + A771726

GEO Data

29126285

23193258

View Report

Human Genome

11031

A375 + DMSO

GEO Data

29126285

23193258

Showing 1 to 4 of 4 entries

First

Previous

1

Next

Last

Positional weight matrices for NFE2L2 (8 entries)

Show 5 entries

Search:

Sequence logo	PWM ID	Matrix type	Matrix category
	V\$NRF2_Q4	factor-specific	matrix compiled from individual genomic sites
	V\$MAF_Q6_01	family	matrix compiled from individual genomic sites
	V\$NFE2L2_01	factor-specific	compiled matrix imported from public database
	V\$NRF2_Q6	factor-specific	matrix compiled from individual genomic sites
	V\$NRF2_Q4_01	factor-specific	matrix compiled from individual genomic sites

Showing 1 to 5 of 8 entries

First

Previous

1

2

Next

Last

Transcription factors which interact with NFE2L2

Show 5 entries

Search:

Species	Factor
Human	beta-catenin, BRD4, c-Jun, JunD, KDM1A, MafG, MafG, MafK, MafK, NF-E2 p45, RXRalpha, TIF1-alpha
Mouse	PPARGgamma1

Showing 1 to 2 of 2 entries

First

Previous

1

Next

Last

Protein Features [what is this?](#)

Overview of protein sequence and structure

[+ View related proteins](#)**Post-translational modifications of NFE2L2 protein**0 

 Acetylated {ace}	 Phosphorylated {p}	 Other
 Sumoylated {sumo}	 Ubiquitinated {ub}	Abbreviations key

[+ Acetylated forms \(2 entries\)](#)[+ Phosphorylated forms \(1 entry\)](#)[+ Sumoylated forms \(1 entry\)](#)[+ Ubiquitinated forms \(1 entry\)](#)**Known types of modification** : phosphorylation; serine phosphorylation; threonine phosphorylation; ubiquitination [details](#)**View complexes containing NFE2L2 protein**[+ View complexes \(57 entry\)](#)**Annotations** [what is this?](#)[Display all annotations](#)**Description**

- Nuclear factor erythroid-derived 2-like 2, a transcription factor that regulates ROS metabolism and inflammation, upregulated in diabetic nephropathy, and pancreas, esophageal, and endometrial carcinomas; mRNA is decreased in obstructive pulmonary disease [11429414 ↗](#) [18074351 ↗](#) [19417020 ↗](#) [10559251 ↗](#) [17384144 ↗](#) [18566336 ↗](#) [11035812 ↗](#)

Function

- Activated by DETA-NO treatment in SH-Sy-5y cells [14985350 ↗](#)
- Activated by LPS in monocytic and THP-1 cells [16177082 ↗](#)
- NF-E2L2 silencing leads to decrease in GSH activity and increase in ROS and TBARS levels in E47 cells treated with arachidonic acid [16551616 ↗](#)
- Protects from arachidonic acid and BSO induced CYP2E1 mediated toxicity in E47 cells [16551616 ↗](#)

Related to

- CNC (D. melanogaster)

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Locus Report - Human

NFE2L2 (NF-E2L2)

logout

help

The N-terminal part of the molecule does not exhibit significant homology with other members of the NF-E2 family (2587222).

Table of Contents

Expression

- K562 cells treated with t-BHQ (tert-butylhydroquinone) 15640523
- KCL22 and KCL22/SR 15050748
- TBHQ-treated HepG2/GFP-B 11708801

Disease related

- Decreased mRNA expression correlates with chronic obstructive pulmonary disease 18566336
- Decreased mRNA expression may correlate with Parkinson disease 21747966
- Gene mutation is associated with advanced esophageal squamous cancer 21969819
- Gene polymorphism correlates with colorectal adenoma 18074351
- Increased protein expression correlates with endometrial serous carcinoma 20530669

more

Identifiers [what is this?](#)

Accessions mapped to this record

BIOBASE gene accession : GN000003944, G004136, MO000031658

BIOBASE protein accession : PR000007881, MO000025668, MO000108716, MO000123529, MO000273683, MO000279044, MO000293187, MO000308238, MO000308245, MO000308552, MO000315794, MO000481153, MO000485021, T01443

Gene

Affymetrix	11739057_a_at, 11743380_s_at, 1567013_at, 16905475, 201146_at, 2588831, 2588833, 2588834, 2588835, 2588836, 2588837, 2588838, 2588839, 2588840, 2588841, 2588842, 2588843, 2588844, 2588863, 2588864, 2588865, 2588866, 2588867, 2588868, 2588890, 2588896, 2588906, 2588909, 2588910, 2588915, 2588916, 2588924, 8056977, 82873_at, 853_at, 91941_at, g5453775_3p_at, S74017_at, TC02005045.hg,
Agilent	A_19_P00315584
Ensembl	ENSG00000116044, ENST00000397062, ENST00000397063, ENST00000421929, ENST00000423513, ENST00000430047, ENST00000446151, ENST00000448782, ENST00000449627, ENST00000458603, ENST00000462023, ENST00000464747, ENST00000477534, ENST00000586532, ENST00000588123
EntrezGene	4780
Genbank	12698719, 15079436, 17975438, 20149575, 224028256, 224028258, 5453775, 62087151, 693841, AB208786, AC079305, AF323119, BC011558, NM_001145412, NM_001145413, NM_006164, S74017
HGMD	NFE2L2
HumanProteinAtlas	ENSG00000116044
Illumina	0001990333, 0004560465, ILMN_1696318
OMIM	600492

UniGene	Hs&744006
WikiPathways	WP2435 , WP2586 , WP2857 , WP2873 , WP2882 , WP2884 , WP3 , WP3611 , WP3612 , WP3613 , WP3624 , WP3670 , WP3953 , WP408 , WP4206 , WP4269 , WP4357 , WP4673 , WP4674 , WP4698 , WP4874 , WP4925 , WP5094 , WP5113

mRNA

RefSeq	NM_001313900 , NM_001313901 , NM_001313902 , NM_001313903 , NM_001313904
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Protein

Genbank	12698720 , 15079437 , 20149576 , 224028257 , 224028259 , 5453776 , 62087152 , 62822161 , 693842 , AAB32188.1 , AAH11558.1 , AAK01657.1 , AAY14710.1 , BAD92023.1 , NP_001138884.1 , NP_001138885.1 , NP_006155.1 , NP_006155.2
UniProt	Q16236

References (290 entries)

Show 5 entries

Search:

Sl.No	PMID	Citation
1	33961781	Dual Proteome-scale Networks Reveal Cell-specific Remodeling of the Human Interactome Cell 184 3022-3040 (2021) Show abstract
2	32296183	A reference map of the human binary protein interactome. Nature 580 402-408 (2020) Show abstract
3	32128917	Yu, YP, Cai, LC, Wang, XY, Cheng, SY, Zhang, DM, Jian, WG, Wang, TD, Yang, JK, Yang, KB, Zhang, C, BMP8A promotes survival and drug resistance via Nrf2/TRIM24 signaling pathway in clear cell renal cell carcinoma. Cancer Sci 111 (5) 1555-1566 (2020) Show abstract
4	31666108	Li, J, Wang, Q, Yang, Y, Lei, C, Yang, F, Liang, L, Chen, C, Xia, J, Wang, K, Tang, N, GSTZ1 deficiency promotes hepatocellular carcinoma proliferation via activation of the KEAP1/NRF2 pathway. J Exp Clin Cancer Res 38 (1) 438-438 (2019) Show abstract
5	30896860	Huang, H, Wu, Y, Fu, W, Wang, X, Zhou, L, Xu, X, Huang, F, Wu, Y, Downregulation of Keap1 contributes to poor prognosis and Axitinib resistance of renal cell carcinoma via upregulation of Nrf2 expression. Int J Mol Med 43 (5) 2044-2054 (2019) Show abstract

Showing 1 to 5 of 290 entries

First

Previous

1

2

3

4

5

Next

Last