Introduction

Description

Forkhead box C2, a transcriptional activator that regulates canonical Wnt receptor signaling, angiogenesis, lymph vessel development, mitochondrion morphogenesis, and adipocyte metabolism; gene mutation causes with lymphedema syndrome

Gene symbol

FOXC2

Synonyms

(LD); MFH1; FOXC2; MFH-1; FKHL14; forkhead box C2; Mesenchyme fork head 1; forkhead box C2 (MFH-1, mesenchyme forkhead 1)

Gene Ontology what is this?

Molecular function

core promoter binding [E], DNA binding [E], transcription factor activity, sequence-specific DNA binding [E] details

Biological process

blood vessel maturation [E], epithelial to mesenchymal transition [E], glucose homeostasis [P], mesoderm development [P], mRNA transcription [E]... details

Cellular component

nuclear body [Y], nucleoplasm [Y], nucleus [E] details

Orthologs & Molecular Hierarchy what is this?

Hierachy of orthologous relationships for this locus

+ View orthologous relationships

Biomarker Associations what is this?

Diseases associated with FOXC2 (15 entries)

Show 5 entries Search:

	Type of Association	Indication

Lung Neoplasms	15 associations	2 associations	8 associations	5 associations		4 associations	2 associations	
Spinal Cord Diseases	9 associations	9 associations				9 associations	3 associations	
Cholangiocarcinoma	8 associations	3 associations	5 associations			3 associations	4 associations	
Lymphedema	8 associations	6 associations	2 associations			6 associations		
Esophageal Squamous Cell Carcinoma	7 associations		7 associations				2 associations	

Showing 1 to 5 of 15 entries First Previous 1 2 3 Next Last

GENE

Mutations

Inherited FOXC2 mutations

The Human Gene Mutation Database (HGMD®) report ↗ provides information on the following inherited FOXC2 mutations (subscription required):

Mutation Type	Count	Mutation Type	Count
Missense/nonsense	36	Small indels	2
Splicing	0	Gross deletions	4
Regulatory	1	Gross insertions	2
Small deletions	29	Complex rearrangements	2
Small insertions	28	Repeat variations	0

Mutant Phenotype what is this?

Mutant phenotype of closely related homolog(s)

Mouse Foxc1 (78.2% identity to Human FOXC2 [7e-69])

Viability effects : inviable details

Anatomical effects : blood vessels; brain; cardiovascular system; cornea; endothelium/endothelial cells; epithelium/epithelial cells; eye; kidney; mesenchyme/mesenchymal cells; mesoderm/mesoderm-derived tissues; skeleton details

Physiological effects : regulated expression; signal transduction details

C. elegans lin-31 (61.7% identity to Human FOXC2 [7e-30])

Show 5 entries Search:

Cell fate/lineage defects	Recessive
Egg laying is defective	Recessive
Egg laying is defective	Null

Showing 1 to 5 of 10 entries First Previous 1 2 Next Last

S. cerevisiae FKH1 (45.0% identity to Human FOXC2 [2e-17])

Viability :

Null Viable; Overexpression or ectopic expression Lethal

Show 5 entries Search:

Phenotypic effect details	Mutation type
Altered sensitivity to divalent cations, heavy metals, or salt	Null
Cell cycle abnormal	Null
Killer toxin resistant	Null
Large cells	Null

Showing 1 to 4 of 4 entries First Previous 1 Next Last

Expression what is this?

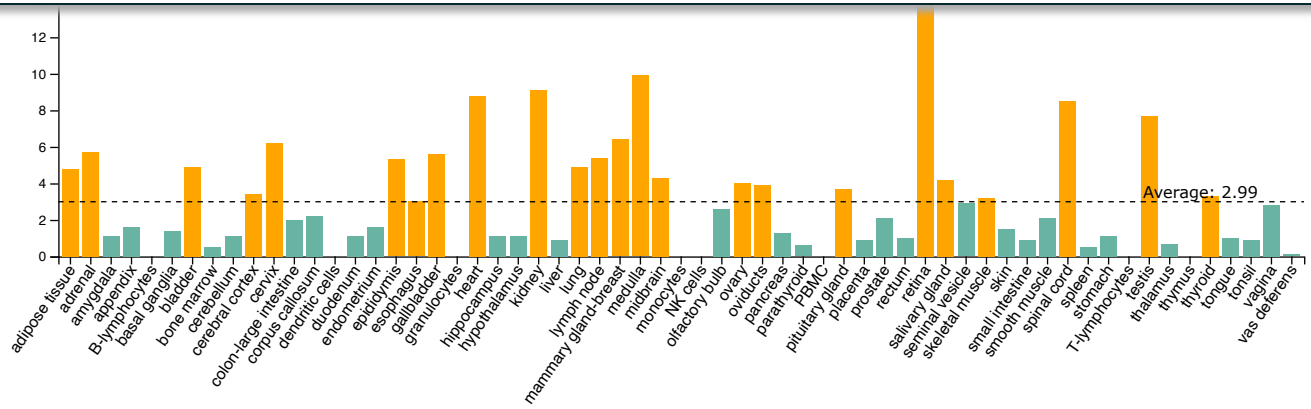
Tissue expression

Consensus normalized transcript expression levels provided by Human Protein Atlas (v20)

Relative tissue specificity: 0.12

Sorting: Alphabetical

Locus Report - Human
FOXC2 (FOXC2)



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

Regulation of FOXC2 expression

Proteins, complexes, or pathways that influence FOXC2 expression (1 entry)

Show 5 entries Search:

Regulator details	Effect
TNF-alpha	Upregulated by

Showing 1 to 1 of 1 entries First Previous 1 Next Last

Transcriptional Regulation what is this?

Regulation of FOXC2 gene expression

Analyze FOXC2 with MATCH Suite

Predicted promoter sequences : Match

Best supported : PM000915306

All promoters for the gene : PM000915306

Show 5 entries Search:

Identifier	Relative Location	Genomic Location	Binding Factor(s)	DNA Binding Reaction	Effect
HS$FOXC2_01	-1845 to -1838	Chr16 86565490 86565497 +	FOXF2(h)	FOXF2(h) --/ FOXC2(h)	transrepression

Showing 1 to 1 of 1 entries First Previous 1 Next Last

In vivo fragments within the promoter(s) of the FOXC2 gene that are bound by transcription factors (859 entries)

Show 5 entries Search:

Promoter	Transcription Factor	Genomic Location	Cell Source	Matrix	Relative Location	CSS	MSS	Sequence	Reference
PM000915306	POU2F1(h)	16:86556323..86556832	HeLa S3	V$POU2F1_Q4	-10561	0.894	0.921	AATGGTAAT	19171782
PM000915306	ASH-1(h)	16:86556727..86556934	NCI-H889	V$ASCL1_01	-9962	0.855	0.897	AAAGCAGGTGGTG	GEO Data 29126285 27452466 23193258
PM000915306	SIX2(h)	16:86556693..86556900	HEK	V$SIX2_03	-9917	0.694	0.756	TTTTCAAGTTAGAAGT	GEO Data 26884396 29126285 23193258
PM000915306	SIX2(h)	16:86556708..86556862	fetal kidney, 17 weeks	V$SIX2_03	-9917	0.694	0.756	TTTTCAAGTTAGAAGT	GEO Data 29126285 23193258
PM000915306	FOXA1(h)	16:86557748..86557913	VCaP + R1881	V$HNF3A_Q6	-9123	0.943	0.931	GTAAAGAA	GEO Data 25552417 29126285 23193258

Showing 1 to 5 of 859 entries First Previous 1 2 3 4 5 Next Last

Predicted enhancers / silencers for FOXC2 regulation (127 entries)

Show 5 entries Search:

Accession	Effect	Chromosomal location	Length (bp)	Identification method	Active in tissue (cell type or line)	Reference
EN000022667	activation	chr16:85962299..85962496	198	chromatin interaction study	brain	HACER
EN000022676	activation	chr16:86018219..86018863	645	chromatin interaction study	blood (B lymphocytes), blood (monocytes), blood (mast cells), brain, placenta (placental epithelial cell)	HACER

				promoter	fibroblast), heart (cardiac fibroblasts), kidney (kidney epithelial cell), lymph node (endothelial cell of lymphatic vessel), muscle (smooth muscle cell of prostate), muscle (enteric smooth muscle cell), muscle (vascular associated smooth muscle cell), skin (skin fibroblasts), stroma (stromal cells), teeth (fibroblast of periodontium)	
EN000022691	activation	chr16:86572337..86572438	102	pair-wise expression correlation with RefSeq promoter, pair-wise expression correlation with robust FANTOM5 promoter	blood vessels (pericyte cell), nervous tissue (astrocytes)	FANTOM5
EN000022692	activation	chr16:86586215..86586629	415	pair-wise expression correlation with RefSeq promoter, pair-wise expression correlation with robust FANTOM5 promoter	blood vessels (fibroblast of tunica adventitia of artery), bone marrow (mesenchymal cell), muscle (vascular associated smooth muscle cell)	FANTOM5

Showing 1 to 5 of 127 entries First Previous 1 2 3 4 5 Next Last

PROTEIN

Pathways & Interactions what is this?

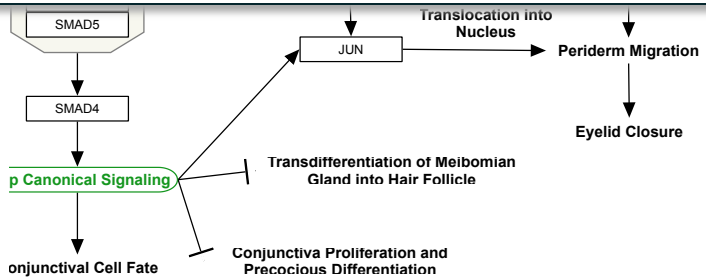
Pathways

Pathways from WikiPathways (8 entries)

Provided by the WikiPathways database.

Show 5 entries Search:

Name	Display below	WikiPathways external link
22q11.2 copy number variation syndrome	View	WikiPathways
Adipogenesis	View	WikiPathways
BMP signaling in eyelid development	View	WikiPathways
Epithelial to mesenchymal transition in colorectal cancer	View	WikiPathways
GDNF/RET signaling axis	View	WikiPathways



RESET

Protein-protein interactions

+ Proteins bound by FOXC2 (41 partners)

Events acting on FOXC2

+ Proteins or complexes that phosphorylate FOXC2 (4 partners)
+ Proteins or complexes that affect FOXC2 in other ways (2 partners)

Events triggered by FOXC2

+ Proteins or complexes affected by FOXC2 in other ways (19 partners)

Genes regulated (directly or indirectly) by FOXC2

Show 5 entries Search:

Gene details	Effect
ITGB3	Upregulated by

Regulation of gene expression by FOXC2

Transcription factor classification :

FOXC2 (Fkh-L14); 3.3.1.3.2
Fork head / winged helix factors; 3.3 (Identified by homology between HNF-3A and fkh. The domain comprises approx. 110 AA. Analysis of the crystal structure has revealed a compact structure of three alpha-helices, the third alpha-helix being exposed towards the major groove of the DNA. The domain also exerts minor groove contacts. Upon binding to DNA, it induces a bend of 13 degree.)

Genes bound by FOXC2 (6 entries)

Show 5 entries Search:

Gene	Location within Gene	Binding Site Identifier	DNA Binding Reaction	Effect	Quality Score
CTNND1(h)	267 to 288	HS$CTNND1_01	FOXC2(h) --/ CTNND1(h)	transrepression	5
etsrp(z)		BRARE$ETV2_01	FOXC2(h) --> etsrp(z)	DNA binding	4
MET(h)	-1636 to -1502	HS$MET_57	FOXC2(h) --> MET(h)	transactivation	3
MET(h)	-1502 to -1322	HS$MET_58	FOXC2(h) --> MET(h)	transactivation	3
MET(h)	-693 to -451	HS$MET_59	FOXC2(h) --> MET(h)	transactivation	3

Showing 1 to 5 of 6 entries First Previous 1 2 Next Last

Artificial sites bound by FOXC2 (1 entry)

Show 5 entries Search:

Description	Binding Site Identifier	Quality Score
artificial sequence	AS$FREAC3_01	5

Showing 1 to 1 of 1 entries First Previous 1 Next Last

Positional weight matrices for FOXC2 (8 entries)

Show 5 entries Search:

Sequence logo	PWM ID	Matrix type	Matrix category
	V$FOXC2_01	factor-specific, recommended by prediction	HT-SELEX
	V$FOXC2_02	factor-specific	HT-SELEX
	V$FOXC2_03	factor-specific	HT-SELEX
	V$FKHL14_Q2	factor-specific	matrix compiled from individual genomic sites
	V$FOXC2_04	factor-specific, methylated	Methyl-HT-SELEX

Showing 1 to 5 of 8 entries First Previous 1 2 Next Last

Transcription factors which interact with FOXC2

	ZNF536

Showing 1 to 1 of 1 entries First Previous 1 Next Last

Protein Features what is this?

Overview of protein sequence and structure

Chromosome : 16q24.1

Isoforms : FOXC2

[+] View associated sequences and their domains

[+] View related proteins

Post-translational modifications of FOXC2 protein

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

[+] Phosphorylated forms (2 entries)

[+] Sumoylated forms (1 entry)

View complexes containing FOXC2 protein

[+] View complexes (42 entry)

Annotations what is this?

Display all annotations

Description

- Forkhead box C2, a transcriptional activator that regulates canonical Wnt receptor signaling, angiogenesis, lymph vessel development, mitochondrion morphogenesis, and adipocyte metabolism; gene mutation causes with lymphedema syndrome 11078474 12453913 17372167 11551504 15744037 18621714

Domains

- Gene is located on chromosome 16q22-24 8674414

- May protect against type 2 diabetes 11551504
- Mutations in the corresponding gene are responsible for the hereditary lymphedema distichiasis syndrome 11078474
- Protein is upregulated in melanoma and breast and colon adenocarcinoma 20060810

more

Identifiers what is this?

Accessions mapped to this record

BIOBASE gene accession : GN000008337, G006084

BIOBASE protein accession : PR000016213, MO000026498, MO000329246, MO000481467, MO000482643, MO000484217, T02518

Gene

Affymetrix	11715312_at, 16821660, 214520_at, 239058_at, 31698_at, 3672647, 3672648, 3672649, 3672650, 3672651, 3672652, 3672653, 3672654, 3672655, 3672656, 3672657, 3672658, 7997733, Hs.239571.0.S1_3p_at, Hs.252844.0.A1_3p_at, TC16000670.hg, Y08223_at,
Agilent	A_14_P125820
Ensembl	ENSG00000176692, ENST00000649859
EntrezGene	2303
Genbank	109731036, 109731689, 1869804, 4885236, BC113437, BC113439, NM_005251, Y08223
HGMD	FOXC2
HumanProteinAtlas	ENSG00000176692
Illumina	0001990358, ILMN_1705201
OMIM	602402
PDB	1D5V, 6AKO, 6AKP, 6O3T
RefSeq	NM_005251.3, NP_005242.1
UniGene	Hs&436448
WikiPathways	WP1591, WP236, WP2857, WP3927, WP4239, WP4657, WP4823, WP4830

Protein

Genbank	109731037, 109731690, 1869805, 4885237, AAI13438.1, AAI13440.1, CAA69400.1, NP_005242.1
UniProt	Q99958

References (48 entries)

Show 5 entries Search:

2	32296183	A reference map of the human binary protein interactome. Nature 580 402-408 (2020) Show abstract
3	28818916	A pathology atlas of the human cancer transcriptome. Science 357 (2017) Show abstract
4	28514442	Architecture of the human interactome defines protein communities and disease networks. Nature 545 505-509 (2017) Show abstract
5	26496610	A human interactome in three quantitative dimensions organized by stoichiometries and abundances. Cell 163 712-723 (2015) Show abstract

Showing 1 to 5 of 48 entries

First Previous 1 2 3 4 5 Next Last