

Introduction

Description

Runt-related transcription factor 3, plays a role in TGF-beta receptor signaling, epithelial cell proliferation, T cell lineage commitment, and inflammatory response; promoter hypermethylation correlates with Barrett esophagus and various other cancers

Gene symbol

RUNX3

Synonyms

AML2; RUNX3; CBFA3; PEBP2aC; PEBP2A3; FLJ34510; MGC16070; RP3-398I9.1; CBF-alpha 3; PEBP2alphaC1; Acute myeloid leukemia 2 protein; RUNX family transcription factor 3; runt-related transcription factor 3; runt related transcription factor 3; Core-binding factor, alpha 3 subunit; Polyomavirus enhancer binding protein 2 alpha C subunit

Gene Ontology [what is this?](#)

Molecular function

ATP binding [P], DNA binding, protein kinase binding [E], sequence-specific DNA binding [E], SMAD binding [E], transcription factor binding [E]... [details](#)

Biological process

cellular response to starvation [E], hemopoiesis [P], mesoderm development [P], negative regulation of cell growth [E], response to acid chemical [E]... [details](#)

Cellular component

Hierarchy of orthologous relationships for this locus

[+ View orthologous relationships](#)

Biomarker Associations [what is this?](#)

Diseases associated with RUNX3 (69 entries)

Show 5 entries		Type of Association				Indication		
Disease details-all	Significance	Causal 28 associations	Correlative 199 associations	Preventative 6 associations	Negative	Disease Mechanism 30 associations	Prognosis 52 associations	Therapeutic Target 10 associations
Stomach Neoplasms	25 associations	3 associations	20 associations	2 associations		4 associations	7 associations	2 associations
Carcinoma, Hepatocellular	17 associations	5 associations	12 associations			5 associations	1 associations	
Urinary Bladder Neoplasms	15 associations		15 associations				8 associations	
Pancreatic Neoplasms	13 associations		13 associations				3 associations	
Esophageal Neoplasms	9 associations		9 associations				4 associations	

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Inherited RUNX3 mutations

The [Human Gene Mutation Database \(HGMD®\) report](#) provides information on the following inherited RUNX3 mutations (subscription required):

Mutation Type	Count	Mutation Type	Count
Missense/nonsense	1	Small indels	0
Splicing	0	Gross deletions	0
Regulatory	4	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 **Runx3** (86.7% identity to Human RUNX3 [0.0])

Anatomical effects : dorsal root ganglion; neurons; thymocytes; thymus [details](#)

Physiological effects : motor function; regulated expression [details](#)

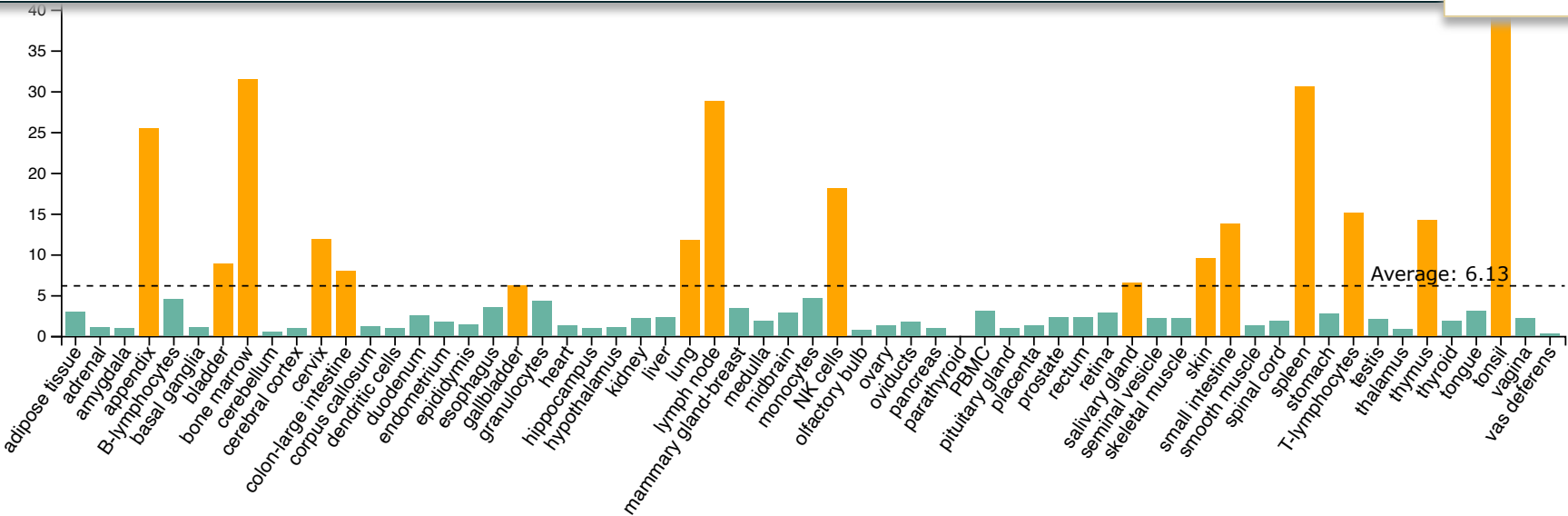
Expression [what is this?](#)

Tissue expression

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

Relative tissue specificity: 0.18

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

Regulation of RUNX3 expression

Proteins, complexes, or pathways that influence RUNX3 expression (2 entries)

Show 5 entries Search:

Regulator details	Effect
GATA-1	Upregulated by
RAR-alpha	Upregulated by

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Transcriptional Regulation [what is this?](#)

Regulation of RUNX3 gene expression

Predicted promoter sequences : Match →Best supported : [PM000581634](#)All promoters for the gene : [PM000993606](#), [PM000581634](#)**In vivo fragments within the promoter(s) of the RUNX3 gene that are bound by transcription factors (1730 entries)**Show **5** ▾ entriesSearch:

Promoter	Transcription Factor	Genomic Location	Cell Source	Matrix	Relative Location	CSS	MSS	Sequence	Reference
PM000993606	c-Maf(h)	1:24939472..24939680	CD4+ T cells + TH1	V\$CMAF_Q5	-10176	0.883	0.827	ATTCCCCAGCA	GEO Data ↗ 29126285 ↗ 23193258 ↗
PM000993606	NGFI-B(h)	1:24939304..24939584	K562	V\$NUR77_Q5_02	-10132	0.723	0.795	GCATGGACTTT	ENCODE Data ↗ 22955616 ↗
PM000993606	FOXA1(h)	1:24939465..24939601	MCF-7 + E2	V\$HNF3A_Q6	-9984	1.000	0.980	GTAAACAG	GEO Data ↗ 29126285 ↗ 25752574 ↗ 23193258 ↗
PM000993606	FOXA1(h)	1:24939464..24939609	MCF-7 + E2 + TNF	V\$HNF3A_Q6	-9984	1.000	0.980	GTAAACAG	GEO Data ↗ 29126285 ↗ 25752574 ↗ 23193258 ↗
PM000993606	FOXA2(h)	1:24939471..24939569	Caco-2	V\$HNF3B_Q6	-9983	1.000	0.973	TGTAAACAG	GEO Data ↗ 25921584 ↗ 29126285 ↗ 2319325 ↗

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Accession	Effect	location	(bp)	Identification method	Active in tissue (cell type or line)	Reference
EN000000791	activation	chr1:24482076..24482156	81	pair-wise expression correlation with RefSeq promoter, pair-wise expression correlation with robust FANTOM5 promoter	blood (T cells), cartilage (chondrocytes)	FANTOM5 ↗
EN000000794	activation	chr1:24506635..24506974	340	pair-wise expression correlation with RefSeq promoter, pair-wise expression correlation with robust FANTOM5 promoter	blood (natural killer cells), blood (T cells), blood, cartilage (chondrocytes), lung, neurons (neuronal stem cell)	FANTOM5 ↗
EN000000795	activation	chr1:24530069..24530294	226	pair-wise expression correlation with robust FANTOM5 promoter		FANTOM5 ↗
EN000000797	activation	chr1:24642128..24642519	392	pair-wise expression correlation with RefSeq promoter	fat (preadipocyte)	FANTOM5 ↗
EN000000802	activation	chr1:24724588..24724717	130	chromatin interaction study	blood vessels (blood vessel endothelial cell), bone marrow (mesenchymal cell), brain, epithelium/epithelial cells (ciliated epithelial cell), urinary system (sensory epithelial cell)	HACER ↗

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Translational Regulation [what is this?](#)

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Identifier	Region	Location	Location Reference Point	Binding Factor(s)
HS\$RUNX3_01	3' UTR	736 to 757	stop codon (end of coding sequence (CDS))	hsa-miR-106b-5p(h)
HS\$RUNX3_02	3' UTR	around 2473	stop codon (end of coding sequence (CDS))	hsa-miR-130a-3p(h)
HS\$RUNX3_03	3' UTR	around 2481	stop codon (end of coding sequence (CDS))	hsa-miR-495-3p(h)
HS\$RUNX3_04	3' UTR	2061 to 2083	stop codon (end of coding sequence (CDS))	hsa-miR-106a-5p(h)
HS\$RUNX3_05	3' UTR	2460 to 2481	stop codon (end of coding sequence (CDS))	hsa-miR-301a-3p(h)

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RNA Features [what is this?](#)

Overview of RNA sequence

Nucleotide Sequence : CCCGCCA...GGAAGGA (1..4270; 4270 nt) [details](#)**Sequence source** : REFSEQ#NM_004350

FASTA ↓

PROTEIN

Drug Interactions [what is this?](#)

Drug(s) targeting RUNX3 (2 entries)

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Leucovorin	small molecule, approved	DGIdb	29156001
			17372756
			29156001

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

Pathways

Pathways from Reactome (18 entries)

Provided by the [Reactome](#) database, release 78 ([ReactomePathways.gmt](#)).

Show entries Search:

Name	Reactome pathway report link	Reactome pathway browser link
Binding of TCF/LEF:CTNNB1 to target gene promoters	R-HSA-4411364	Open in Reactome Browser
Formation of the beta-catenin:TCF transactivating complex	R-HSA-201722	Open in Reactome Browser
Gene expression (Transcription)	R-HSA-74160	Open in Reactome Browser
Generic Transcription Pathway	R-HSA-212436	Open in Reactome Browser
Regulation of RUNX3 expression and activity	R-HSA-8941858	Open in Reactome Browser

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Pathways from WikiPathways (7 entries)

Provided by the [WikiPathways](#) database.

Show entries Search:

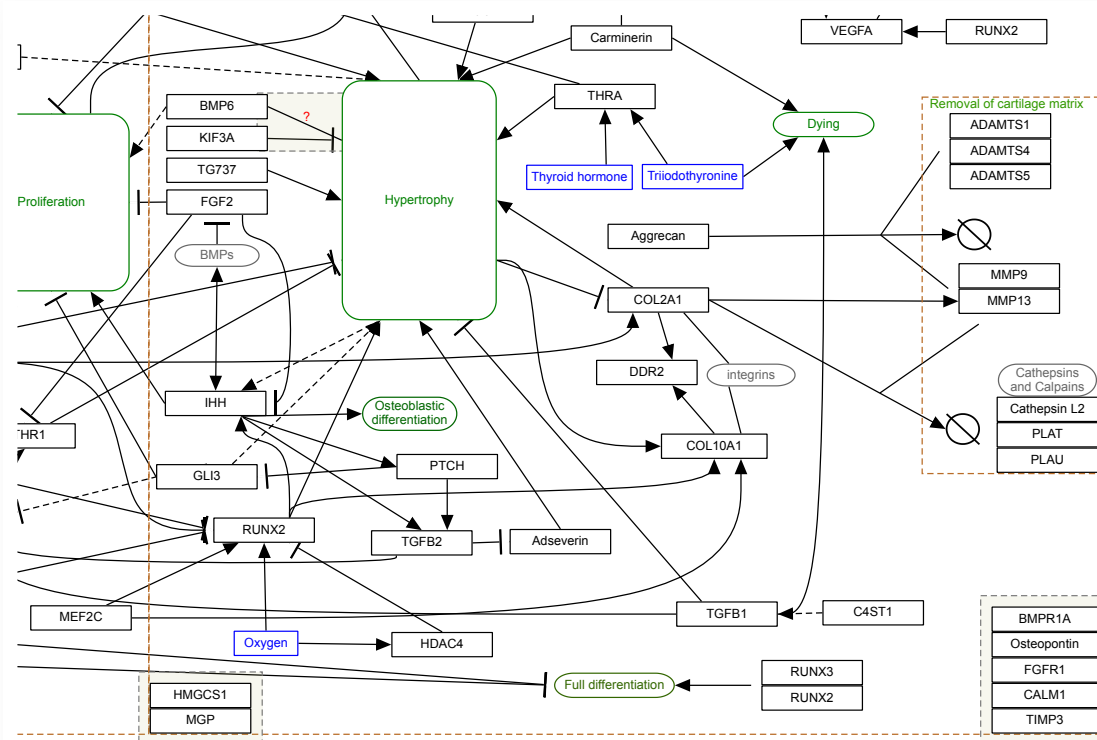
Name	Display below	WikiPathways external link
Endochondral ossification	View	WikiPathways

WikiPathways ↗

View

WikiPathways ↗

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[+ Protein-protein associations \(3 partners\)](#)

Events acting on RUNX3

[+ Proteins or complexes that affect RUNX3 in other ways \(41 partners\)](#)

Events triggered by RUNX3

[+ Proteins or complexes affected by RUNX3 in other ways \(49 partners\)](#)

Genes regulated (directly or indirectly) by RUNX3

Show 5 ▾ entries	Search:
Gene details	Effect
ITGAL	Upregulated by
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Transcription Factor Activity [what is this?](#)

Regulation of gene expression by RUNX3

Transcription factor classification :

Runx3 (PEBP2alphaC, CBF-alpha3, AML-2); [6.4.1.0.3](#)

Runt domain factors; [6.4](#) (The members of this transcription factor class have been identified on the basis of their homology to a defined region within the Drosophila protein Runt. The runt domain (of RUNX1) contains twelve beta strands, seven of which shape the fold of an immunoglobulin-like beta sandwich (S-type Ig fold) also found in the DNA-binding domains of other transcription factors (NF-kappaB, NFAT, p53, STAT, and the T-domain) that is preceded by an N-terminal alpha helix. The runt domain is responsible for both DNA-binding and heterodimerization which occur at distinct, non-overlapping sites within the domain. Heterodimerization with CBFbeta leads to conformational changes in the runt domain (S-switch) that stabilize DNA binding .)

Genes bound by RUNX3 (24 entries)

Show 5 ▾ entries	Search:				
Gene	Location within Gene	Binding Site Identifier	DNA Binding Reaction	Effect	Quality Score

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BCL2(h)		HS\$BCL2_13	Runx3(h) --> BCL2(h)	DNA binding	3
BCL2L11(h)	-3130 to -3111	HS\$BCL2L11_08	Runx3(h) --> BCL2L11(h)	DNA binding	2
BCL2L11(h)	-2758 to -2739	HS\$BCL2L11_09	Runx3(h) --> BCL2L11(h)	DNA binding	2

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Artificial sites bound by RUNX3 (1 entry)
Show entriesSearch:

Description	Binding Site Identifier	Quality Score
Artificial sequence	AS\$RUNX3_	2

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ChIP-seq or similar experiments for RUNX3(1 entry)
Show entriesSearch:

ChIP Experiment Report	Chromosome	Binding Fragments	Cell	Reference
View Report	Human Genome	67399	GM12878	ENCODE Data ↗ 22955616 ↗

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Positional weight matrices for RUNX3 (15 entries)
Show entriesSearch:

Sequence logo	PWM ID	Matrix type	Matrix category
 	V\$AML_Q6	family	matrix compiled from individual genomic sites

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	V\$AML2_01	factor-specific	multiplexed massively parallel SELEX
	V\$AML2_Q3	factor-specific	matrix compiled from individual genomic sites
	V\$AML2_Q3_01	factor-specific	matrix compiled from individual genomic sites

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Transcription factors which interact with RUNX3

Show entriesSearch:

Species	Factor
Human	CBF-beta , CBF-beta-isoform2 , Runx2-isoform2 , Sp110
Mammalia	p300

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Protein Features [what is this?](#)

Overview of protein sequence and structure

Chromosome : 1p36**Isoforms** : [Runx3-isoform1](#) , [Runx3-isoform2](#)

+ View associated sequences and their domains

+ View related proteins

Post-translational modifications of RUNX3 protein



[+](#) Acetylated forms (2 entries)[+](#) Sumoylated forms (2 entries)[+](#) Ubiquitinated forms (1 entry)**Known types of modification** : serine phosphorylation [details](#)

View complexes containing RUNX3 protein

[+](#) View complexes (27 entry)

Annotations [what is this?](#)

[Display all annotations](#)

Description

- Runt-related transcription factor 3, plays a role in [TGF-beta](#) receptor signaling, epithelial cell proliferation, T cell lineage commitment, and inflammatory response; promoter hypermethylation correlates with Barrett esophagus and various other cancers [10419474 ↗](#) [12875960 ↗](#) [15273736 ↗](#) [12907736 ↗](#) [12807883 ↗](#) [14715269 ↗](#) [14743205 ↗](#)

Function

- Associates with beta-subunit protein [7622058 ↗](#)
- Transcription activator [7622058 ↗](#)

Domains

- Factor was found to be associated with the nuclear matrix [9192636 ↗](#)

- DNA hypermethylation and subsequent inactivation correlates with breast cancer [16598897](#)
- Expression of the corresponding gene is downregulated in acute myeloid leukemia [15674361](#)
- Expression of the corresponding gene is downregulated in gastric cancer [15685235](#)
- Expression of the corresponding gene is downregulated in peritoneal metastases of gastric cancers [16166423](#)

[more](#)

Identifiers [what is this?](#)

Accessions mapped to this record

BIOBASE gene accession : GN000003848, G003994, MO000030783

BIOBASE protein accession : PR000007707, MO000026238, MO000198039, MO000338419, MO000483594, MO000484972, MO000485018, MO000572671, T02223

Gene

Affymetrix	106_at, 11740486_a_at, 11743428_a_at, 11752954_x_at, 11755054_x_at, 16683624, 204197_s_at, 204198_s_at, 234928_3p_x_at, 234928_x_at, 2401988, 2401990, 2401992, 2401993, 2401995, 2401996, 2401997, 2402004, 2402008, 2402013, 2402015, 2402016, 2402017, 2402018, 2402026, 2402027, 2402028, 2402029, 7913805, g4757917_3p_a_at, Hs.170019.0.S1_3p_a_at, Hs.170019.1.S1_3p_at, Hs.170019.1.S1_3p_a_at, Hs.170019.1.S1_3p_x_at, TC01002370.hg, TC01005339.hg, TC01005340.hg, TC01005341.hg, Z35278_at,
Agilent	A_23_P51231
Ensembl	ENSG00000020633 , ENST00000308873 , ENST00000338888 , ENST00000399916 , ENST00000479341 , ENST00000496967
EntrezGene	864
Genbank	12044652 , 33878242 , 3900882 , 4490532 , 4757917 , 4826532 , 50834307 , 559440 , 608132 , 72534651 , 8928573 , AF022726 , AJ238394 , AL023096 , AL445471 , BC013362 , CQ834770 , NM_001031680 , NM_004350 , U14520 , X79550 , Z35278
HGMD	

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OMIM	600210
RefSeq	NM_001031680.2 , NM_001320672.1 , NM_004350.3 , NP_001026850.1 , NP_001307601.1 , NP_004341.1 , XM_005246024.4 , XM_011542351.1 , XP_005246081.1 , XP_011540653.1
UniGene	Hs&170019
WikiPathways	WP2840 , WP3945 , WP474 , WP4808 , WP4816 , WP560 , WP706

Protein

Genbank	15426512 , 3900883 , 4490533 , 4757918 , 4826533 , 50834308 , 559441 , 55959931 , 56202495 , 608133 , 72534652 , 8928574 , AAA86465.1 , AAB80759.2 , AAH13362.1 , CAA18856.1 , CAA56093.2 , CAA84541.1 , CAB42882.1 , CAC42093.2 , CAH05600.1 , CAI20422.1 , NP_001026850.1 , NP_004341.1
UniProt	Q13761

References (154 entries)

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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	32323849	Xiao, Z, Tian, Y, Jia, Y, Shen, Q, Jiang, W, Chen, G, Shang, B, Shi, M, Wang, Z, Zhao, X, RUNX3 inhibits the invasion and migration of esophageal squamous cell carcinoma by reversing the epithelial?mesenchymal transition through TGF?/?Smad signaling. Oncol Rep 43 (4) 1289-1299 (2020) Show abstract
3	32296183	A reference map of the human binary protein interactome. Nature 580 402-408 (2020) Show abstract
4	28818916	A pathology atlas of the human cancer transcriptome. Science 357 (2017) Show abstract



Locus Report - Human
RUNX3 (Runx3)

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Angileri, F, Ming, B, Zheng, F, Zeng, Q, Mao, X, Peng, Y, Mao, Y, He, P, Wang, QK, Qi, L, Hu, FB, Liang, L, Wu, Y, Genome-wide
Analysis of DNA Methylation and Acute Coronary Syndrome. Circ Res 120 (11) 1754-1767 (2017) [Show abstract](#)

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