SnapShot: Forkhead Transcription Factors II

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Human Gene Symbol (Localization)	Potentially Regulated by	Potentially Regulates	Cellular and Developmental Roles	Mutant Mouse Phenotype	Role in Cancer/ Human Disease
FOXJ1 (17q25.1)	FOXD1, bleomycin	IFNG, IL2, NFKBIB, NFkB, protein-DNA	T-lymphocyte proliferation.	Random determination of left-right asymmetry, no cilia, growth failure, hydrocephalus. Die perinatally.	
FOXJ2 (12p13.31)					
FOXJ3 (1p34.1)					
FOXK1 (7p22.1)			Regulates cell cycle progression in myogenic progenitor cells.	Atrophic skeletal muscles, impaired satellite cell function.	
FOXK2 (17q25.3)					
FOXL1 (16q24.1)	2,4-dinitrophenol-ovalbumin conjugate, LPS, GLI1, TAC1, Hedgehog	proteoglycan, SDC1, BMP2, BMP4	Involved in proteoglycan biosynthesis.	Gastric mucosa hyperplasia, suppressed gastric acid secretion.	Mesenchymal modifier of APC/Min in gastrointestinal carcinogenesis.
FOXL2 (3q22.3)		GDF9, INHBA, AMH	Granulosa cell differentiation; development of ovarian follicle.	Eyelid and forehead dysmorphology; gonadal dysgenesis or premature ovarian failure in females. High rate of perinatal mortality.	Associated with Blepharophimosis-Ptosis-Epicanthus Inversus (BPES); Premature ovarian failure.
FOXM1 (12p13.33)	GLI1, doxorubicin, NRAS, fulvestrant, butyric acid, FGF7, CDKN1A, YY1, MSA, vitamin D3, TNFSF11, IL6, CDC2	CDC25B, CENPA, AURKB, CCNA2, CCNF, CENPB, BIRC5, CCNB1, CDKN1A, ESR1, ADAM17, GLB1	Controls progression into S phase; regulates genes required for mitotic entry; liver development.	Reduced hepatoblast and cardiomyocyte mitosis, ventricular hypoplasia. Die perinatally.	Upregulated in pancreatic cancer.
FOXN1 (17q11.2)	WNT5B, WNT4, BMP4, Noggin	FAM57A, SERPINB1, GZMA, MREG, IL7, TRG, PPP1R16B, C19ORF28, CD274, IVL	Epithelial cell proliferation; keratinocyte differentiation; hair follicle and thymus development.	Hairless, abnormal thymus and T cell development. Premature death.	Associated with immunodeficiency, alopecia, nail dystrophy.
FOXN2 (2p22-p16)					Upregulation associated with advanced papillary serous ovarian carcinoma in humans.
FOXN3 (14q24.3-q31)	INSR, STK11, camptothecin, ER, MEN1		Involved in G2/M phase of cell cycle.		Recruits SKIP to repress genes important for tumorigenesis.
FOXN4 (12q24.12)		NEUROD4, NEUROD1, PROX1	Neuron fate commitment, amacrine and horizontal cell genesis.	Disrupts commitment of retinal progenitors. Die postnatally.	
FOXO1 (13q14.11)	Akt, IGF1, LY294002, Insulin, IRS1, IRS2, wortmannin, PTEN, INS, PDPK1, IL6, FOXO1A, C5b9, TNF	PCK1, BCL2L11, IGFBP1, CDKN1B, FASLG, SERPINE1, TNFSF10, CXCR4, CCNG2, GADD45A, PRL, MYOD1, BCL2L1	Mediates insulin signaling, suppresses proliferation and/or induces apoptosis; development of blood vessels, diaphragm, and yolk sac.	Incomplete vascular development. Die by E10.5. Heterozygotes display decreased hepatic glycogen levels.	Fused to PAX3 or PAX7 in rhabdomyosarcoma.
FOXO2 (1p34.1)					
FOXO3 (6q21)	Akt, LY294002, IGF1, hydrogen peroxide, PI3K, EPO, TP53, Pi3 Kinase, SGK, IKBKB, CHUK, SHC1, etoposide, IL3	BCL2L11, CDKN1B, CCNG2, FASLG, FBXO32, CDKN1A, RBL2, GADD45A, FOXO3A, BNIP3L, SOD2, NOS2A, BBC3, HBP1	Differentiation of erythrocytes; suppresses spontaneous T cell activation and autoimmunity; suppresses proliferation and/or induces apoptosis.	Females have follicular activation leading to oocyte death and sterility.	Fused to MLL gene in secondary acute myeloblastic leukemia.
FOXO4 (Xq13.1)	IGF1, JINK1/2, MAPK10, MAPK8, RALA, wortmannin, Akt, RGL2, LY294002, RALGPS1, Ras, naltrindole, INS1	CDKN1B, CDKN1A, VEGFA, BCL6, RBL2, CDC42EP3, LEMD3, GADD45B, SGK, OVOL1, EPO, GADD45A, CTGF, JAG1, IER3	Negative regulation of cell proliferation; cell-cycle progression; cell differentiation.		Fused to MLL gene in acute lymphocytic leukemia.
FOXP1 (3p14.1)	ITGAM, AGN194204, PMA, FOXP1		Inhibits macrophage differentiation; differentiation of cardiomyocytes; heart development.	Defects in cardiac morphogenesis. Die at E14.	May function as tumor suppressor.
FOXP2 (7q31)	En, GATA6, FOXP2	SFTPC, SCGB1A1, FOXP2	Development of caudate nucleus, cerebellum, and putamen of CNS.	Motor abnormalities, absence of ultrasonic vocalization. Mice die by 3 weeks after birth.	Associated with speech and language disorder.
FOXP3 (Xp11.23)	TGFB1, Cd3, prostaglandin E2, CD28, cyclosporin A, Tcr, TGAL copolymer, PTGER4, CBLB, PTGER2, Flagellin, LEPR, PLP1, AG490, CTLA4	IL4, IL2, IL5, IL2RA, SMAD7, ITGAE, ERBB2, SELL, IgG2a, IgM, IgG1, CD40LG	Regulatory T cell development.	Multiorgan inflammatory response, eosinophilia, dysregulated cytokine production, hyperimmunoglobulinemia E. Males die 3 weeks after birth.	Breast cancer supressor. Associated with neonatal diabetes, enteropathy and endocrinopathy.
FOXP4 (6p21.1)	FOXP4	FOXP4	Heart development.	2 hearts develop, esophagus and trachea do not separate. Die ~E12.5.	
FOXQ1 (6p25.3)	flutamide, TITF1, DHT	Telokin	Modulates natural killer cell function.	Mice have a silky coat.	
FOXR1 (11q23.3)					
FOXR2 (Xp11.21)					

See online version for legend and references.
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SnapShot: Forkhead Transcription Factors II

Cell

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Forkhead transcription factors were first discovered more than 10 years ago in *Drosophila* and are characterized by a shared 100 amino acid DNA-binding motif, termed the "winged helix" or "forkhead" domain. Conserved forkhead domains have been identified in eukaryotic organisms from yeast to humans. The human genome contains more than 40 *FOX* genes. The forkhead transcription factors have been shown to play diverse roles in development, metabolism, immunology, cancer, and cell-cycle control.

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