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Gene Section
Review

FOXQ1 (forkhead box Q1)

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Abstract

Review on FOXQ1, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: HFH1

HGNC (Hugo): FOXQ1

Location: 6p25.3

DNA/RNA

Description

The FOXQ1 gene is 2338 base pairs in length and is intronless.

Transcription

In mouse Foxq1 has been reported to be regulated by Hoxa1 (Martinez-Ceballos et al., 2005), Hoxc13 (Potter et al., 2006) and Tgfβ (Zhang et al., 2011). In human FOXQ1 has been shown to be a target of the Wnt pathway (Christensen et al., 2013; Xia et al., 2014).

Protein

Description

The forkhead box Q1 gene codes for a 403 amino acid long protein with a size of 41.5 kDa. FOXQ1 is a member of the Forkhead box (Fox) superfamily.

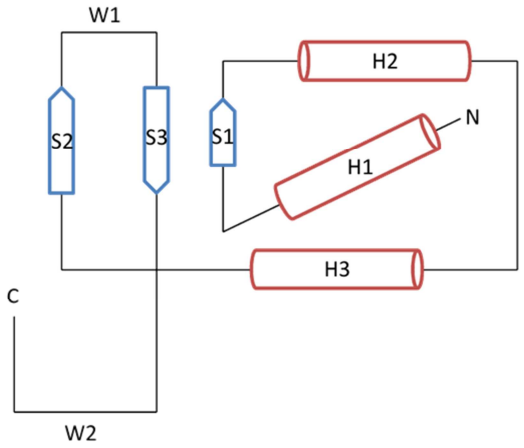

Figure 1. Structure of the winged helix domain. α-helices are shown as red cylinders (H1, H2 and H3), β-strands as blue arrows and W1 and W2 denote the wings (Clark et al., 1993; Gajiwala and Burley, 2000).

The family members share a conserved DNA-binding domain named forkhead box or winged helix domain.
The domain consists of three a-helices, three β-sheets and two loops termed wings.

Expression

Predominantly in the stomach, trachea, bladder and salivary gland (Bieller et al., 2001).

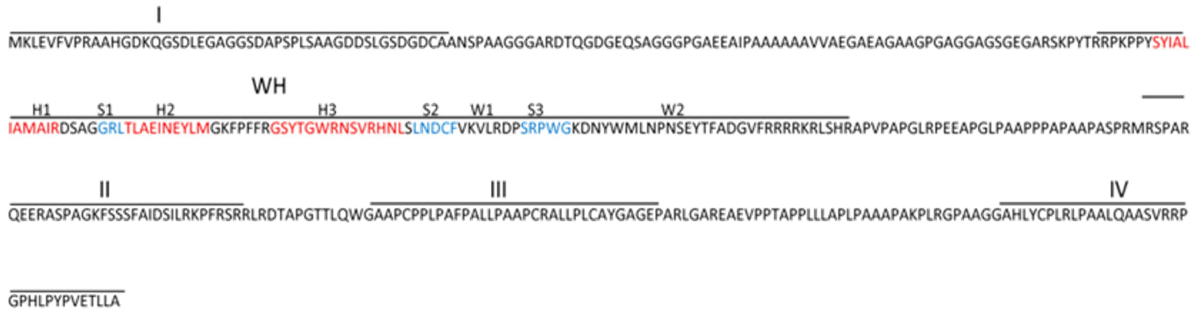

Figure 2. Graphical illustration of the FOXQ1 amino acid sequence and domains. (I) Acid and serine-rich domain. (WH) winged helix domain. (II) Serin-rich domain. (III) Proline-rich domain. (IV) Functional conserved domain (Hong et al., 2001; Wu et al., 2013).

Function

In mice Foxq1 is involved in hair follicle differentiation (Hong et al., 2001; Potter et al., 2006).

A mutation in the Foxq1 gene is responsible for an impaired differentiation of the hair shaft in the satin mice (Hong et al., 2001). In the digestive system Foxq1 has been shown to regulate acid secretion and expression of Muc5ac (Goering et al., 2008; Verzi et al., 2008).

Homology

According to NCBI the following genes have been suggested to be putative homologues: FOXQ1 (H. sapiens), Foxq1 (M. musculus), Foxq1 (R. norvegicus), Foxq1a (D. rerio) and Foxq1b (D. rerio). Conserved domains from CDD found in protein sequences by rpsblast searching was FH (cl00061).

Mutations

Note

Mutations in the Foxq1 gene is responsible for the hair follicle defects seen in the satin mouse mutant. Three mutations have been described leading to similar phenotypes of the animals. Foxq1^{sa} has a 67 bp deletion from 686-752 and a base pair change CA-AT at position 766-767. Foxq1$^{sa\text{-}el}$ has a point mutation a position 383 changing T to G thus replacing isoleucine with serin at position 128 in the protein. Foxq1$^{sa\text{-}J}$ has C to T mutation in position 490 changing the amino acide arginine to cysteine at position 164 in the protein (Hong et al., 2001; Wu et al., 2013).

Implicated in

Bladder cancer

Oncogenesis

FOXQ1 was overexpressed in bladder cancer samples. Depletion of FOXQ1 expression in bladder cancer cell lines reduced invasiveness and EMT markers (Zhu et al., 2013).

Breast cancer

Prognosis

FOXQ1 expression in breast cancer patients is associated with poor survival, high grade, metastatic status and basal-like phenotype (Qiao et al., 2011).

Oncogenesis

FOXQ1 overexpression was observed in invasive breast cancer cell lines compared to non-invasive. FOXQ1 expression increases breast cancer cell proliferation, migration and invasion in vitro and metastasis in vivo (Zhang et al., 2011). FOXQ1 promotes an EMT phenotype through transcriptional regulation of CDH1 (Qiao et al., 2011; Zhang et al., 2011).

Colorectal cancer

Oncogenesis

Several studies have shown FOXQ1 to be overexpressed in colorectal tumor samples compared to healthy colonocytes (Bieller et al., 2001; Sabates-Bellver et al., 2007; Kaneda et al., 2010; Christensen et al., 2013).

The increased expression of FOXQ1 could be due to a hyperactive Wnt pathway in these tumors. Wnt activity directly correlates with FOXQ1 expression in colorectal cancer cell lines and β-catenin can bind to the promoter of FOXQ1 and increase transcription (Christensen et al., 2013). FOXQ1 expression can induce an EMT phenotype (Qiao et al., 2011; Abba et al., 2013). FOXQ1 does not increase growth but seems to protect from apoptosis (Kaneda et al., 2010; Qiao et al., 2011; Abba et al., 2013). The anti-apoptotic effect was mediated through FOXQ1 regulation of p21 (Kaneda et al., 2010).

Gastric cancer

Prognosis

The expression of FOXQ1 was a prognostic factor for overall survival and correlated with tumor size, grade and tumor-node metastasis stage (Liang et al., 2013).

Oncogenesis

FOXQ1 increases migration and proliferation by downregulating NRXN3.

Glioma

Disease

Tumors that arise from the glial cells, the most common site is the brain.

Oncogenesis

FOXQ1 increased migration and proliferation by downregulating NRXN3 (Sun et al., 2013).

Hepatocarcinoma

Cytogenetics

FOXQ1 correlated with overall worse survival and higher recurrence (Wang et al., 2013; Xia et al., 2014).

Oncogenesis

In hepatocarcinoma FOXQ1 directly activated the EMT transcription factor ZEB2. This led to an EMT phenotype and increased lung metastasis. FOXQ1 and ZEB2 expression correlated positively in hepatocarcinoma samples but inversely with CDH1. FOXQ1 induced metastasis through regulation of VersicanV1, which promoted tumor-associated-macrophages attraction. Also, similarly to colorectal cancer expression of FOXQ1 was regulated by the Wnt pathway in hepatocarcinoma (Xia et al., 2014).

Non-small-cell lung carcinoma

Prognosis

FOXQ1 expression was associated with poor prognosis and EMT (Feng et al., 2012).

Ovarian cancer

Oncogenesis

FOXQ1 expression increased ovarian cancer cell proliferation, invasion and induced an EMT phenotype (Gao et al., 2012).

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