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Gene Section
Review

ID1 (inhibitor of DNA binding 1, dominant negative helix-loop-helix protein)

Eduardo Castañón, Ignacio Gil-Bazo

New target therapies laboratory, Division of Oncology, Center for Applied Medical Research, 31621 Pamplona, Spain (EC, IGB)

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Identity

Other names: ID, bHLHb24
HGNC (Hugo): ID1
Location: 20q11.21

DNA/RNA

Description

DNA contains 1239 bp encoding 2 coding exons.

Transcription

Id1 gene has 2 transcripts, called Id1-001 (or Id1A) and Id-1-002 (or Id1B). mRNA Id1A contains 994 bps whereas mRNA Id1B contains 1233 bps.
Id1A is considered the "canonical sequence".

Protein

Description

ID1 belongs to the helix-loop-helix protein family. It is composed by 155 aa.
It has a main domain located on 143-155 aa responsible for the helix-loop-helix conformation.
Its main motif, encoded by 14 aa is responsible for the nuclear export signaling.

Expression

High levels of ID1 are found in brain, liver, lung, skin and thyroid gland cells. It is also expressed in fetal cells and in the umbilical vein endothelial cell.

Localisation

Nucleus.

Function

Although it does not bind directly to DNA, by binding basic helix-loop-helix transcription factors through its HLH motif, ID1 may control tissue-specific genes related to cell growth, proliferation, differentiation and angiogenesis.

Homology

H.sapiens: ID1; P.troglodytes: ID1; C.lupus: ID1; B.taurus: ID1; M.musculus: Id1; R.norvegicus: Id1; G.gallus: ID1; D.rerio: id1.

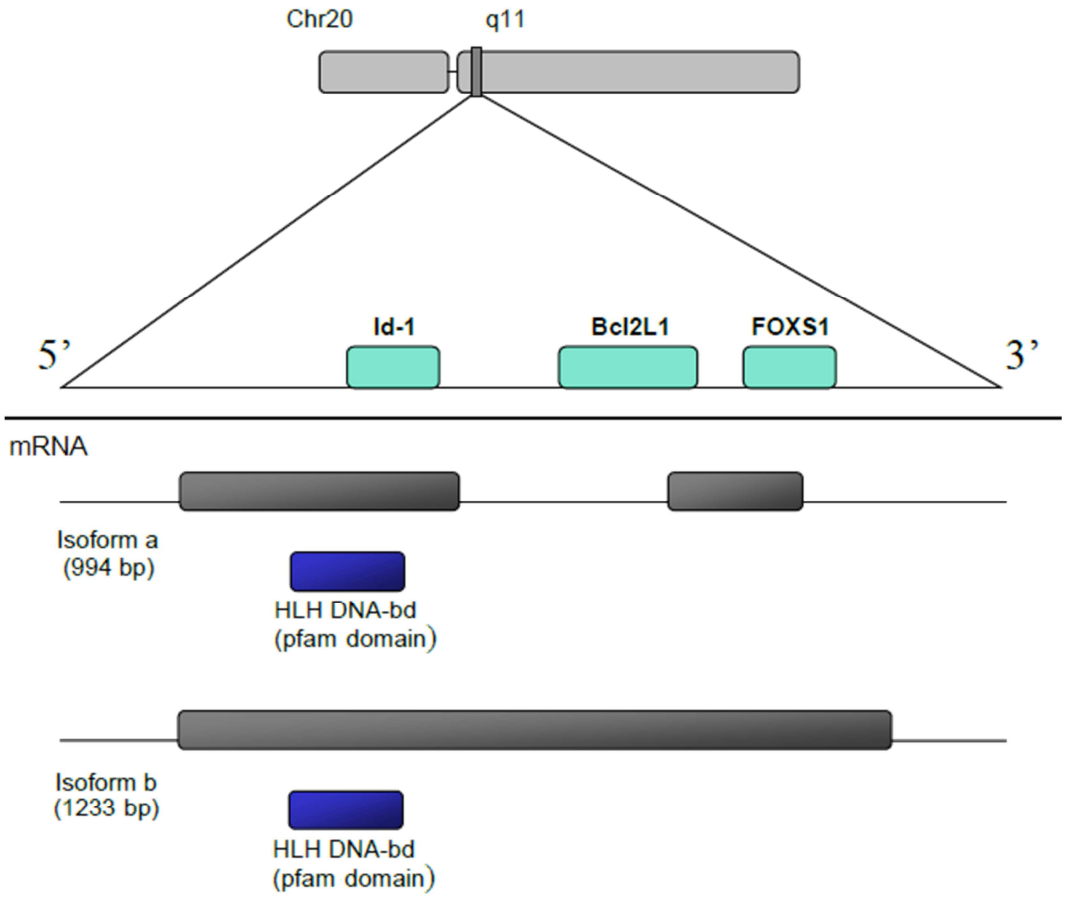
Mutations

Germinal

No germinal mutations have been reported.

Somatic

No somatic mutations have been reported.



Implicated in

Non small cell lung cancer

Note

ID1 levels are correlated with a worse prognosis in lung adenocarcinoma in both, disease free survival and overall survival.

A higher expression of Id1 has been reported in squamous cell carcinoma and adenocarcinoma of the lung.

ID1 expression are detected in more resistant tumors to either chemo and radiation therapy.

When silencing Id1 in in vitro models, a reversal of resistance to the treatment (both chemotherapy and radiation) was observed.

Gastric cancer

Note

Gastric cancer prognosis has also been linked to ID1 expression levels.

Whereas poor differentiated gastric tumors express higher levels of ID1, those gastric cancers with a higher differentiation, and thus, a better prognosis, express a lower quantity of ID1.

Nevertheless, the impact of ID1 expression on clinical outcome has not reached statistical significance when a multivariate analysis was carried out.

Breast cancer

Note

In breast cancer, especially in those node negative tumors, ID1 expression has become an independent prognostic factor.

Higher levels of ID1 are related to a worse prognosis (measured by both, overall survival and disease free survival).

This may be explained by the possible relation between ID1 and the steroid-receptor, this latter considered a factor which may change therapeutic options in breast cancer patients.

Prostate cancer

Note

In prostate cancer it has been observed that levels of ID1 are correlated to the grade of differentiation measured by the Gleason score, detecting higher levels of ID1 in those prostate tumors with a higher Gleason score.

Comparing prostate cancer with benign prostate hyperplasia, ID1 expression differences may also be seen; ID1 is not expressed in benign prostate hyperplasia (BPH), whereas ID1 expression is remarkably higher in prostate cancer cells.

Melanoma

Note

In melanoma ID1 is also positively related to tumor thickness and also with overall survival. Also, ID1 is highly expressed in those BRAF mutated melanomas compared to BRAF wild type melanomas. ID1 negative regulates CDKN2A, which has been related to malignant melanoma development. ID1 is expressed in the earliest stages of melanoma.

Glioblastoma

Note

In recent studies, ID1 has been catalogued as a marker of brain stem cells localized at the perivascular niche. Those stem cells with higher levels of ID1 have a major capability of tumor initiation and therapeutic resistance.

Hepatocarcinoma

Note

In Hepatitis B virus-induced hepatocarcinoma, levels of ID1 may predict both disease free survival and overall survival, in a negative manner. Also, ID1 has been related to bad prognostic features such as portal vein invasion, lymph node metastasis and a worse Child Pugh grade.

Anaplastic thyroid tumor

Note

ID1 is highly expressed in anaplastic thyroid tumors rather than in regular thyroid cells; it may be explained by the role ID1 plays on cell growth and differentiation.

Neurogenesis

Note

Lacking of Id1 alleles (with simultaneous Id3 downregulation) triggers neural differentiation in mice embryos development resulting in a lethal event. It has also been reported that when Id1 and Id3 are not expressed, vascular sprouting in brain does not occur.

Heart and vessel formation

Note

Id1 has also being related to play a crucial role in heart development, since Id1 knockout mice showed ventricular defects and myocardium trabeculation impairment.

ID1 is also expressed in endothelial progenitor cells, and its suppression is related to angiogenesis inhibition and in a blockade of endothelial cells mobilization.

Hematopoiesis

Note

Higher ID1 levels are found in pro-B cells, whereas it is downregulated in pre-B and mature cells. When blocking Id1 in those cells, B-cell development is disrupted.

Metastasis

Note

Higher levels of ID1 expression are found in those breast cancers which are more prone to metastasize to the lung. Id1 has been described as part of the genes signature for breast cancer metastasis to the lung.

Stemcellness and selfrenewal

Note

Satellite cells are muscle stem cells related to injured muscle renewal. ID1 expression has been recently correlated to muscle stem cell self-renewal ability, showing that when ID1 is expressed, a higher capability of self-renewal may be observed. Culture cells with high ID1 expression, may retain selfrenewal ability after several passages comparing to those cells with lower levels of ID1.

Stem cells are characterized by their anchorage to an special microenviroment, also known as niche. ID1, by repressing the activation of Rap1GAP (an inhibitor of an important neural cell adhesion protein known as RAP1) assure stem cell joints to the niche. When ID1 is downregulated, neural stem cells detach from the brain stem cell niches, such as the ventricular zone in embryonic brain and the subventricular zone of post-nata brain. This detachment from the niches, may also trigger neuronal and oligodendrogial differentiation.

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