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Gene Section
Mini Review

RARRES1 (retinoic acid receptor responder (tazarotene induced) 1)

Kwok-Wai Lo, Grace TY Chung

State Key Laboratory in Cancer in South China, Department of Anatomical and Cellular Pathology, Prinve of Wales Hospital, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China

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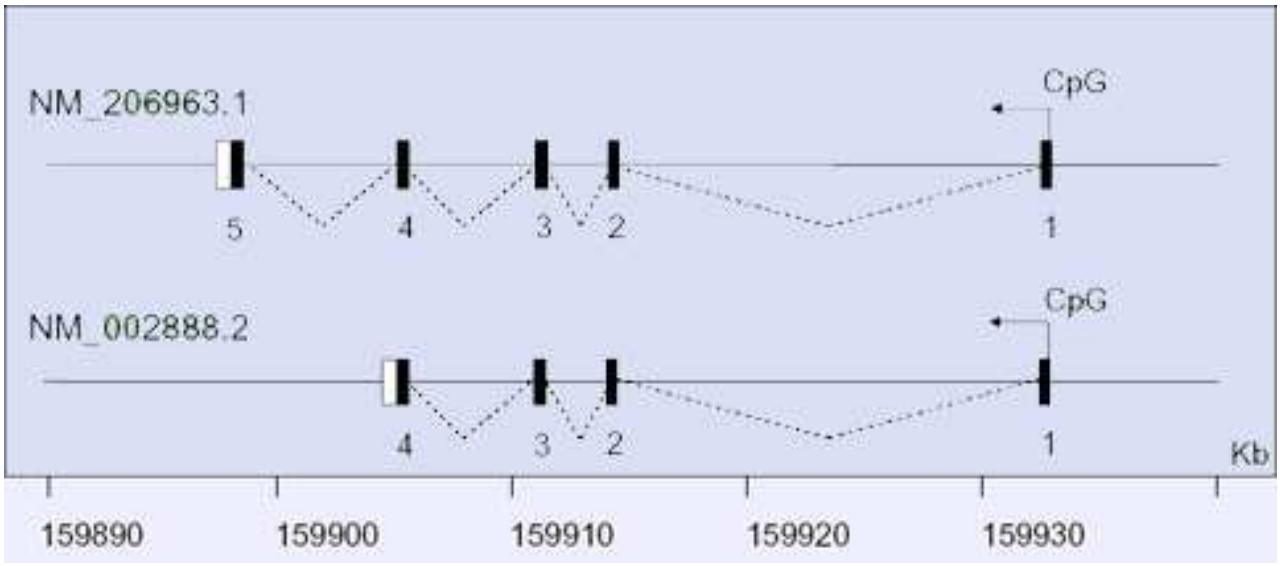
Identity

Hugo: RARRES1
Other names: TIG1
Location: 3q25.32
Local order: Telomeric to MFSD1 and centromeric to GFM1 and LXN
Note: RARRES1 (retinoic acid receptor responder 1) is also known as TIG1 (Tazarotene-induced gene 1). The gene was initially identified as a target gene that was induced by the synthetic retinoid tazarotene (AGN 190168) in human skin raft cultures. It is upregulated by retinoic acid receptor-specific but not by retinoid X receptor-specific retinoids.
As noted in the early published articles, the authors mentioned that RARRES1 (TIG1) is located at 3p12-13. The location was subsequently confirmed to be incorrect. UCSC Genome Browser on Human Mar. 2006 Assembly shows that the RARRES1 should be located between 3q25.32 and 3q25.33.

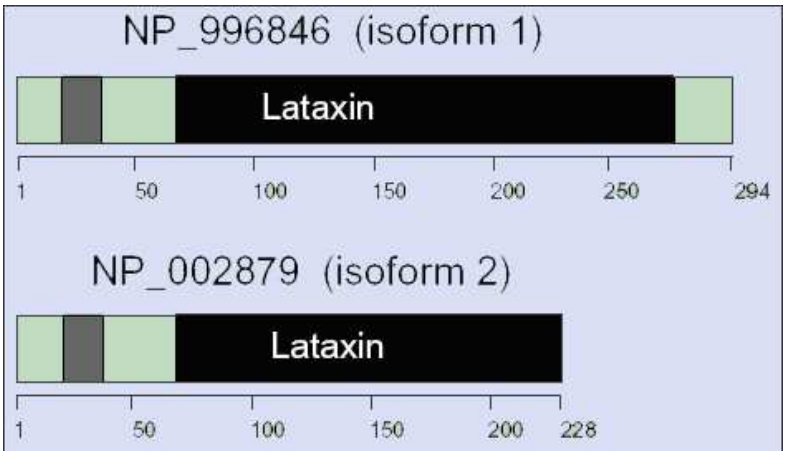
DNA/RNA

Description

The RARRES1 gene contains 6 exons and spans 35377 bases.



Two transcript variants (isoform 1: NM_206963.1 and isoform 2: NM_002888.2) are shown. Black boxes represent the exons of RARRES1. CpG: location of CpG island.



The gray box indicates the single membrane-spanning hydrophobic region. Lataxin domain for 2 RARRES1 isoforms is shown as black box.

Transcription

Two alternatively spliced transcripts were identified (isoform 1 and isoform 2). Exons 1 to 4 are common to both isoforms. Exon 5 and 6 are present in isoform 1 (NM_206963.1) only. The cDNA of isoform 1 is 1545 bp while isoform 2 is 886 bp.

Pseudogene

No known pseudogenes.

Protein

Description

Called Retinoic acid receptor responder protein 1 (synonyms: Tazarotene-induced gene 1 protein/RAR-responsive protein TIG1); Two isoform, isoform 1 (NP_996846) and isoform 2 (NP_002879), produced by alternative splicing were reported. Isoforms 1 and 2 contain 294 and 228 amino acids respectively. Molecular weight of Isoform 1 is 33258 Da. The two isoforms show difference in the 3'end-region. RARRES1 is predicted to be a transmembrane protein with a small N-terminal intracellular regions, a single membrane-spanning hydrophobic region, and a large C-terminal extracellular region containing a glycosylation signal.

Expression

High level of RARRES1 transcripts was detected in multiple tissues including prostate, heart, lung, liver, colon and small intestine. Expression of RARRES1 protein was demonstrated in colorectal tissues.

Localisation

Based on the predicted amino acid sequence, RARRES1 is suspected to be a transmembrane protein. However, immunohistochemical analysis showed that RARRES1 protein localizes at the supranuclear regions of colorectal adenocarcinoma, adenoma and adjacent normal epithelial cells. The precise localization of RARRES1 protein needed to be further investigated.

Function

RARRES1 was suggested to be a tumor suppressor of a variety of human cancers. Inactivation of RARRES1 is involved in the malignant progression of prostate cancer. Restoration of RARRES1 expression in malignant prostate cell lines led to a decrease of invasiveness and tumorigenicity in nude mice. It is speculated that RARRES1 may function as a cell adhesion molecule. Since the protein shows sequence similarity to Latexin, the only known mammalian carboxypeptidase inhibitor, RARRES1 may also have protease inhibitor activity and inhibit the degradation of extracellular matrix.

Homology

RARRES1 belongs to the proteinase inhibitor I47 (latexin) family, its c-terminal region shows 30% sequence similarity with Latexin.

Mutations

Note: No germline or somatic mutation associated with disease is reported.

Implicated in

A variety of human cancers

Note: The association of RARRES1 with human cancer was first revealed by the subtractive differential gene display analysis of benign and malignant prostate cell lines. The gene was expressed in benign prostate cell lines and not in malignant ones. It is now considered as a putative tumor suppressor gene in a variety of human cancers although its function remains unclear. Its expression is commonly suppressed in prostate carcinoma, lung cancer, nasopharyngeal carcinoma, and leukemia by promoter hypermethylation. Restoring RARRES1 expression in prostate cancer cells resulted in decrease of in vitro invasiveness and in vivo tumorigenicity. RARRES1

also implicated in therapeutic effects of retinoic acid in psoriasis.

Disease

Prostate carcinoma, nasopharyngeal carcinoma, head and neck cancer, lung cancer, gastric carcinoma, colorectal adenocarcinoma, endometrial cancer, breast cancer, acute myeloid leukemia, Chronic myeloid leukemia.

Prognosis

Down-regulation of RARRES1 is significantly related with the late stage colorectal adenocarcinoma (Dukes's stage D). However, no difference in survival was found comparing patient with negative, weak and strong RARRES1 expression in tumors.

Cytogenetics

No translocations and amplifications of this gene have been reported.

Hybrid/Mutated Gene

No hybrid gene involving RARRES1 has been described.

Breakpoints

Note: No breakpoints involving this gene have been described.

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