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Gene Section

Mini Review

TFRC (transferrin receptor (p90, CD71))

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Identity

Other names: CD71; OKT-9; TFR1 (Transferrin receptor 1); TFR; TRFR; p90; Mtvr-1 (mammary tumor virus receptor 1, in mice)
HGNC (Hugo): TFRC
Location: 3q29

DNA/RNA

Note
History and Nomenclature: The TFRC gene was assigned to chromosome 3 in 1982. It was located in 3q22 - qter the following year. It precisely maps to 3q29. Transferrin receptor was first detected as the proliferation-associated receptor for transferrin on leukemia cells. Transferrin receptor 2 is a distinct protein belonging to transferrin receptor-like family and its gene TFR maps to chromosome 7q22.

Transcription

13 alternative splicing variants have been described. The full-length transcript contains 19 exons enco-ding 760 amino acids.

Pseudogene

There is no known pseudogene derived from TFRC.

Protein

Description

A plasma membrane transport glycoprotein composed of disulfide-linked polypeptide chains, each 84.8-kDa molecular weight. Belongs to the peptidase m28 family.

Expression

Expressed in a wide range of cell types and tissues. Expression level is highest in lymphocytes, placenta and neoplastic cells.

Localisation

TFRC is a cell surface membrane protein.

Function

TFRC is primarily involved in iron homeostasis by regulating cellular iron uptake in interaction with the HFE protein. It is also crucial in iron transportation from mother to fetus.
Transferrin receptor is the main receptor for transferrin and allows transferrin-bound iron uptake by the cell. Its expression is regulated by cellular iron requirements. Conserved iron-response elements in the 3'-untranslated region of transferrin receptor mRNA enhances binding of iron regulato-ry proteins 1 and 2. The hereditary hemochroma-tosis protein HFE competes for binding with transferrin for an overlapping binding site. It is also involved in materno-fetal iron transport via the placenta.

Mutations

Note
There are no disease-causing mutations in the TFRC gene. However, there are missense coding region variants that may have functional effects. The only one with appreciable frequency (rs3817672) is in exon 4 and encodes S142G amino acid substitution. This polymorphism does not have a homogeneous global distribution. Its minor allele in Caucasians is the major allele in Asians and Africans.

There is no nonsense mutation described in TFRC. TFRC is not involved in any known translocations. Tfrc knockout mice are not viable and die during embryonic development due to erythropoietic and neuronal development problems. The short arm of chromosome 3 also harbors other iron-related genes: transferrin (3q22.1), lactotrans-ferrin (3q21-q23), melanotransferrin (3q28-q29) and ceruloplasmin (3q23-q25). Trisomy of chromo-some 3, gain of the whole 3q arm and gain of 3q27-qter have been noted in various malignancies including both solid tumors and hematopoietic ones.

Implicated in

Cancer Susceptibility

Note

Overexpression of TFRC in malignant cells mediates higher iron uptake required for cell division. Expression is activated by c-Myc. No mutation or variation in TFRC causes cancer and TFRC is not involved in cancer-associated translocations.

TFRC variant S142G modifies the associations of HFE C282Y mutation in cancer susceptibility for hepatocellular carcinoma, breast cancer, leukemia, colorectal cancer and multiple myeloma. Biological plausibility of these associations has been supported by the successful use of monoclonal antibodies against transferrin receptor in cancer treatment in vitro and in vivo.

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