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Gene Section
Short Communication

GATA2 (GATA binding protein 2)

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Abstract

Review on GATA2, with data on DNA, on the protein encoded, and where the gene is implicated.

Keywords
GATA2; DCML deficiency; Emberger syndrome; 3q21q26 syndrome; leukemias; solid tumors.

Identity

Other names: MGC2306; NFE1B; ENSG00000179348

HGNC (Hugo): GATA2

Location: 3q21.3 128,479,427-128,493,185 reverse strand

DNA/RNA

Description

Genomic DNA 13,759bp, 6 exons ((two untranslated first exons that utilized differentially and five translated exons).

Transcription

The distal (IS) exon specifically utilized in hematopoietic and neural cells, while the proximal (IG) exon is utilized ubiquitously, producing 3383-bp and 3484-bp transcripts, respectively. These two variant transcripts encode the same protein. Trancription is oriented from telomere to centromere.

Protein

Description

Contains 2 zinc finger domains, ZF1 (aa 294 to 344) and ZF2 (aa 349 to 398).

Expression

Strictly regulated and tissue specific. Gene activity depends on several trans regulators and cis-acting regulatory elements scattered in a wide range around the gene. 3.1-kbp upstream of IS exon recapitulates endogenous Gata2 gene expression in yolk sacs and paraaortic splanchnopleura hematopoietic cells in mice. An enhancer in 77-kbp upstream of GATA2 gene and GATA-box-E-box composite element in the fourth intron are important in adult hematopoiesis and implicated in the leukemogenesis in humans (see below). In non-hematopoietic tissues, the element in the fourth intron works as an endothelial specific enhancer, whereas enhancer(s) located between +75- and +113-kbp to the translational initiation site are responsible to the Gata2 expression in caudal periureteric mesenchyme/ urogenital sinus and rostral metanephric mesenchyme in mice, respectively. It has been considered that currently not-identified enhancer(s) for urogenital organs development are located more distal region of Gata2 gene..

Localisation

Nuclear.

Function

Binds to the consensus sequence 5'-(A/T)GATA(A/G)-3'. Transcriptional activator which is expressed very early in hematopoiesis and plays a role in development and regulation of every early pluripotent hematopoietic precursor, but also of eosinophils, basophils and mast cells. Early stages of erythroid differentiation depends of GATA2, but during maturation GATA2 expression decreases progressively at the benefit of GATA1. GATA2 suppresses differentiation of bone marrow

mesenchyme stem cells to adipocytes and sustains the hematopoietic stem cell environment. GATA2 also plays roles in development of neural system, urogenital organs and vascular system.

Homology

Member of the GATA family which contains 6 known members; only GATA1, GATA2 and GATA3 are involved in hematopoiesi

Mutations

Germinal

Loss-of-function mutations and dominant-negative mutations have been found as a cause of Familial myelodysplastic syndrome (MDS), DCML deficiency and Emberger syndrome, which are in a group of complex syndromes predisposing to leukemia with overlapping clinical features. Mutation in GATA-box-E-box composite element in the fourth intron, which leads to reduction of GATA2 gene expression, has been found in a pedigree of MonoMAC syndrome family.

Somatic

Chromosomal rearrangements involving the 77-kbp upstream region of GATA2 gene on 3q21 and MECOM (EVI1) gene on 3q26 are associated with MDS and acute myeloid leukemia (AML). This type of hematopoietic malignancies is referred to as 3q21q26 syndrome. Mutations are found as a cause of acute myeloid transformation of chronic myeloid leukemia (CML).

Implicated in

DCML deficiency

Disease

Immunodeficiency syndrome associated with loss of dendritic cells, monocytes, B and NK cells, leading to the increasing incidence of mycobacterial, fungal and viral infections. This disease occurs sporadically or in an autosomal dominant inheritance with incomplete penetrance. Patients with DCML deficiency have high incidence of developing hematopoietic malignancies. DCML deficiency with mycobacterium avium complex infection has been described as "monoMAC (monocytopenia with Mycobacterium avium complex) syndrome".

Prognosis

Prone to develop MDS and AML.

Emberger syndrome

Disease

Sporadic or autosomal dominant disease with incomplete penetrance, which has a characteristic feature of primary lymphoedema with myelodysplasia. The lymphedema generally confined to the lower limbs and genitals.

Prognosis

Prone to develop AML.

3q21q26 syndrome

Disease

Hematopoietic malignancies, including MDS and AML, caused by a chromosomal aberration between the regions 3q21 and 3q26. The 77-kbp upstream region of GATA2 gene on 3q21 is rearranged proximal to the Evi1 locus on 3q26 by the translocation or inversion. Aberrant expression of EVI1 gene lead by the activity of GATA2 enhancer is appeared to be involved in the pathogenesis and poor prognosis of this disease.

Prognosis

Unfavorable prognosis.

Cytogenetics

inv(3)(q21q26), t(3;3)(q21;q26).

Acute promyelocytic leukaemia (APL)

Disease

GATA2 may be involved in APL leukemogenesis by physical interaction with the PML component of PML-RARa fusion or with the variant PLZF-RARa fusion, generated respectively by t(15;17) or t(11;17) translocation.

Myelodysplasic syndrome

Disease

GATA2 is expressed in MDS, but not in normal controls; the frequency of expression increases with the severity of dysplasia (100% in RAEB/RAEB-T).

Myeloid transformation of chronic myelooid leukemia CML

Disease

Out of 85 unselected cases of CML blast transformation, 9 showed a GATA2 mutation: 8 with a T-->G substitution at aa359 in ZF2 (L359V) and 1 with a 6 aa deletion (aa 341 to 346) in ZF1. All 9 transformations were myeloid, with a myeloblastic or monoblastic morphology. L359V leads to a gain of function of GATA2 protein.

Aplastic anemia (AA)

Disease

Hypothetical. In knockout mice, GATA2 haploinsufficiency leads to a decrease of hematopoietic stem cells number and efficiency. In human, GATA2 mRNA expression is largely reduced in patients with AA.

Prostate cancer

Disease

High expression of GATA2 is associated with aggressiveness, high metastasis ratio and resistance for therapy in prostate cancer through, in part, the activation of androgen-receptor target genes in ligand-independent pathway.

Prognosis
Unfavorable prognosis.

Non-small cell lung cancer

Disease
GATA2 is required for the survival of Ras-mediated NSCLC by controlling IL-1/NF-κB signaling. Knockdown of GATA2 expression lead to a reduction of tumor burden in mouse model of NSCLC, suggesting that GATA2 is a therapeutic target of Ras mutant cancers.

Glioma

Disease
The level of GATA2 expression that might be regulated by EGFR/ERK signaling pathway is correlated with prognosis of glioma patients.

Neuroblastoma

Disease
The expression level of GATA2 is reverse-correlated with aggressiveness, as GATA2 may negatively regulate proliferation of neuroblastoma cells.

Renal cell carcinoma (RCC)

Disease
The expression level of GATA2 is reverse-correlated with aggressiveness, possibility of metastasis, and risk of recurrence in clear cell RCC.

Hepatocellular carcinoma

Disease
The expression level of GATA2 is reverse-correlated with poor prognosis of hepatocellular carcinoma. Knockdown of GATA2 expression enhances the proliferation of a human liver cancer cell line in vitro.

Colorectal cancer

Disease
High level of GATA2 expression is correlated with aggressive feature, high recurrence rate and poor outcome of colorectal cancer.

Breast cancer

Disease
Roles of GATA2 in pathogenesis of breast cancer are contraversial. Reports describing that GATA2 level was increased in breast cancer showed that GATA2 might be related to tumor progression by repressing PTEN activity and/or promoting expression of aromatase gene, whereas another report showed that the expression GATA2 gene was silenced by aberrant hyper-methylation of GATA2 promoter region.

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