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Gene Section
Mini Review

EBAG9 (Estrogen receptor-binding fragment-associated antigen 9)

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Identity

Hugo: EBAG9
Other names: EB9; PDAF; RCAS1
Location: 8q23.2

DNA/RNA

Description

The EBAG9 gene contains 7 exons and 6 introns. It was predicted to span over approximately 24.6 kb of the genomic DNA with mRNA size approximately 1182 bp. The exon 3 was the smallest at 79 bp; the other exons ranged from 92-720 bp. The EBAG9 was isolated from MCF-7, human breast cancer cell library and it has been reported identical with RCAS1 (receptor-binding cancer antigen expressed on SiSo cells) gene from human uterine adenocarcinoma cell line.

Transcription

The EBAG9 mRNA is up-regulated by estrogen in MCF-7 cells and its promoter responds to estrogen through the complete palindromic estrogen responsive element (ERE) that was located in the 5'-up stream region of the gene.

Pseudogene

One pseudogene located in chromosome 10 associated with RCAS1/EBAG9.

Protein

Description

The EBAG9/RCAS1 consists of 213 amino acids (aa) corresponding to a molecular weight of 24.4 kDa. The EBAG9/RCAS1 has an N-terminal trans-membrane segment (8-27 aa) and a coiled-coil structure in the C-terminal portion (179-206 aa), indicating that the EBAG9/RCAS1 is a type II membrane protein able to form oligomers through the coiled-coil structure, which is expressed on the surfaces of human cancer cells.

Expression

The EBAG9/RCAS1 mRNA is expressed in ovary, testis, prostate, thymus, muscle, and heart. At the protein level the EBAG9/RCAS1 not detected in normal ovary tissues or any of the other above. Neither mRNA nor protein was detected in small intestine, colon, lymph node or peripheral blood lymphocytes.

Localisation

Mainly in the golgi, membrane and cytoplasm of cancer tissues, but its expression is very low or hardly detected in normal tissues.

Function

The biological functions of the EBAG9/RCAS1 secreted by non-cancerous tissues remain unknown.
In cancer cells, the EBAG9/RCAS1 is a ligand for a putative receptor present on various human cell lines and normal peripheral lymphocytes such as T-, B- and natural killer (NK)-cells. The expression of this receptor is enhanced by activation of these lymphocytes. The EBAG9/RCAS1 acts to inhibit the growth of receptor-binding cells and induced apoptotic cell death. Over-expression of the EBAG9/RCAS1 is known to inhibit the growth and induced apoptosis of immune cells. As the results, cancer cells might evade immune surveillance by expressing the EBAG9/RCAS1 and inducing the apoptosis of the EBAG9/RCAS1 receptor-positive immune cells.

Homology

Mouse and human EBAG9/RCAS1 shows a high degree of homology at the amino acid level (98%). Mouse (Mus musculus) ebag9 gene spans about 30 kb in genomic DNA and consists of 7 exons. Dog (Canis familiaris) EBAG9/RCAS1 also shows highly homologues to human (96,2%) and to mouse (96,7%). For chimpanzee (Pan troglodytes) 100%, rat (Rattus norvegicus) 94% and chicken-ebag9 (Gallus gallus) 91%.

Mutations

Germinal

Not known in Homo sapiens.

Somatic

Not known in Homo sapiens.

Implicated in

Immunity

Note: During pregnancy, EBAG9/RCAS1 may play a role in the down-regulation of the maternal immune response and may participate in the initiation of the labor. In the healthy women, higher EBAG9/RCAS1 expression was observed in the periovulatory and the secretory menstrual cycle phases than in the proliferation phase. The changes in EBAG9/RCAS1 expression were combined with significant differences in the number of immune cells and their activity. It suggested that EBAG9/RCAS1 endometrial expression may favor the coexistence of active lymphocytes and endometrial cells.

Disease

The elevated serum level of EBAG9/RCAS1 reported to be associated with a poor immunological prognosis in HIV-1-infected patients, and also associated with the apoptosis of CD4+ T cells in HIV infection. In addition, the induction and secretion of EBAG9/RCAS1 in HIV-Trans-acting transcriptional activator-stimulated CD4+ T cells and monocytes suggested that EBAG9/RCAS1 may involved in the CD4+ T cell apoptosis observed in HIV-1 infection along with FasL and TRAIL.

Malignancy.

Disease

The EBAG9/RCAS1 reported to be over-expressed in many human cancers. Among them: breast, female-genital, gastrointestinal, blood, lung, pancreas, liver, renal, billiary-tract, hepatic, prostate, thyroid, gall bladder, and brain cancer.

Prognosis

The EBAG9/RCAS1 over-expression could be used as a predictor of poor prognosis in malignant diseases.

Oncogenesis

The EBAG9/RCAS1 plays a role in the immune escape of cancer cells. The EBAG9/RCAS1 could help cancer cells to survive and avoid immunosurveillance. This gene over-expression might cause progression, invasion and metastasis. The EBAG9 acts as one of the estrogen responsive genes in estrogen receptor-positive tumors and mediate estrogen function. Overall, the EBAG9/RCAS1 has an etiological role in the development and progression of cancer cells.

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