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Gene Section
Mini Review

RSF1 (remodeling and spacing factor 1)

Tian-Li Wang, Joon T Park

Departments of Gynecology/Obstetrics and Oncology Johns Hopkins Medical Institutions CRBII, Rm: 306 1550 Orleans Street Baltimore, MD 21231, USA (TLW, JTP)

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Identity

Other names: HBXAP; XAP8; RSF-1; p325

HGNC (Hugo): RSF1

Location: 11q13.5

Local order: Gene orientation: centromere -3' RSF1 5'-telomere.

DNA/RNA

Description

Rsf1 gene is encoded by 16 exons spanning 154.607 Mb that are located on chromosome 11p14.1.

Transcription

5.131 Kb mRNA, the coding sequence is from 121 bp-4446 bp.

Protein

Note

1441 amino acids, highly acidic protein (pI 4.94), with calculated molecular mass of 164 kD. SDS-PAGE detected native RSF1 at molecular mass of 200 to 300 kD.

Contain a DDT domain, Zinc finger PHD-type domain which was found in nuclear proteins thought to be involved in chromatin-mediated transcriptional regulation.

RSF1 also contains 3 nuclear localization signal near C-terminus.

Description

Using a variation of the yeast 2-hybrid screen aiming to identify proteins interacting with hepatitis B virus X protein (HBX), Shamay et al (2002a) cloned RSF1 from a spleen cDNA library. Therefore, the initial name of RSF1 was called Hepatitis B virus X-Associated Protein (HBXAP). Using 5'RACE, 3 splice variants were cloned and named HBXAP-alpha, -beta, -gamma, which contains 1431, 1400, and 1189 amino acids, respectively. By characterizing a protein remodeling complex RSF, Loyola A et al has identified two interacting subunits: RSF1 and SNF2H. They used peptide sequence information of RSF1 to clone the full-length cDNA. The deduced sequence contains 1441 amino acids which includes 252 additional amino acids at N-terminus as compared to HBXAP-gamma. Reconstitute experiment by isolating protein complex from coinfection of viruses caring each subunit can recapitulate the chromatin assembly ability and ATPase activity of native complex. They also showed that SNF2H binds to DNA independently of histones. However, RSF1 couldn't bind to DNA unless histones are present.

Genomic organization of human RSF1.

Diagram of the RSF1 protein.

Expression

Highly expressed in heart, skeletal muscle, kidney, and placenta, and expressed weakly in brain and colon.

Localisation

Mainly located at cell nucleus. During mitosis, the expression in the nucleus is decreased.

Function

RSF1 functions as transcription coactivator when associated with hepatitis B virus X protein (HBX). Shamay et al (2002b) observed the direct interaction between the RSF1 variant, HBXAP-gamma, and HBX. HBXAP-gamma increased hepatitis B viral transcription in an HBX-dependent manner. Furthermore, in the presence of both HBX and HBXAP, the transcription of a nuclear factor kappa-B (NFKB) was significantly increased. However, in the presence of HBXAP alone, the transcription of a NFKB was decreased in a dose-dependent manner. Examination of HBXAP-gamma deletion mutants showed that the interaction between HBX and HBXAP-gamma was mediated by the PHD domain in HBXAP-gamma.

RSF1 functions as chromatin remodeling and spacing when associated with SNF2H. Loyola et al reconstituted the RSF complex by overexpressing two subunits, RSF1 and SNF2H. RSF1 assembled nucleosome randomly as a histone chaperone in the nuclei. The resulting nucleosomes were then redistributed into a regularly spaced nucleosome array by the ATP-utilizing nucleosome mobilization factor SNF2H. At the cellular level, Rsf1/SNF2H complex participated in chromatin remodeling by mobilizing nucleosomes in response to a variety of growth modifying signals and environmental cues. Sheu JJ et al found that the induction of RSF1 expression affected the molecular partnership of SNF2H and translocated SNF2H into nuclei where it colocalized with RSF1. To determine which domain in the RSF1 is involved in the binding to SNF2H, a series of RSF1-deletion mutants were generated. Only the fragment that contains DDT, Glu-rich, and PHD motifs could be immunoprecipitated with SNF2H. Ectopic expression of this RSF1 fragment disrupted RSF1/SNF2H complex and resulted in remarkable growth inhibition in ovarian cancer cells with RSF1 gene amplification and overexpression, but not in the cells without detectable RSF1 expression. This finding suggests that interaction between RSF1 and SNF2H may define a survival signal in the tumors overexpressing RSF1.

Mutations

Somatic

Chromosome 11q is one of the most common targets for allelic imbalance alteration in human cancers. Several candidate tumor-promoting genes were postulated previously. In ovarian carcinoma, Shih et al, has pinpointed a minimal amplicon spanning from 76.6 to 78.4 Mb on the chromosome 11q, which harbor 13 genes. Rsf1 was identified as the gene with most consistent correlation between gene amplification and transcription up-regulation.

Implicated in

Ovarian cancer

Prognosis

Shih et al found that amplification of Rsf1 locus was correlated with shorter overall survival of ovarian cancer patients.

Cytogenetics

Amplification of 11q13 detected an ovarian cancer cell line, OVCAR3.

Oncogenesis

Shih et al found that the amplification of chr11q13 is associated with RSF1 protein over-expression. siRNA knockdown experiment in OVCAR3 cell, which harbor Rsf-1 amplification, demonstrated it is essential for tumor cell survival.

Mao TL et al found that RSF1 overexpression was observed in 25% of high-grade ovarian serous carcinomas and in less than 7% of low-grade ovarian serous carcinoma and ovarian endometrioid. RSF1 does not express in any of the ovarian serous borderline tumors, ovarian clear cell carcinomas, ovarian mucinous carcinomas, and normal ovaries. Overexpression of RSF1 was significantly associated with high-grade ovarian serous carcinoma ($P < 0.05$) as compared with other types of ovarian tumors, demonstrating that RSF1 expression is primarily confined to high-grade serous carcinoma, the most aggressive ovarian cancer.

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