Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section

Review

CSE1L (CSE1 chromosome segregation 1-like (yeast))

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Identity

Other names: CAS, CSE1, MGC117283, MGC130036, MGC130037, XPO2

HGNC (Hugo): CSE1L

Location: 20q13.13

DNA/RNA

Note

CDS: 2915 bp.

Description

The CSE1L gene consists of 25 exons (Brinkmann et al., 1999). The CSE1L gene is high-frequency amplified in various cancer types (Tai et al., 2010a).

Transcription

Multiple transcript variants encoding several different isoforms in a tissue-specific manner have been described for CSE1L gene (Brinkmann et al., 1999).

Protein

Note

CSE1L is a multiple function protein. The protein is involved in nuclear protein transport (Lindsay et al., 2002), cell apoptosis (Brinkmann et al., 1996), microtubule assembly (Scherf et al., 1996), cell secretion (Tsao et al., 2009), and cancer cell invasion (Liao et al., 2008; Tung et al., 2009; Stella Tsai et al., 2010) etc.

Description

CSE1L gene encodes a 971-amino acid protein with an approximately 100-kDa molecular mass (Brinkmann et al., 1995).

Expression

CSE1L is expressed in various tissues, and particularly it is highly expressed in most cancer (Tai et al., 2010a; Brinkmann et al., 1995). The expression level CSE1L is positively correlated with high tumor stage, high tumor grade, and worse outcomes of cancer patients (Tai et al., 2010a). The increased expression of CSE1L in cancer is mainly due to the amplification of the copy number of the CSE1L gene in cancer tissue (Tai et al., 2010a). The association of CSE1L with microtubules is related with pseudopodia extension and the migration of cancer cells (Tai et al., 2010b). CSE1L is also a secretory protein, and it is present is the sera of cancer patients. The secretion of CSE1L is related with the invasion of cancer cells (Tung et al., 2009; Stella Tsai et al., 2010).

Localisation

Nucleus, cytoplasm.

Function

A cell apoptosis susceptibility protein; a microtubule-associated protein; an export receptor of importin-a in the nuclear protein import cycle; involved in tumor cell invasion and metastasis in cancer progression.

Homology

The yeast chromosome segregation gene CSE1.

Implicated in

Breast cancer

Prognosis

Benign breast lesions show weak cytoplasmatic CSE1L staining, while in ductal and lobular in situ carcinomas, 70%-90% of breast tumor cells showed heavy CSE1L staining cytoplasm. Also, in invasive ductal and lobular carcinomas, 70-90% of the tumor cells showed heavy CSE1L staining pattern predominantly in nuclei (Behrens et al., 2001).

Ovarian carcinoma

Prognosis

In serous ovarian carcinoma, moderate to strong immunostaining of CSE1L was observed in 34 of 41 cases (83%) of serous carcinomas, and CSE1L immunoreactivity was positively related to the frequency of apoptotic bodies ($p = 0.0170$), the tumor grade ($p = 0.0107$), and adverse outcomes ($p = 0.0035$). CSE1L protein reactivity was present in 100% of 69 ovarian carcinomas, and a significant reciprocal correlation was observed between high levels of CSE1L and the histological type, FIGO (International Federation of Obstetrics and Gynecology) stage III and grade 3, residual tumors of > 2 cm, and 20q13.2 (ZNF217 gene) amplification (> four copies in > 20% cells). A tissue array study composed of 244 serous ovarian tumors of different grades (0-3) and stages (I-IV) showed a higher expression of CSE1L in poorly compared to highly differentiated invasive ovarian tumors (Brustmann, 2004; Peiro et al., 2002; Ouellet et al., 2006).

Melanomas

Prognosis

Analysis of the expression of CSE1L in 27 control benign and 55 malignant melanocytic lesions (including 32 primary and 23 metastatic lesions), and the results showed that only 13 of the 27 benign melanocytic lesions stained positive for CSE1L. However, 5 of 7 lentigo maligna melanomas, 11 of 12 superficial spreading melanomas, and all acrolentiginous ($n = 7$) and nodular ($n = 6$) melanomas showed medium to high intensity immunoreactivity for CSE1L staining. All metastatic melanomas ($n = 23$) showed strong CSE1L staining. Also, CSE1L detection in clinical stages according to the International Union Against Cancer (UICC) showed an increase from 43% ± 34% CSEL-positive cells in stage I, to 53% ± 26% in stage II, 68% ± 24% in stage III, and 72% ± 24% in stage IV (Böni et al., 1999).

Lymphomas

Prognosis

In normal lymphoid tissue and malignant lymphomas, low-grade non-Hodgkin's lymphoma revealed weak CSE1L staining, with 10% to 60% of all cells positive. In contrast, highly malignant non-Hodgkin's lymphoma and malignant cells of Hodgkin's disease displayed very strong CSE1L positivity, with staining of up to 80% of atypical cells (Wellmann et al., 1997).

Endometrial carcinomas

Prognosis

An analysis of 89 endometrial carcinomas and 56 samples of non-neoplastic adjacent endometrium showed that CSE1L was expressed in 93% of endometrial carcinomas neoplastic tissues, while lower levels of CSE1L expression were observed in the adjacent endometrium compared to the carcinomas ($p = 0.003$). Also, CSE1L expression was higher in grade 3 tumors ($p = 0.002$) (Peiró et al., 2001).

Hepatocellular carcinomas

Prognosis

The expression of CSE1L was not detected in normal hepatocytes, while strong CSE1L expression was detected in hepatocellular carcinoma. Study also showed that the immunohistochemical staining intensity score of CSE1L was significantly higher in human hepatocellular carcinoma than in non-tumor tissue ($p < 0.05$) (Wellmann et al., 2001; Shiraki et al., 2006).

Lung cancer

Prognosis

The immunophenotypic profiling of non-small cell lung cancer progression using tissue microarray with 59 tissue samples, including 33 primary tumors without distant metastasis and 26 non-small cell lung cancer with brain metastases and showed that elevated expression of CSE1L was significantly associated with the metastatic potential of non-small cell lung cancer (Papay et al., 2007).

Gliomas

Prognosis

The results of array-based comparative genomic hybridization showed that 57.1% of the glioblastoma multiforme cases had high-frequency amplification of the CSE1L gene. Idbaih et al. investigated a series of 16 low-grade gliomas and their subsequent progression to higher-grade malignancies using a one-megabase bacterial artificial chromosome (BAC)-based array comparative genomic hybridization technique, and reported that the CSE1L gene was associated with the progression of gliomas (Hui et al., 2001; Idbaih et al., 2008).

Colorectal carcinoma

Prognosis

The expression of CSE1L was also reported to be higher in the primary and metastatic human colorectal carcinoma compared to the normal colon mucosa ($p < 0.0001$). Also, the concentration of CSE1L in serum is positively correlated with the stage of colorectal cancer (Stella Tsai et al., 2010; Seiden-Long et al., 2006).

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