

In non-Hodgkin lymphomas, cIAP1 was expressed in 73%, cIAP2 in 48% and XIAP in 15%. cIAP was positive in all precursor B-cell lymphoblastic lymphoma/leukemia and nodal marginal zone B-cell lymphoma, over 90% of follicular lymphoma and diffuse large B-cell lymphoma, and approximately 50 to 60% of myeloma, Burkitt lymphoma, lymphoplasmacytic lymphoma, small lymphocytic lymphoma/chronic lymphocytic leukemia, extranodal marginal zone B-cell lymphoma of mucosa associated lymphoid tissue (MALT-lymphoma), splenic marginal zone lymphoma, and mantle cell lymphoma.

In Hodgkin lymphomas, cIAP was positive in 75%, and were not correlated with histologic type (Akyurek et al., 2006). Treatment of diffuse large B-cell lymphoma cells with bortezomib caused apoptosis via involving the mitochondrial pathway and activation of caspases, and finally down-regulate the expression of cIAP1, XIAP and survivin (Uddin et al., 2008). Among multiple myeloma patients with increased multidrug-resistant (MDR) 1 expression after chemotherapy, those with a poor outcome exhibited significant increase in survivin, cIAP1, cIAP2, and XIAP expression by chemotherapy compared with those with a good prognosis. Similarly, in the lung resistance protein (LRP) expression-increased group, patients with a poor outcome showed significant increase of cIAP1 and cIAP2 expression compared with those with longer survival (Nakagawa et al., 2006). An integrated analysis of high-density oligonucleotide array CGH and gene expression profiling data from 155 multiple myeloma samples identified a promiscuous array of abnormalities contributing to the dysregulation of NF- κ B in approximately 20% of patients. Mutations in 10 genes causing the inactivation of TRAF2, TRAF3, CYLD, cIAP1/cIAP2 and the activation of NF- κ B1, NF- κ B2, CD40, LTBR, TACI, and NIK that result primarily in constitutive activation of the noncanonical NF- κ B pathway, with the single most common abnormality being inactivation of TRAF3 (Keats et al., 2007).

Myelodysplastic syndrome

Note

Overexpression of mRNA for survivin, cIAP1, NAIP and XIAP was significant in myelodysplastic syndrome bone marrow cells compared with control samples. However, the expression of mRNA for survivin, cIAP1 and cIAP2 exhibited a remarkable decrease after the development of overt leukemia (Yamamoto et al., 2004).

Squamous cell carcinoma of head and neck (HNSCC)

Note

Nuclear cIAP-1 expression was positive in 30% of HNSCC, was correlated with lymph node metastasis and advanced disease stage, and tends to be correlated with poor patient prognosis. Nuclear cIAP-1 expression

was inversely correlated with caspase-3 expression, but was correlated with Smac/DIABLO expression. Nuclear cIAP-1 expression appears to be a useful marker for predicting poor patient prognosis in HNSCCs, and may play roles in HNSCC through the signaling pathway mediated by Smac/DIABLO and caspase-3 (Tanimoto et al., 2005). Nuclear, cytoplasmic and concurrent cIAP-1 immunoreactions were significantly correlated with lymph node metastasis in tongue SCCs. Concurrent cIAP-1 expression was inversely correlated with caspase-3, but was positively correlated with Ki-67 expression. Both nuclear and cytoplasmic patterns of cIAP-1 expression were useful markers for predicting cervical lymph node metastasis in tongue SCC (Qi et al., 2008).

Squamous cell carcinoma (SCC) of esophagus

Note

High copy-number amplification at 11q21-q23 was identified in cell lines derived from esophageal SCCs using comparative genomic hybridization. Only cIAP1 was consistently overexpressed in cell lines that showed amplification. cIAP1 protein was overexpressed in the primary tumors from which those cell lines had been established. cIAP1 is likely to be a target for 11q21-23 amplification and may be involved in the progression of esophageal SCC (Imoto et al., 2001).

Squamous cell carcinoma (SCC) of uterine cervix

Note

In the 2 of 9 cell lines of cervical SCC showed amplification and consistent overexpression of cIAP1, as well as significant resistance to radiation-induced cell death as compared with cell lines showing no cIAP1 amplification. Both overall survival and local recurrence-free survival rates were significantly lower among patients with tumors showing high levels of nuclear cIAP1 staining than among patients whose tumors revealed little or no nuclear cIAP1. Multivariate analyses showed nuclear cIAP1 staining to be an independent predictive factor for local recurrence-free survival after radiotherapy among patients with cervical SCC (Imoto et al., 2002).

Adenoid cystic carcinoma of lacrymal gland

Note

Expression of cIAP1, cIAP2, XIAP and survivin was higher in adenoid cystic carcinoma than in pleomorphic adenoma of the lacrymal gland (Liao et al., 2009).

Nasopharyngeal carcinoma (NPC)

Note

Among the IAPs family, only transcription of survivin, HIAP-1 and HIAP-2/BIRC2 was consistently up-regulated in nasopharyngeal carcinoma (NPC) and

metastatic NPC tissues. Immunohistochemical staining showed that their proteins were more predominantly expressed in tumor cells nests. Survivin, HIAP-1 and HIAP-2 were upregulated by interleukin-1 alpha stimulation or EBV infection, and subsequently resulted in triggering rapid proliferation of NPC (Chua et al., 2008).

Lung cancer

Note

Amplification of chromosome 11q22 was detected in primary tumors and lung cancer cell lines of both non-small cell lung cancer and small cell lung cancer. Gene localized in this region included cIAP1 and cIAP2. Immunohistochemistry and western blot analysis identified cIAP1 and cIAP2 as potential oncogenes in this region as both were overexpressed in multiple lung cancers (Dai et al., 2003).

Malignant pleural mesothelioma

Note

IAP-1 was overexpressed in malignant pleural mesothelioma and is responsible for a large degree of the resistance of cultured mesothelioma cells to cisplatin. Levels of circulating TNF-alpha were significantly higher in mesothelioma patients prior to surgical tumor debulking compared with those after surgery. TNF-alpha could increase mRNA and protein levels of IAP-1, IAP-2 and XIAP. IAP gene expression levels were increased concomitantly with translocation to the nucleus of the TNF-responsive transcription factor NF-KB (Gordon et al., 2007).

Renal cell carcinoma

Note

Overexpression of cIAP1 and cIAP2 occurred in most renal cell carcinoma specimens, but 20% of the patients had lower cIAP levels in malignant than in normal tissue. The cIAP1 expression correlated with the tumor stage, levels being higher in pT1 tumors than in advanced pathological stages. Decreased cIAP1 expression in renal cell carcinoma relative to paired normal samples predicted an abbreviated time to recurrence and tumor-specific survival irrespectively of the tumor stage and grade. The prognostic effect of cIAP1 was most pronounced in patients with pT3 disease. The results of uni- and multivariate analyses suggested a prognostic value of cIAP1 expression for renal cell carcinoma patients, downregulation indicating an aggressive, potentially lethal phenotype (Kempkensteffen et al., 2007).

Pancreatic neoplasms

Note

cIAP1 expression was constantly high in non-neoplastic pancreatic tissues, in pancreatic intraepithelial neoplasia lesions, as well as in a subset of primary and metastatic pancreatic ductal adenocarcinomas, and a preferential cytoplasmic

localisation was observed in the tumor tissues. cIAP expression was rare in a cystic tumors. Survival analyses revealed a shorter survival in patients with cIAP1/cIAP2-positive tumors (Esposito et al., 2007).

Endometrial cancer

Note

cIAP-1 expression was high in endometrial cancer cells expressing phospho-Akt. Akt phosphorylation decreased and apoptosis was strongly increased in PTEN-mutated endometrial cancer cells in the presence of phosphatidylinositol 3 kinase (PI3-K) inhibitor which was accompanied by a down-regulation of cIAP-1. Overexpression of Akt using a constitutively active Akt expression vector resulted in an up-regulation of cIAP-1 expression. Akt regulated endometrial cancer cell survival through the up-regulation of cIAP-1 (Gagnon et al., 2003).

Various cancer cell lines

Note

cIAP1 and XIAP were expressed in most cancer lines analysed, with substantial variability in their relative levels. Higher levels of cIAP1 protein were associated with resistance to several anticancer drugs (Tamm et al., 2000). IAPs were induced by NF-KB or v-Rel in multiple cell lines and conversely, HIAP1 and HIAP2 activated NF-kappaB possibly forming a positive feedback loop (LaCasse et al., 1998). cIAP1 and cIAP2 promoted cancer cell survival by functioning as E3 ubiquitin ligases that maintain constitutive ubiquitination of the RIP1 adaptor protein (Bertrand et al., 2008).

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This article should be referenced as such:

Maeshima A, Tsuda H. BIRC2 (baculoviral IAP repeat-containing 2). *Atlas Genet Cytogenet Oncol Haematol.* 2010; 14(5):440-443.
