Gene Section
Review

BCL2L1 (BCL2-like 1)

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Identity

Other names: BCL-XL/S; BCL2L; BCLX; Bcl-X; Bcl2-L-1; DKFZp781P2092; bcl-xL; bcl-xS
HGNC (Hugo): BCL2L1

Location: 20q11.21

Local order: According to GeneLoc and NCBI Map Viewer, genes flanking BCL2L1 in plus strand direction are: COX4I2 (20q11.21; cytochrome c oxidase subunit IV isoform 2 (lung)); MYLK2 (20q11.21; myosin light chain kinase 2).

Note: The Bcl2L1 proteins are encoded by BCL2L1 gene. Bcl2L1 proteins belong to the BCL-2 protein family; the members of this family form hetero- or homodimers and act as anti- or pro-apoptotic regulators that are involved in a wide variety of cellular activities. Bcl2L1 proteins are located outer mitochondrial membrane, and have been shown to regulate mitochondrial membrane channel (VDAC) opening. VDAC regulates mitochondrial membrane potential, and thus controls the production of reactive oxygen species and release of cytochrome C by mitochondria, both of which are the potent inducers of cell apoptosis.

DNA/RNA

Description

Bcl2L1 DNA contains 58394 bps (genomic size) and RNA 2575 bps. Bcl2L1, member of the Bcl-2 protein family, plays a role in the regulation of apoptosis. Two major isoforms exist due to alternative splicing of the BCL2L1 mRNA: Bcl-xS and Bcl-xL.

The bcl-x promoter contains consensus motifs for a number of transcription factors, as Sp1, AP-1, Oct-1, Ets, Rel/NF-kB, STATs, and GATA-1, in which three transcription factor families, STATs, Rel/NF-kB, and Ets family, have been demonstrated to play an important role in the regulation of bcl-x gene expression (Grillot et al., 1997). Bcl-xS has 3 exons (contains exon2b shortly than 2a), and forms a heterodimer with bcl2 to promoting apoptosis.

Bcl-xL has 4 exons (contains exon 2a) and form heterodimer with Bax, Bak and has cell death repressing activity (Tamura et al., 2009).

Bcl-xL protein can be regulated post-transcriptionally and it is mainly controlled at the gene expression level (Grad et al., 2000). Bcl-xL protects cells from apoptosis by regulating mitochondria membrane potential by interacting with pro-apoptotic members Bax or Bim and subsequently prevents the release of cytochrome C. Bcl-xL protein displays remarkable amino acid and structural homology to Bcl-2 (González-García et al., 1994).

At the post-translational level, Bcl-xL is phosphorylated by SAPK/JNK after exposure to microtubule-damaging drugs (Portuchynsky et al., 1998; Basu et al., 2003). Bcl-xL resides in the nuclear envelope, extra-nuclear membranes, including the mitochondrion but also cytosol (González-García et al., 1994).
Polymorphism
In a study of 105 patients with multiple sclerosis relapsing disease it was identified sequence alterations in the promoter region BCL-X gene (Kuhlmann et al., 2002).

Protein

Description
Three alternatively transcript variants, which encode distinct isoforms, have been reported. The longer isoform Bcl-xL acts as an apoptotic inhibitor and the shorter form Bcl-xS acts as an apoptotic activator (Boise et al., 1993). The last one Bcl-x(beta) differs from the longer and the shorter forms by a modification of the last 45 amino acids (Ban et al., 1998). The BH1 and BH2 motifs are required for both heterodimerization with other Bcl-2 family members, and for repression of cell death. The BH4 motif is required for anti-apoptotic activity. Thus, Bcl-xL forms homodimers and heterodimers with Bak (6p21.31; BCL2-antagonist/killer 1) isoform Sigma, Bax (19q13.33; BCL2-associated X protein) and Bcl2 (18q21.3; B-cell leukemia/lymphoma 2). Heterodimerization with Bax does not seem to be required for anti-apoptotic activity. Also interacts with Bad (11q13.1; BCL2-antagonist of cell death), Bbc3 (19q13.3-q13.4; BCL2 binding component 3), Siva isoform 1 (14q32.33), BCL2L11 (2q13; BCL2-like 11 (apoptosis facilitator)), BECN1 (17q21.31; Beclin-1), and PGAM5 (12q24.33; phosphoglycerate mutase family member 5). Like Bcl-xL, Bcl-x(beta) binds to the pro-apoptotic protein Bax, suggesting a functional activity in vivo (Ban et al., 1998).

Expression
The expression of Bcl-xL and Bcl-xS appeared differentially regulated in human tissues. Bcl-xS is expressed at high levels in cells that undergo a high rate of turnover, such as developing lymphocytes. In contrast, Bcl-xL is found in tissues containing long-lived postmitotic cells, such as adult brain (Boise et al., 1993).

Localisation
Bcl-xL resides in the nuclear envelope, extra-nuclear membranes, including the mitochondrion but also cytosol (González-García et al., 1994).

Function
The Bcl-xL isoform is a potent inhibitor of cell death. Its association with SIVA-1 inhibits its anti-apoptotic activity (Chu et al., 2004). The binding of this isoform to the voltage-dependent anion channel (VDAC) regulates cell death by blocking it and preventing the release of the cytochrome into the cytoplasm (Vander Heiden et al., 2001; Malia et al., 2007). In contrast to Bcl-xL isoform, the Bcl-xS isoform promotes apoptosis.
Bcl-xS induces apoptosis in a caspase- and BH3-dependent manner by a mechanism involving cytochrome c release. BAK and BAX can be involved in Bcl-xS induced apoptosis (Kim et al., 2004; Lindenboim et al., 2005). Bcl-xL mutants correlate with their ability to form homodimers (Jeong et al., 2004).

**Mutations**

*Note*

Few mutations are described. Thus, in 50 non-Hodgkin's lymphoma cases it was found one missense mutation in a patient with diffuse large B-cell lymphoma. Sequence analysis of this case showed that AGC (Ser) was mutated to GGC (Gly) in codon 154 (Yamaguchi et al., 2002). In one case of follicular lymphoma mutation analysis revealed one synonymus mutation (Codon 109 ACA-->ACC) (Liu et al., 2006). The experimentally mutagenesis is described on: Uniprot.

**Implicated in**

**Antiapoptotic role**

*Note*

BCL-xL has been shown to inhibit cell death induced by a number of apoptotic stimuli including gamma irradiation, glucocorticoids, and anti-CD3 treatment (Boise et al., 1993; Chao et al., 1995; Chao et al., 1997). Down regulating the basal level of BCL-xL by RNA interference induces apoptosis in aged human fibroblasts without further stress, indicates that Bcl-xL is an important factor in cell-death control in old fibroblasts (Rochette et al., 2008). This was described in other cell type: in hepatocellular carcinoma cells Hepg2 (Lei et al., 2006), in nasopharyngeal carcinoma cells (Liu et al., 2005) or in esophageal cancer cells (Xie et al., 2006). In colorectal carcinoma (CRC) cell lines and in tissue it was shown that Bcl-xL contributes to apoptosis resistance. Same authors demonstrated that CRC cells with reduced Bcl-xL expression were more sensitive towards oxaliplatin- irinotecan, and 5-FU while, Bcl-xL plasmid transfection decreased chemotherapeutic drug-induced apoptosis (Schulze-Bergkamen et al., 2008). In another study using pancreatic, prostate and leukemic cells treated with benzylisothiocyanate Bcl-xL was phosphorylated and in parallel an enhancement of apoptosis (Basu et al., 2008). In HepG2 cells treated with topotecan it was shown that the expression of Bcl-xL was simultaneously down-regulated with the up-regulation of Bcl-xS in cytoplasm, which could explain the induction of apoptosis (Zhang et al., 2008). Bcl-2 and Bcl-xL inhibit apoptosis induced by a variety of agents in MCF-7 cells. MCF-7 cell lines expressing Bcl-xL and Bcl-2 were protected against apoptosis induced by TNFa and doxorubicin (Fiebig et al., 2006). PUMA (19q13.3-q13.4); p53-upregulated modulator of apoptosis) interacts with anti-apoptotic Bcl-2 and Bcl-xL and is dependent on Bax to induce apoptosis. PUMA initiates apoptosis in part by dissociating Bax and Bcl-xL, thereby promoting Bax multimerization and mitochondrial translocation (Ming et al., 2006).

**Autophagy**

*Note*

It was shown that in normal conditions, Beclin 1 (17q21.31; autophagy related) is bound to and inhibited by Bcl-2 or the Bcl-xL. This interaction involves a BH3 domain in Beclin 1 and the BH3 binding groove of Bcl-2/Bcl-xL. But other proteins containing BH3 domains, called BH3-only proteins, can competitively disrupt the interaction between Beclin 1 and Bcl-2/Bcl-xL to induce autophagy (Levine et al., 2008). The overexpression of Bcl-xL enhances autophagic cell death when apoptotic cell death is inhibited in Bax(-/-)/Bak(-/-) double knockout cells (Kim, 2005).

**Quiescence regulation**

*Note*

It was shown that Bcl-xL facilitate G0 quiescence by decreasing RNA content and stabilization an up-regulation of p27 protein (14q32.13; interferon, alpha-inducible protein 27) due to phosphorylation of p27 at Ser(10) by the kinase Mirk (19q13.2) (Janumyan et al., 2008). P27 protein upregulation could delay cell cycle re-entrning throught inhibition of Myc (8q24) activity (Greider et al., 2002).
**Senescence**

**Note**

In human diploid fibroblasts it was demonstrated the role of BCL-xL for pre-senescence state induction with decline of the ability of genotoxic stress to induce apoptosis. It was found that aged cells became progressively more resistant to UV-induced apoptosis with apoptosis reduction of 10-20 folds. In young cells, the level of anti-apoptotic protein BCL-xL decrease after UV irradiation while pro-apoptotic protein Bax increases. The increase in Bax tracked the level of p53 BCL-xL is itself responsible for the pre-senescence decline in the ability of a genotoxic stress to induce apoptosis. Acquired apoptosis resistance at late passage is associated with altered UVB-regulation of Bcl family members. Bcl-xL is a major contributor to UV-induced apoptosis resistance in older cells (Rochette et al., 2008).

**Human neural stem cells**

**Disease**

Bcl-xL enhances dopaminergic neuron generation from human neural stem cells and mouse embryonic stem cells (Shim et al., 2004).

**Oncogenesis**

Using human cell line hNS1 cell line with v-myc (8q24; v-myc myelocytomatosis viral oncogene homolog) immortalized and non-immortalized it was found that Bcl-xL controls the balance between the generation of neurons and glia from differentiating immortalized and non-immortalized hNSCs differentiation (Liste et al., 2007).

**Cutaneous cell carcinoma**

**Disease**

Squamous cell carcinoma, a non melanoma skin cancer, is a common malignancy in the worldwide Caucasian population. Keratocarcinoma is a common neoplasm of the skin and is typically characterised by rapid growth. These two forms are difficult to distinguish by histology.

**Oncogenesis**

In a series of twenty five squamous carcinoma (SCC) and sixty four keratocarcinoma (KA), stained for bcl-xL, the authors detected that the two lesions differed significantly in expression of Bcl-xL which was present in 84% of the SCC compared with only 15% in the KA (Vasiljevic et al., 2009).

**Colorectal cancers**

**Oncogenesis**

Bcl-xL shows a strong correlation with TGF-beta1 (19q13.2, transforming growth factor, beta 1) and Bax (19q13.33; BCL2-associated X protein) in colorectal cancers especially in deeply invading cancers (pT3+pT4) instead of superficially growing tumors (pT1+pT2) (Sulkowski et al., 2009). In a study with fifty-six pair tissue samples from patients with colon cancer Bcl-xL expression was higher in cancerous tissue than in normal tissue and it was associated with the pathological grade and lymph node metastasis. Furthermore, in vitro transfection with Bcl-xL siRNA inhibited the colony formation and invasion ability of human colon cancer cell line HT29 (Zhang et al., 2008). Caco-2 colon cancer cells treated with Bcl-xL antisense oligonucleotides in combination with IR or cisplatin showed reduction of the Bcl-xL protein level by almost 50% and increase of apoptosis and reduction of cell proliferation suggesting that Bcl-xL is an important factor contributing to the treatment resistance (Wacheck et al., 2003). siRNA Bcl-xL specific could knockdown Bcl-xL protein expression and inhibit proliferation more effectively in 5-FU-resistant cells than in 5-FU-sensitive cells (Zhu et al., 2005). Bcl-xL was found correlated with Hif1 alpha (14q23.2; hypoxia inducible factor 1, alpha subunit) in moderately and poorly differentiated rectal and colonic tumors (Wincewicz et al., 2007).

**Renal cell carcinoma**

**Disease**

The expression of Bcl2 and/or Bcl-xL in normal tissue is low in normal kidney.

**Oncogenesis**

Renal cell carcinoma (RCC) expressing high levels of Bcl-xL and/or Bcl2 do not show any apoptotic cells, and conversely when the expression of these proteins was not detected, apoptosis was highly present (Gobé et al., 2002).

**Pancreatic carcinoma**

**Oncogenesis**

A study using 25 patients showed an inverse association for the Bcl-xL, score and apoptotic index. Bcl2 and Bax protein levels did not show any association with the apoptotic index and were overexpressed in most of the pancreatic cancer samples (Sharma et al., 2005).

**Prostate carcinoma**

**Disease**

Bcl-xL protein was detected in the epithelial cells of normal prostate gland and prostate cancers.

**Oncogenesis**

Increased levels of Bcl-xL were found to be correlated with higher grade indicating a possible role of Bcl-xL in prostate cancer progression (Krajewski et al., 1994). Interactions of Bcl-xL with Bax (19q13.33; BCL2-associated X protein) and Bak (6p21.31; BCL2-antagonist/killer 1) were evidenced in lysates from high-grade prostate cancer tissues and Bcl-xL would
exert an inhibitory effect over Bak via heterodimerization (Castilla et al., 2006) whereas blocking Bcl-xL expression in prostate cancer cells decreased cell proliferation (Vilenchik et al., 2002). These interactions may provide mechanisms for suppressing the activity of proapoptotic Bax and Bak in prostate cancer cells and that Bcl-xL expression contributes to androgen resistance and progression of prostate cancer.

**Lung carcinoma**

**Oncogenesis**

Biopsies from 30 cases of squamous cell carcinoma of the lung in stage III were assessed for the expression of Bcl-2, Bcl-xL, TP53 (17p13; Tumor protein p53) and Bax (19q13.33; BCL2-associated X protein) at the mRNA protein levels and immunohistochemistry. The apoptotic index correlated with Bax expression but not with Bcl-2, Bcl-xL or p53 levels (Shabnam et al., 2004).

**Bladder cancer**

**Oncogenesis**

In a study with 42 samples of bladder transitional cell carcinoma Bcl-x overexpression was observed in 45.2% but this overexpression was not correlated with recurrence or survival (Kirsh et al., 1998). In another study on 72 patients with muscle-invasive bilharzial squamous cell carcinoma of the urinary bladder, Bcl-xL overexpression was associated with tumor progression (Hameed et al., 2008).

**Hepatocellular carcinoma**

**Oncogenesis**

In a study using 33 hepatocellular carcinomas (HCC) Bcl-xL overexpression was found in 63.6% cancer specimens (Watanabe et al., 2004). In another study, performed on 42 patients with HCC, it was shown that Bcl-xL expression was present in cancerous and non-cancerous tissue whereas elevated levels Bcl-xL were found in tumor tissue in the cytoplasm and the nuclei from two thirds of the patients (Watanabe et al., 2002). Bcl-2 and bcl-xL may play an important role in regulating the apoptosis of normal liver and HCC (Guo et al., 2002).

**Breast cancer**

**Oncogenesis**

Most breast cancer cells overexpress Bcl-xL and Bcl-2 (Simonian et al., 1997). Increased levels of Bcl-xL expression were found in primary human breast carcinomas, mainly in undifferentiated tumors (Olopade et al., 1997; Sierra et al., 1998). Using orthotopic xenograft tumors in nude mice obtained from human breast cancer cells lines MDA-MB 435, MDA-MB 468 and MCF-7 it was observed that the overexpression of Bcl-2 or Bcl-xL influenced tumorigenicity. Overexpression of Bcl-xL was associated with the loss of apoptosis in breast cancer cells in vivo (Fernández et al., 2002).

**Soft tissue sarcomas**

**Oncogenesis**

In a study of eighty-two soft tissue sarcomas (STS), a combined high Bad/Bcl-xL mRNA expression levels revealed a 20-fold increase and a worse prognosis (Köhler et al., 2002).

**Giant cell tumor of bone**

**Disease**

Giant cell tumor of bone (GCTb) is a benign but locally aggressive tumor that infrequently shows metastatic spread to the lungs (Bertoni et al., 2003).

**Oncogenesis**

Using array comparative genomic hybridization performed on 20 frozen tumor samples of GCTb, the authors showed that the most frequent region of change identified was amplification of a 1 Mbp region at 20q11.1, which contains BCL2L1 gene. These results were confirmed by Southern blot (Smith et al., 2006).

**Non-Hodgkin's lymphoma**

**Oncogenesis**

In non-Hodgkin's lymphoma, Bcl-xL is overexpressed when compared with normal B cells (Xerri et al., 1999). Rituximab (Rituxan, IDEC-C2B8) has been shown to sensitize non-Hodgkin’s lymphoma (NHL) cell lines to chemotherapeutic drug-induced apoptosis and selectively down-regulated Bcl-xL (Jazirehi et al., 2003). The down-regulation of Bcl-xL by Rituximab is dependant on up-regulation of Raf kinase inhibitor protein RKIP on the ERK1/ERK2 pathway (Jazirehi et al., 2004). In a study of 15 patients with reactive hyperplasia, BCL-xL was overexpressed in follicular lymphoma. No significant rise of BCL-xL expression was observed in 24 patients with T-cell lymphoma and 24 patients with a diffuse large B-cell lymphoma (Liu et al., 2006). In another study of 50 non-Hodgkin’s lymphoma cases Bcl-xL one missense mutations of the transcript in a patient with diffuse large B-cell lymphoma was found. Sequence analysis of this case showed that AGC (Ser) was mutated to GGC (Gly) in
codon 154 with a possibly role in the tumorigenesis of non-Hodgkin's lymphoma (Yamaguchi et al., 2002).

**Follicular lymphomas**

**Oncogenesis**

In follicular lymphoma and primary cutaneous follicle center lymphomas, bcl-xL gene overexpression was linked to short overall survival times. In a study of 20 patients with primary cutaneous follicle center lymphomas Bcl-xL expression is significantly higher in biopsies of patients, who developed relapse or disease progression later compared with patients who did not. Higher levels of bcl-xL gene expression were significantly correlated with shorter progression-free survival. This suggesting that bcl-xL overexpression is inversely correlated with progression-free survival suggests that bcl-xL, through its anti-apoptotic effect, might contribute to tumor cell survival (Soltani-Arabshahi et al., 2009). In another study were analysed 27 samples of follicular lymphoma, bcl-xL gene overexpression was linked to short overall survival times (Zhao et al., 2004). Moreover, in follicular lymphoma, high Bcl-xL level was associated with multiple extranodal involvement, elevated lactate dehydrogenase level, high-risk international prognostic index and a short overall survival time. In one case of follicular lymphoma mutation analysis revealed one synonymous mutation (Codon 109 ACA-->ACC) (Liu et al., 2006). In a recent study of follicular lymphoma, it has been demonstrated that TRAIL was cytotoxic only in follicular lymphoma B cells. The engagement of CD40 by its ligand CD40 induces a rapid RNA and protein up-regulation of c-FLIP and Bcl-xL. The antiapoptotic signaling of CD40, which interferes with TRAIL-induced apoptosis in follicular lymphoma B cells, involves NF-kappaB-mediated induction of c-FLIP and Bcl-xL, which can respectively interfere with caspase 8 activation or mitochondrial-mediated apoptosis (Travert et al., 2008).

**Chronic lymphocytic leukemia**

**Oncogenesis**

B cell chronic lymphocytic leukemia (B-CLL) cannot be cured with conventional chemotherapy because B-CLL cells are resistant to programmed cell death and arrested in G0/G1 phase of the cell cycle. In B-CLL cells, levels of the anti-apoptotic Bcl-xL showed a positive correlation with levels of the 80 kDa regulatory component (Ku80) of the DNA-dependent protein kinase that is involved in DNA double-stranded break repair (Klein et al., 2000). It has also been demonstrated in B-CLL that CD40 stimulation enhanced the constitutive anti-apoptotic profile of B-CLL cells by upregulation of Bcl-xL. Functionally, CD40-stimulated B-CLL cells became resistant to drug-induced apoptosis (Kater et al., 2004). More recently, in 60 chronic lymphocytic leukemias (CLL) treated with ABT-737 and its orally active analog, ABT-263, revealed that the resistance occurred upstream of mitochondrial perturbation and involved de novo synthesis of the anti-apoptotic protein BCL-xL, which could be responsible for resistance to ABT-737. After therapy with ABT-737-related inhibitors, resistant CLL cells might develop in lymph nodes in vivo and that treatment strategies targeting multiple Bcl2 antiapoptotic members simultaneously may have synergistic activity (Vogler et al., 2009).

**Acute lymphoblastic leukemia (ALL)**

**Oncogenesis**

Dexamethasone (Dex) is a glucocorticoid inducing apoptosis. Dex induced significant down-regulation of the anti-apoptotic Bcl-2 family members Bcl-2 and Bcl-xL. In 12 primary childhood ALL samples, Dex-induced apoptosis was associated with activation of Bax and down-regulation of Bcl-2 and/or Bcl-xL (Laane et al., 2007). The first study which has demonstrated a role of Bcl-xL in childhood acute lymphoblastic leukemia was published in 1997. The expression and the regulation of Bcl-2, Bcl-xL, and Bax has been correlated with p53 status and sensitivity to apoptosis in childhood acute lymphoblastic leukemia (Findley et al., 1997). The resistance to glucocorticoid treatment is often associated with treatment failure in children with acute lymphoblastic leukaemia (ALL). In 30 consecutive children with ALL treated with prednisone, Bcl-2 and Bcl-xL protein in 28 samples. Prednison treatment induced a decrease in Bcl-2 and Bcl-xL levels in 17 and 16 of the 28 patients, respectively. A statistically significant decrease was only observed for Bcl-xL protein expression in T phenotype ALL, in the poor responder group and in patients with >20000/mm(3) white cell count (WBC) at diagnosis. This study suggested a role of Bcl-xL in the mechanisms of protection of leukemic cells from apoptosis induced by glucocorticoids (Casale et al., 2003). In a series of 62 consecutive children, only the good response to prednisone and the low intensity of Bcl-xL expression were independent significant prognostic factors (Casale et al., 2003).

**References**


Chao DT, Korsmeyer SJ. BCL-XL-regulated apoptosis in T cell development. Int Immunol. 1997 Sep;9(9):1375-84
BCL2L1 (BCL2-like 1) Varna M, et al.


Grad JM, Zeng XR, Boise LH. Regulation of Bcl-xL: a little bit of this and a little bit of STAT. Curr Opin Oncol. 2000 Nov;12(6):543-9


Greider C, Chappapathayya A, Parkhurst C, Yang E. BCL-x(L) and BCL2 delay Myc-induc- ed cell cycle entry through elevation of p27 and inhibition of G1 cyclin-dependent kinases. Oncogene. 2002 Nov 7;21(51):7765-75


Chu F, Borthakur A, Sun X, Barking J, Gudi R, Hawkins S, Prasad KV. The Siva-1 putative amphipathic helical region (SAH) is sufficient to bind to BCL-XL and sensitize cells to UV radiation induced apoptosis. Apoptosis. 2004 Jan;9(1):83-95


Jeong SY, Gaume B, Lee YJ, Hsu YT, Ryu SW, Yoon SH, Youle RJ. Bcl-x(L) sequesters its C-terminal membrane anchor in soluble, cytosolic homodimers. EMBO J. 2004 May 20;23(11):2456-55


Shabnam MS, Srinivasan R, Wali A, Majumdar S, Joshi K, Behera D. Expression of p53 protein and the apoptotic...


Castilla C, Congregado B, Chinchón D, Torrubia FJ, Japan MA, Saez C. Bcl-xL is overexpressed in hormone-resistant prostate cancer and promotes survival of LNCaP cells via interaction with proapoptotic Bak. Endocrinology. 2006 Oct;147(10):4960-7


Rochette PJ, Brash DE. Progressive apoptosis resistance prior to senescence and control by the anti-apoptotic protein BCL-XL. Mech Ageing Dev. 2008 Apr;129(4):207-14


correlated with lower apoptotic cell numbers and shorter progression-free survival in PCFCL. J Invest Dermatol. 2009 Jul;129(7):1703-9


Tan KB, Lee YS. Immunoexpression of Bcl-x in squamous cell carcinoma and keratoacanthoma: differences in pattern and correlation with pathobiology. Histopathology. 2009 Sep;55(3):338-45


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