Global Journals LaTeX JournalKaleidoscope™
Artificial Intelligence formulated this projection for compatibility purposes from the original article published at Global Journals. However, this technology is currently in beta. *Therefore, kindly ignore odd layouts, missed formulae, text, tables, or figures.*

# "Cell Cycle Aberration in Ameloblastoma: As Evidenced by an Immunohistochemical Expression of p53 and Survivin"

Dr. Zulfin Shaikh[1] and Dr. Niranjan K C[2]

[1] SDM College of Dental Sciences and Hospital, Dharwad. Rajiv Gandhi University of Health Sciences, Bangalore

*Received: 6 December 2013 Accepted: 3 January 2014 Published: 15 January 2014*

## Abstract

Evasion from apoptosis by aberrations of apoptotic regulatory factors has been found to cause accumulation of neoplastic cells in various tumours. Survivin, an inhibitor of apoptosis protein localizes to the nucleus as well as in the cytoplasm depending on its function such as cell division and inhibiting apoptosis. The regulation of Survivin seems to be linked to p53, a tumour suppressor gene. Though there are studies showing the role of p53 and Survivin in oral carcinogenesis, but the field of odontogenic tumours yet needs to be explored. The aim of this study was to correlate the expression of p53 and Survivin in normal tissues (tooth germ) and Ameloblastoma as well as to assess differential localization of Survivin. Qualitative and quantitative assessment of immunexpression of p53 and Survivin (nuclear and cytoplasmic) was evaluated in a total of 35 cases which included 10 tooth germs and 25 Ameloblastoma. The expression levels of p53 and nuclear Survivin were significantly higher in Ameloblastoma quantitatively but there was no significant correlation between p53 and cytoplasmic expression of Survivin. There was up-regulation of both p53 and Survivin in Ameloblastoma. This study highlights the nuclear and cytoplasmic expression of Survivin and p53 in tumorigenesis of Ameloblastoma.

***Index terms***— apoptosis, survivin, p53, ameloblastoma, immunohistochemical expression, tumorigenesis, aberrations, tumour suppressor gene, inhibitor of apoptosis pr

## 1 Introduction

dontogenic tumours comprise a complex group of lesions exhibiting considerable variations in clinical and histological behavior [1]. A series of genetic and molecular alterations appear to promote the development and progression of these tumours [2]. Ameloblastoma is an epithelial odontogenic tumour characterized by a benign but locally invasive behavior, with a high risk of recurrence. Ameloblastoma shows Author ?: Assistant Professor, Department of Oral and Maxillofacial Pathology and Microbiology, Al-badar Dental College and Hospital, Gulbarga, Karnataka, India. Author ?: Associate Professor, Department of Oral and Maxillofacial Pathology and Microbiology, SDM College of Dental Sciences and Hospital, Dharwad, Karnataka, India. e-mail: niranjankc29@gmail.com solid/multicystic, unicystic, peripheral and desmoplastic [3].

Regulation of the cell cycle and control of apoptosis are thought to be intimately linked processes in maintaining homeostasis and developmental morphogenesis [4]. TP53 is one of the most frequently altered tumour suppressor genes and its gene products play an important role in response to genomic damage by inducing cell cycle arrest and apoptosis [2]. TP53 encompasses 16-20kb of DNA on human chromosome 17pl3.1 [5].

Apoptosis, also known as programmed cell death or physiological cell death, has diverse roles in development and normal homeostasis as well as in a variety of pathological conditions [6]. Survivin, a member of inhibitor of apoptosis protein family (IAP), has a molecular weight of 16.5kDa and the gene is located on chromosome 17q25

[7]. It is a unique bifunctional protein which suppresses apoptosis by inhibiting caspase-3 and caspase-9 and regulates G2/M phase of the cell cycle by associating with mitotic spindle microtubules. It is highly expressed in embryonic tissues and neoplasm's but is absent in terminally differentiated cells [8]. Several studies have proposed that the sub-cellular distribution of Survivin is regulated by active import into the nucleus and CRM1-mediated export to the cytoplasm [9][10][11]. Recent studies have suggested that the nuclear pool of Survivin is involved in promoting cell proliferation, whereas the cytoplasmic pool of Survivin controls cell survival [9,10,12,13].

Mutation of p53 in tumours causes over expression of Survivin which rescues cells from p53 induced apoptosis [14]. Survivin is highly expressed in most human tumours of the oral cavity, lung, colon, breast, liver, gastrointestinal and prostate [15][16][17][18][19][20][21]. The expression of Survivin in odontogenic epithelial cells has already been described [22][23][24], but to date, no study has investigated the relationship between nuclear and cytoplasmic expression of Survivin in odontogenic tumours. The role of p53 in various tumours has been extensively studied but there are few reports about its assess nuclear and cytoplasmic localization of Survivin in Ameloblastoma to gain a better insight into its tumorigenesis.

# 2 II.

# 3 Materials and Methods

Twenty five formalin fixed paraffin embedded tissue blocks with histological diagnosis of Ameloblastoma were retrieved from the archives of the Department of Oral and Maxillofacial Pathology, SDM College of Dental Sciences and Hospital, Dharwad. The study sample being an odontogenic tumour, the control tissue included ten tooth germs taken from the postmortem fetal oral tissues fixed in 10% formalin. All the tooth germs taken were between 20 th to 25 th weeks of gestation.

The study was approved by the institutional ethics committee. Immunostaining was performed using the super sensitive polymer -Horseradish Peroxidase (HRP) detection system, a biotin free detection system supplied by Biogenex life sciences limited [California, USA]. The paraffin-embedded tissues were cut into fourmicrometer thick sections, mounted on aminopropyltriethoxysilane (APES) coated slides, deparaffinized in xylene, rehydrated in alcohol and then treated with 3% hydrogen peroxide for 10 minutes.

The tissue sections were then incubated with primary antibodies against p53 [Mouse monoclonal, Clone DO7, IgG2b immunoglobulin; Biogenex Ltd, USA; diluted at 1:150] and Survivin [Rabbit monoclonal, Clone EP28880Y, IgG immunoglobulin; Biogenex Ltd, USA; diluted at 1:40] as per the instructions given by the manufacturer. Next, the tissue sections were incubated with the secondary antibody and immunoreactivity was visualized with 3, 3-diaminobenzidine solution. Finally, the sections were counterstained with Harri's hematoxylin.

Two independent observers scored all samples in a blinded manner and no interobserver variability was observed. An immunoreactivity scoring system was applied as follows [25]: (i) the staining intensity was graded on a four point scale such as '0' for no staining, '1' for mild staining, '2' for moderate staining and '3' for by 100 and the score was expressed as the percentage of positive cells. Nuclear (A) and cytoplasmic (B) expression of Survivin was assessed separately. The results were subjected to statistical analysis. Mann Whitney U test was performed to determine the significance of p53 and Survivin expression between tooth germ and Ameloblastoma. Wilcoxon Signed Ranks test was used to assess the significance between p53 and Survivin expression in each group. Pearson's correlation test was done to determine the correlation between p53 and Survivin expression in each group. A p-value of $<0.05$ was considered as statistically significant.

III.

# 4 Results

The study sample of 25 Ameloblastoma included 12 follicular, 4 plexiform and 9 cases of unicystic subtypes. Out of ten tooth germs five showed hard tissue formation. a) p53 expression in tooth germ and Ameloblastoma p53 expression was localized to the nucleus [Figure 1] with predominant intense staining compared to that of tooth germ [Table 1]. Out of ten tooth germs, p53 expression was seen in six tooth germs and was more evident in inner enamel epithelial cells than in stellate reticulum & outer enamel epithelial cells [Figure 1a]. In Ameloblastoma, p53 was expressed in all the tissues. In follicular and plexiform subtypes, p53 expression was seen in peripheral ameloblast-like and few central stellate reticulum-like cells [Figure 1b & 1c] and in unicystic variant, expression was seen in basal and suprabasal cells [Figure 1d]. p53 expression was statistically significant between tooth germ and Ameloblastoma in the number of positive cells but no significance was seen in relation to the staining intensity [Table 2]. 2]. The staining intensity was predominantly moderate in Ameloblastoma compared to tooth germ [Table 3]. Out of ten tooth germs, Survivin was expressed in five tooth germs with cytoplasmic expression in inner enamel epithelial cells, stellate reticulum & outer enamel epithelial cells with focal nuclear expression in inner enamel epithelial cells [Figure 2a]. In follicular and plexiform ameloblastoma, Survivin showed cytoplasmic expression both in peripheral ameloblast-like and central stellate reticulumlike cells with focal nuclear expression in peripheral cells [Figure 2b & 2c]. Among unicystic ameloblastoma, cytoplasmic expression of Survivin was seen in basal and suprabasal cells with focal nuclear staining in basal cells [Figure 2d]. Similar to p53, Survivin expression was statistically significant between tooth germ and Ameloblastoma but no significance was seen with respect to staining intensity [Table 4]. Four tooth germs showed both p53 and Survivin expression, three showed negative staining for both p53 and Survivin, two tooth germs had only p53

expression and one tooth germ showed only Survivin expression. A positive correlation was found between p53 and Survivin expression in Ameloblastoma [r=0.251, p=0.226]. We found that p53 and Survivin expression was statistically significant in Ameloblastoma with respect to staining intensity [Table 5]. Quantitatively, p53 and nuclear Survivin was statistically significant in Ameloblastoma [p=0.000] but no significance was seen in p53 and cytoplasmic expression of Survivin in Ameloblastoma [p=0.330]. Due to focal expression of Survivin in the nucleus of normal and neoplastic cells, a statistical correlation could not be obtained between cytoplasmic and nuclear Survivin. IV.

# 5 Discussion

Various concepts have been proposed which explain the pathogenesis of odontogenic tumours, but what causes odontogenic cells to transform into an odontogenic tumour is yet to be explored [23]. p53, a tumour suppressor gene, acts as a 'molecular policeman' by monitoring the integrity of the genome. If DNA is damaged, p53 accumulates and switches off cell replication to allow extra time for repair mechanisms to act. If the repair fails, p53 triggers cell suicide by apoptosis [26].

Survivin, an inhibitor of has been shown by disruption of Survivin induction pathways leading to increase in apoptosis and decrease in tumour growth. Besides its role as an IAP, Survivin acts as a subunit of the chromosomal passenger complex (CPC) and as a regulator of microtubule dynamics [8,27]. The CPC also composed of the Aurora-B kinase, Borealin and INCENP corrects attachment errors between chromosomes and the mitotic spindle, regulates the quality-control checkpoint and ensures the correct completion of cytokinesis [10].

The typical chromosomal passenger localization pattern of Survivin can be observed not only in normal but also in tumour cells [27,28]. LI et al. have suggested that nuclear Survivin is involved in the promotion of cell proliferation, whereas cytoplasmic Survivin may help control cell survival [29]. Thus, Survivin exists in two subcellular pools (cytoplasmic and nuclear) in response to its function in the regulation of both cell survival and cell division.

Experiments have revealed that transient expression of wild-type p53 results in marked repression of Survivin at both the mRNA and protein levels [14]. Upregulation of Survivin and mutation of p53 occurring concomitantly in many human tumours implicates that these two events are related [30,33]. p53 expression in tooth germs in contrast to previous studies [34,35], can be explained by the fact that p53 activation is not limited to DNA damage; it is also activated in response to myriad stresses like oxidative stress, osmotic shock, heat shock, hypoxia, ribonucleotide depletion and deregulated oncogene expression leading to accumulation of p53 in stressed cells [36]. Absence of staining in other tooth germs correlates with the literature that p53 does not normally accumulate to amounts detectable by immunohistochemical staining because of its short half-life (6-20 minutes) [34,35,37].

EL-SISSY NA et al. reported faint p53 staining and attributed this to slow tumour growth, expansion and correlated with the benign nature of Ameloblastoma resulting from relatively quiescent tumour cells [34]. Thus, the presence of predominant intense p53 staining in the present study may be suggestive of rapid growth, predominant cytoplasmic expression of Survivin in the peripheral ameloblast-like cells and stellate reticulumlike cells with focal nuclear expression is suggestive of its role in evading apoptosis rather than in the proliferation of neoplastic cells in Ameloblastoma.

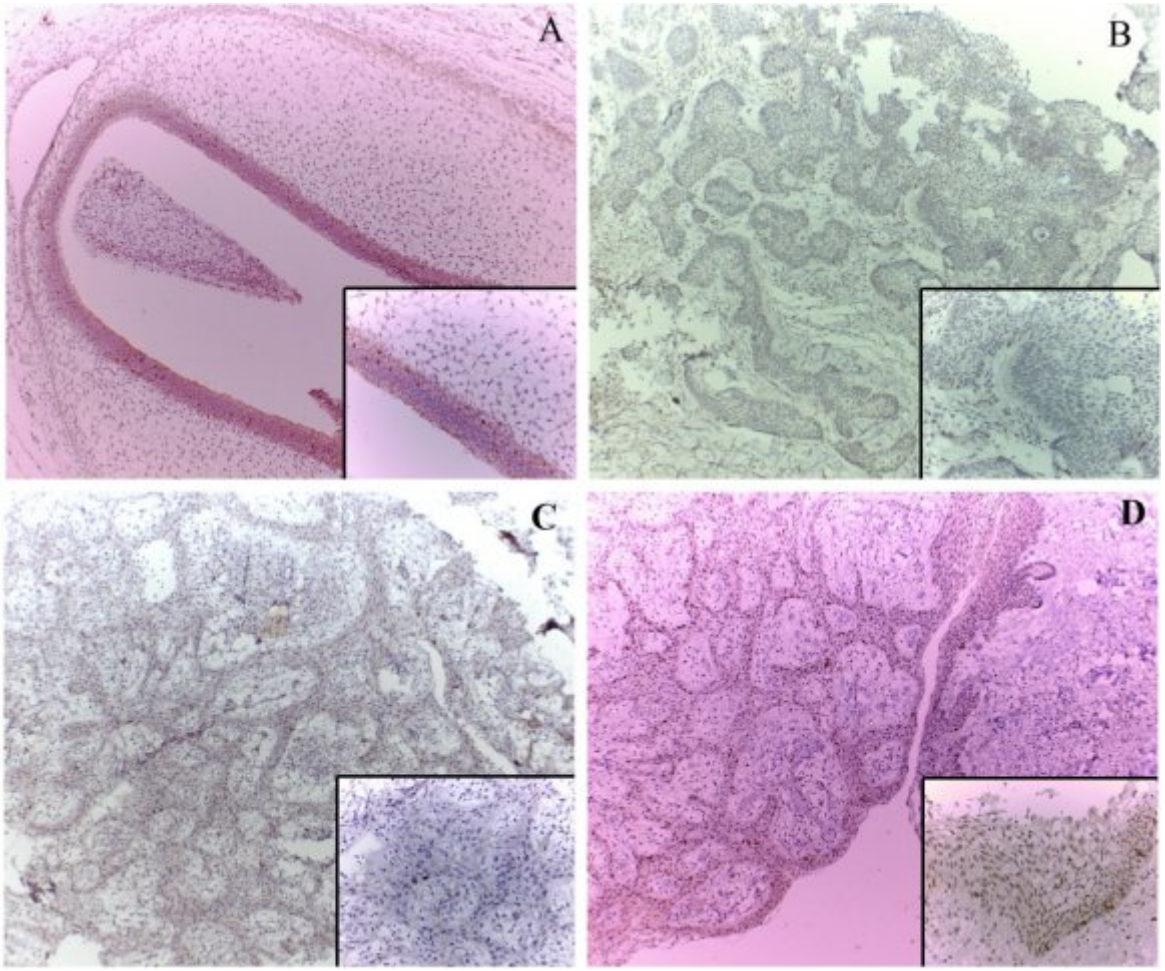
Co-expression of p53 and Survivin in the present study implicates that these two proteins may have a combined role in inhibiting apoptosis, where mutant p53 led to up-regulation of Survivin. But the expression of only p53 or Survivin in few tissues also cannot be ignored. Though possible explanation was obtained through literature review, the significance of clinical and other molecular factors needs to be explored. The present study was done to throw light on nuclear and cytoplasmic expression of Survivin in relation to p53 in Ameloblastoma which would add-up to the existing understanding about its biological behavior and explore new and better therapeutic results. Further molecular studies with large sample size are required to confirm these findings. apoptotic protein (IAP) inhibits caspase activation. This expansion and locally aggressive behavior of Ameloblastoma [38].

Survivin is chiefly expressed in the undifferentiated proliferating cells like stem cells, basal cells of the oral epithelium, embryonic and fetal tissues but becomes undetectable in most terminally differentiated cells [39]. Absence of Survivin expression in five tooth germs may be due to differentiation of inner enamel epithelial cells into ameloblast because hard tissue formation was evident in these tooth germs. KUMAMOTO et al. suggested that cells neighboring the basement membrane are proliferative cells and those away from the basement membrane are apoptotic [23]. Studies in the literature have described cytoplasmic expression of Survivin to be associated with

Figure Legends

**2** 


Figure 1: Figure 2 :




1

Figure 2: Figure 1 :

**1**

determine the role of p53 and Survivin, in addition to intense staining, and (ii) the number of positively stained cells with brown colour were counted among 400 tumour cells using an occulometer eye-piece grid at the objective magnification x40. The results were multiplied

| Group | Total no. of cases | Negative staining | Mild staining | Moderate staining | Intense staining | Average % of positive cells |
|---|---|---|---|---|---|---|
| Tooth germ | 10 | 1 | 1 | 6 | 2 | 24.89% |
| Ameloblastoma | 25 | 0 | 1 | 9 | 15 | 75.97% |
| Follicular | 12 | 0 | 1 | 5 | 6 | 79.37% |
| Plexiform | 4 | 0 | 0 | 0 | 4 | 81.62% |
| Unicystic | 9 | 0 | 0 | 4 | 5 | 68.91% |

Figure 3: Table 1 :

**2**

| | N | Sum of Ranks | Mean Rank | U-value | Z-value | p-value |
|---|---|---|---|---|---|---|
| Qualitative analysis | | | | | | |
| Tooth germ | 10 | 123.50 | 12.35 | 68.50 | - 2.296 | 0.038 |
| Ameloblastoma | 25 | 506.50 | 20.26 | | | |
| Quantitative analysis | | | | | | |
| Tooth germ | 10 | 74.00 | 7.40 | 19.00 | - 3.874 | 0.000* |
| Ameloblastoma | 25 | 556.00 | 22.24 | | | |

Statistically significant

b) Survivin expression in tooth germ and Ameloblastoma

Survivin expression was predominantly localized to the cytoplasm [Figure

Figure 4: Table 2 :

**3**

| Group | Total no. of cases | Negative staining | Mild staining | Moderate staining | Intense staining | Average % of positive cells |
|---|---|---|---|---|---|---|
| Tooth germ | 10 | 0 | 4 | 4 | 2 | 29.10% |
| Ameloblastoma | 25 | 0 | 6 | 13 | 6 | 78.25% |
| Follicular | 12 | 0 | 5 | 7 | 0 | 78.06% |
| Plexiform | 4 | 0 | 0 | 4 | 0 | 79.12% |
| Unicystic | 9 | 0 | 1 | 2 | 6 | 56.66% |

Figure 5: Table 3 :

**4**

| | N | Sum of Ranks | Mean Rank | U-value | Z-value | p-value |
|---|---|---|---|---|---|---|
| Qualitative analysis | | | | | | |
| Tooth germ | 10 | 161.00 | 16.10 | 106.00 | -0.752 | 0.506 |
| Ameloblastoma | 25 | 469.00 | 18.76 | | | |
| Quantitative analysis | | | | | | |
| Tooth germ | 10 | 73.00 | 7.30 | 18.00 | -3.913 | 0.000* |
| Ameloblastoma | 25 | 557.00 | 22.28 | | | |

Statistically significant

c) p53 and Survivin expression in tooth germ and Ameloblastoma

Figure 6: Table 4 :

**5**

"Cell Cycle Aberration in Ameloblastoma: As Evidenced by an Immunohistochemical Expression of p53 and Survivin"

| | N | Sum of Ranks | Mean Rank | Z-value | p-value |
|---|---|---|---|---|---|
| Qualitative analysis | | | | | |
| Tooth germ | 10 | 28.00 | 8.00 | -0.378 | 0.705 |
| Ameloblastoma | 25 | 171.00 | 18.2 | -2.854 | 0.004* |
| Quantitative analysis | | | | | |
| Tooth germ | 10 | 28.00 | 8.60 | -0.676 | 0.499 |
| Ameloblastoma | 25 | 276.00 | 24.25 | -0.821 | 0.411 |
| Statistically significant | | | | | |

Figure 7: Table 5 :

# .1 Acknowledgements

We wish to thank Dr. Kaveri Hallikeri, Professor and Head, SDM College of Dental Sciences and Hospital, Dharwad, Dr. Amsavardani Tayaar @ Padmini. S, Professor, SDM College of Dental Sciences and Hospital, Dharwad and Dr. M V Muddapur, Statistician, SDM College of Dental Sciences and Hospital, Dharwad for their valuable support in the course of the study.

[ Current Opinion in Cell Biology ()] , *Current Opinion in Cell Biology* 2006. 18 p. .

[Knauer et al. ()] , S K Knauer , C Bier , N Habtemichael . *The Survivin-Crm1 Rep* 2006. 7 p. .

[ Cancer Res ()] , *Cancer Res* 2007.

[ Int J Clin Exp Pathol ()] , *Int J Clin Exp Pathol* 2013. 6 p. .

[Loro et al. ()] 'Apoptosis in normal and diseased oral tissues'. L L Loro , O K Vintermyr , A C Johannessen . *Oral Dis* 2005. 11 p. .

[Cell Cycle Aberration in Ameloblastoma: As Evidenced by an Immunohistochemical Expression of p53 and Survivin] *Cell Cycle Aberration in Ameloblastoma: As Evidenced by an Immunohistochemical Expression of p53 and Survivin*,

[Philipsen ()] *Cell Cycle Aberration in Ameloblastoma: As Evidenced by an Immunohistochemical Expression of p53 and Survivin*, H P Philipsen . 2005. Lyon: IARC Press. (WHO Classification of Tumors: Pathology and genetics of head and neck tumors)

[Li et al. ()] 'Control of apoptosis and mitotic spindle checkpoint by survivin'. F Li , G Ambrosini , E Y Chu . *Nature* 1998. 396 p. .

[Halasova et al. ()] 'Expression of anti-apoptotic protein survivin and tumor suppressor p53 protein in patients with pulmonary carcinoma'. E Halasova , M Adamkov , E Kavcova . *Eur J Med Res* 2009. 14 p. .

[Ranade et al. ()] 'Expression of Survivin and p53 proteins and their correlation with hormone receptor status in Indian breast cancer patients'. K J Ranade , A V Nerurkar , M D Phulpagar . *Indian J Med Sci* 2009. 63 p. .

[Kumamoto and Ooya ()] 'Expression of survivin and X chromosome-linked inhibitor of apoptosis protein in ameloblastomas'. H Kumamoto , K Ooya . *Virchows Arch* 2004. 444 p. .

[Parenti et al. ()] 'Expression of survivin, p53 and caspase 3 in Barrett's esophagus carcinogenesis'. A Parenti , G Leo , A Porzionato . *Human Pathol* 2006. 37 p. .

[Miller et al. ()] 'Human p53 localized to short arm of chromosome 17'. C Miller , T Mohandas , D Wolfd . *Nature* 1986. 319 p. .

[Mirza et al. ()] 'Human survivin is negatively regulated by wild-type p53 and participates in p53-dependent apoptotic pathway'. A Mirza , M Mcguirk , T N Hockenberry . *Oncogene* 2002. 21 p. .

[El-Sissy ()] 'Immunohistochemical detection of p53 protein in ameloblastoma types'. N A El-Sissy . *Eas Mediterra Health J* 1999. 5 p. .

[Shintani et al.] *Immunohistochemical expression of nuclear and cytoplasmic survivin in gastrointestinal carcinoma*, M Shintani , A Sangawa , N Yamao .

[Dws ()] 'Immunohistochemical Expression of P53 in Different Types of Ameloblastoma'. Al-Fayad Dws . *Al-Anbar University* 2010. 8 p. .

[Qi et al. ()] 'Intracellular localization of survivin determines biological behavior in colorectal cancer'. G Qi , H Tuncel , E Aoki . *Oncol Rep* 2009. 22 p. .

[Kumamoto ()] 'Molecular alterations in the development and progression of odontogenic tumors'. H Kumamoto . *Oral Med Pathol* 2010. 14 p. .

[Kumamoto ()] 'Molecular pathology of odontogenic tumors'. H Kumamoto . *J Oral Pathol Med* 2006. 35 p. .

[Stauber et al.] *Nuclear and cytoplasmic survivin: molecular mechanism*, R H Stauber , W Mann , S K Knauer .

[Knauer et al. ()] 'Nuclear export is essential for the tumor-promoting activity of survivin'. S K Knauer , O H Krämer , T Knösel . *FASEB J* 2007. 21 p. .

[Kim et al. ()] 'Nuclear interaction of Smac/DIABLO with Survivin at G2/M arrest prompts docetaxel-induced apoptosis in DU145 prostate cancer cells'. J Y Kim , J Y Chung , S G Lee . *Biochem Biophys Res Commun* 2006. 350 p. .

[Li et al. ()] 'Nuclear or cytoplasmic expression of survivin: What is the'. F Li , J Yang , N Ramnath . *Int J Cancer* 2005. 114 (4) p. .

[Deoliveira et al. ()] 'Odontogenic Epithelium: Immunolabeling of Ki-67, EGFR and Survivin in Pericoronal Follicles, Dentigerous Cysts and Keratocystic Odontogenic Tumors'. M G Deoliveira , I Da Silva Lauxen , Acm Chaves . *Head and Neck Pathol* 2010. 5 p. .

[Carvalhais et al. ()] 'P53 and MDM2 expression in odontogenic cysts and tumours'. J N Carvalhais , De Aguiar , V C De Araujo . *Oral Dis* 1995. 5 p. .

[Al-Salihi et al. ()] 'P53 gene mutation and protein expression in ameloblastomas'. K A Al-Salihi , L Y Li , A Azlina . *Braz J Oral Sci* 2006. 5 p. .

[Hollstein et al. ()] 'p53 mutations in human cancers'. M Hollstein , D Sidransky , B Vogelstein . *Science* 1991. 253 p. .

[Bai and Zhu ()] 'p53: Structure, Function and Therapeutic Applications'. L Bai , W G Zhu . *J Cancer Mol* 2006. 2 p. .

[Chen et al. ()] 'Prognostic value of survivin, X-linked inhibitor of apoptosis protein and second mitochondria-derived activator of caspases expression in advanced non-small-cell lung cancer patients'. P Chen , J Li , L P Ge . *Respirology* 2010. 15 p. .

[Barboza et al. ()] 'Proliferating cell nuclear antigen (PCNA) and p53 protein expression in ameloblastoma and adenomatoid odontogenic tumor'. C A Barboza , Pereira Pinto , L , Freitas Rde , A . *Braz Dent J* 2005. 16 p. .

[Adamkov et al. ()] 'Relation between expression pattern of p53 and survivin in cutaneous basal cell carcinomas'. M Adamkov , E Halasova , J Rajcani . *Med Sci Monit* 2011. 17 p. .

[Li ()] 'Role of surviving and its splice variants in tumorigenesis'. F Li . *Br J Cancer* 2005. 92 p. .

[Nassar et al. ()] 'Survivin expression in breast carcinoma: correlation with apoptosis and prognosis'. A Nassar , D Sexton , G Cotsonis . *Appl Immunohistochem Mol Morphol* 2008. 16 p. .

[Andric et al. ()] 'Survivin expression in odontogenic keratocysts and correlation with cytomegalovirus infection'. M Andric , B Dozic , B Popovic . *Oral Dis* 2010. 16 p. .

[L Lo Muzio et al. ()] 'Survivin expression in oral squamous cell carcinoma'. G L Lo Muzio , Pannone , Staibano . *Brit J of Canc* 2003. 89 p. .

[Ito et al. ()] 'Survivin promotes cell proliferation in human hepatocellular carcinoma'. T Ito , K Shiraki , K Sugimoto . *Hepatology* 2000. 31 p. .

[Shi ()] 'Survivin structure: crystal unclear'. Y Shi . *Nat Struct Biol* 2000. 7 p. .

[Knauer et al. ()] 'Survivin's dual role: an export's view'. S K Knauer , W Mann , R H Stauber . *Cell Cycle* 2007. 6 p. .

[Altieri ()] 'Survivin, versatile modulation of cell division and apoptosis in cancer'. D C Altieri . *Onco* 2003. 22 p. .

[Altieri] *The case for survivin as a regulator of microtubule dynamics and cell -death decisions*, D C Altieri .

[Lens et al. ()] 'The case for Survivin as mitotic regulator'. S M Lens , G Vader , R H Medema . *Curr Opin Cell Biol* 2006. 18 p. .

[Choi and Chang ()] 'The expression of MAGE and SSX, and correlation of COX2, VEGF, and survivin in colorectal cancer'. J Choi , H Chang . *Anticancer Res* 2012. 32 p. .