MEDS Clinical Medicine (2026)
Clausius Scientific Press, Canada

DOI: 10.23977/medsc.2026.070313
ISSN 2616-1907 Vol. 7 Num. 3

Expression and Correlation of Survivin and Smac in Pectoral Keloid Tissues

Runfang Chen[1,2,a], Shuang Ding[1,2,b,*], Pandeng Li[3,c]

[1]Department of Clinical Laboratory, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China
[2]School of Medical Technology, Xuzhou Medical University, Xuzhou, China
[3]Department of Burn and Plastic Surgery, The Affiliated Hospital of Xuzhou Medical University, Xuzhou, China
[a]chenrunfang2025@qq.com, [b]67350366@qq.com, [c]climbli@qq.com
**Corresponding author: Shuang Ding *Co-corresponding author: Pandeng Li*

Keywords: Keloid; Survivin; Smac; Immunohistochemistry

Abstract: This study aimed to evaluate the expression of Survivin and Smac in sternal keloid tissue, analyze their correlation, and preliminarily elucidate how these two molecules participate in sternal keloid pathogenesis. Reverse transcription-polymerase chain reaction (RT-PCR) was used to quantify the mRNA levels of Survivin and Smac, and immunohistochemical (IHC) staining was applied to detect the protein expression levels of Survivin and Smac in 20 sternal keloid tissue samples and their matched adjacent normal skin tissue samples; Pearson correlation analysis was further performed to investigate the correlation between Survivin and Smac expressions in keloid tissues. The results revealed statistically significant differences in the mRNA and protein expressions of Survivin and Smac between sternal keloid tissues and adjacent normal skin tissues ($p<0.05$); specifically, the mRNA level and protein positive expression rate of Survivin in sternal keloid tissues were significantly higher than those in adjacent normal skin tissues ($p<0.05$), while the mRNA level and protein positive expression rate of Smac in sternal keloid tissues were obviously lower than those in adjacent normal skin tissues ($p<0.05$), and a significant negative correlation was found between Survivin and Smac protein expressions in sternal keloid tissues ($r = -0.334$, $P<0.01$). It is concluded that the overexpression of Survivin and downregulation of Smac may exert pivotal effects on the proliferation-apoptosis signal transduction pathway of keloids, and the two molecules are probably involved in the initiation and progression of sternal keloids.

1. Introduction

Keloid is a pathological fibroproliferative disorder of the skin and subcutaneous tissue induced by an excessive wound healing response to injury, characterized by unregulated hyperproliferation of fibroblasts that extends beyond the boundaries of the original injury site. Clinically, keloid lesions typically protrude from the skin surface, even exhibit a crab-claw-like invasive growth pattern, and are frequently accompanied by pruritus, persistent pain, recurrent ulceration, and even a

potential risk of malignant transformation. These manifestations not only severely impair patients' physical appearance and quality of life but also pose a threat to their health and even life safety [1]. The pectoral region is one of the most common predilection sites for keloids, with typical clinical features of large lesion area, intractable pruritus and pain, and strong treatment willingness in affected patients. However, the exact molecular pathogenesis of keloids has not been fully elucidated to date.Accumulating evidence has indicated that the abnormal proliferation of keloid tissues is closely associated with the imbalance between fibroblast proliferation and apoptosis [2]. *Survivin* and *Smac* are newly identified apoptosis-associated genes, and the majority of relevant studies have focused on their regulatory effects in malignant tumors [3,4]. Given the similar biological characteristics between keloids and malignant tumors such as invasive growth and anti-apoptosis, the regulatory roles of Survivin and Smac in keloid formation have attracted increasing attention. In the present study, we detected the mRNA and protein expression levels of Survivin and Smac in pectoral keloid tissues by RT-PCR and IHC staining, and further analyzed their correlation, aiming to preliminarily reveal the roles and underlying mechanisms of Survivin and Smac in the formation and development of pectoral keloids.

2. Materials and Methods

2.1 Specimen Collection and Ethical Approval

The clinical specimens used in this study were obtained from the Department of Burn and Plastic Surgery, The Affiliated Hospital of Xuzhou Medical University, including 20 pectoral keloid tissue samples (pathologically confirmed as keloids by postoperative histopathological examination) and 20 matched adjacent normal skin tissue samples (5 cm away from the keloid margin). None of the patients received any preoperative treatment such as local drug injection, radiotherapy or surgical resection. Written informed consent for specimen collection was obtained from all patients or their family members.

2.2 Main Reagents

Rabbit anti-human Survivin polyclonal antibody and rabbit anti-human Smac polyclonal antibody were purchased from Santa Cruz Biotechnology (Santa Cruz, CA, USA); SP immunohistochemical staining kit and 3,3'-diaminobenzidine (DAB) chromogenic kit were obtained from Zhongshan Golden Bridge Biotechnology Co., Ltd. (Beijing, China); Trizol Reagent was purchased from Invitrogen (Carlsbad, CA, USA); RT reverse transcription kit and PCR amplification kit were provided by MBI Fermentas (Vilnius, Lithuania).

2.3 RT-PCR Assay for mRNA Expression Detection

Fresh keloid and normal skin tissues (100 mg each) were harvested and ground into powder in liquid nitrogen, and total cellular RNA was extracted in accordance with the instructions of the Trizol Reagent. The concentration and purity of extracted RNA were detected by a nucleic acid protein analyzer (NanoDrop 2000, Thermo Fisher, USA), and only RNA samples with A260/A280 ratio between 1.8 and 2.0 were used for subsequent experiments. Total RNA (2 μg) was reverse-transcribed into complementary DNA (cDNA) following the protocol of the RT reverse transcription kit.

Specific primers for *Survivin*, *Smac* and the internal reference gene *β-actin* were designed using Primer Premier 5.0 software based on the gene sequences from GenBank (NCBI), and synthesized by Shanghai Jierui Biological Engineering Co., Ltd. (Shanghai, China). The primer sequences and

amplified fragment lengths are shown in Table 1.

The PCR amplification was performed in a 50 μL reaction system containing 25 μL PCR Mix, 1 μL forward primer (10 μmol/L), 1 μL reverse primer (10 μmol/L), 1 μL cDNA template and 22 μL nuclease-free water. The PCR reaction conditions were as follows:① *Survivin*: Pre-denaturation at 95℃ for 3 min, followed by 32 cycles of denaturation at 95℃ for 30 s, annealing at 60℃ for 30 s, extension at 72℃ for 45 s, and a final extension at 72℃ for 7 min;② *Smac*: Pre-denaturation at 95℃ for 3 min, followed by 32 cycles of denaturation at 95℃ for 40 s, annealing at 60℃ for 30 s, extension at 72℃ for 45 s, and a final extension at 72℃ for 45 s;③ *β-actin*: Pre-denaturation at 95℃ for 3 min, followed by 32 cycles of denaturation at 95℃ for 30 s, annealing at 65℃ for 30 s, extension at 72℃ for 7 min, and a final extension at 72℃ for 7 min.

After PCR amplification, 5 μL of the PCR products were subjected to 1.5% agarose gel electrophoresis, and the gel images were captured using a gel imaging analysis system (Tanon 2500, Shanghai, China). The relative mRNA expression levels of *Survivin* and *Smac* were semi-quantitatively analyzed by ImageJ software (Version 1.8.0, NIH, USA), and calculated as the ratio of the gray value of the target gene band to that of the *β-actin* band (*β-actin* corrected value). All experiments were repeated three times to ensure reproducibility.

2.4 Immunohistochemical Staining for Protein Expression Detection

The collected tissue samples were fixed in 4% paraformaldehyde for 24 h, embedded in paraffin, and cut into 4 μm-thick serial sections. Immunohistochemical staining was performed strictly in accordance with the manufacturer's instructions for the SP staining kit. Rabbit anti-human Survivin and Smac polyclonal antibodies were used as the primary antibodies at the dilution ratios of 1:100 and 1:50, respectively.

The staining results were evaluated using a positive coefficient, which was calculated as the product of staining intensity and the percentage of positive cells. All sections were observed under a light microscope at a magnification of ×400, and five high-power fields were randomly selected for assessment in each section.

The criteria for staining intensity were graded as follows [1]: 0 point (almost no staining), 1 point (weak staining), 2 points (moderate staining), and 3 points (strong staining).The criteria for the percentage of positive cells were classified as: 0 point (<5%), 1 point (6%–25%), 2 points (26%–50%), and 3 points (>51%).The positive coefficient was further categorized for result interpretation: negative (-) (0–1 point) and positive (+ to +++) (2–9 points), with weak positive (+) defined as 2–3 points, moderate positive (++) as 4–6 points, and strong positive (+++) as 9 points.

Phosphate-buffered saline (PBS) was used instead of the primary antibody as the negative control for the staining procedure.

Table 1 Primers and amplified fragment lengths for RT-PCR.

Gene name	Primer sequence (5'→3')	Amplified fragment length (bp)
Survivin	(F)5'-gga cca ccg cat ctc tac at -3'	
	(R)5'-gca ctt tct tcg cag ttt cc-3'	338bp
Smac	(F)5'-aac cgc cag gaa tca cat-3'	
	(R)5'-tga ttg gcc agg gca gga tct-3'	303bp
β-actin	(F)5'-cgt ctg gac ctg gct ggc cgc gac c -3'	
	(R)5'-cta gaa gca ttt gcg gtg gac gat g -3'	600bp

2.5 Statistical Analysis

All experimental data were collated and analyzed using the Statistical Product and Service Solutions (SPSS) 17.0 software (IBM, Armonk, NY, USA). Measurement data were expressed as the mean ± standard deviation ($x \pm s$), and the comparison between two groups was performed using the independent-samples t-test. Count data were expressed as n (%) and analyzed using the Kruskal-Wallis H test. The correlation between Survivin and Smac protein expressions in keloid tissues was analyzed using Spearman's rank correlation analysis. A two-tailed *P* value <0.05 was considered statistically significant.

3. Results

3.1 Expression Levels of *Survivin* and *Smac* mRNA in Pectoral Keloid and Normal Skin Tissues

RT-PCR results showed that the relative mRNA expression levels of *Survivin* and *Smac* were significantly different between pectoral keloid tissues and adjacent normal skin tissues ($P<0.05$). The relative mRNA expression level of *Survivin* in pectoral keloid tissues was 0.72±0.01, which was significantly upregulated compared with that in normal skin tissues (0.12±0.02). In contrast, the relative mRNA expression level of *Smac* in pectoral keloid tissues was 0.31±0.02, which was significantly downregulated in comparison with that in normal skin tissues (0.82±0.03) (Table 2, Figure 1,2).

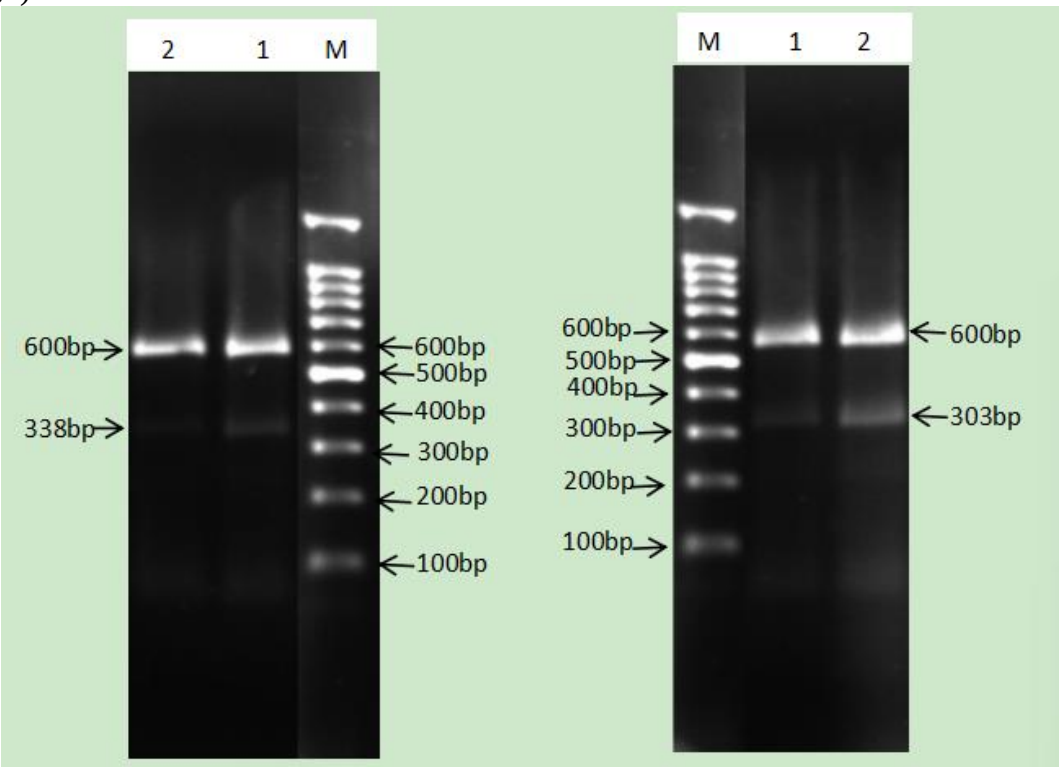

Figure 1 (left) Expression of Survivin mRNA in two types of tissues.

M: Marker; 1: Keloid, 2: Normal skin

Figure 2 (right) Expression of Smac mRNA in two types of tissues.

M: Marker; 1: Keloid, 2: Normal skin

Table 2 Expression of Survivin and Smac mRNA in two tissues.

Group	n	Survivin	Smac
Keloid	20	0.72±0.01*	0.31±0.02*
Normal skin	20	0.12±0.02	0.82±0.03

*Compared with normal skin, p<0.05

3.2 Expression Levels of Survivin and Smac Protein in Pectoral Keloid and Normal Skin Tissues

IHC staining results demonstrated the distinct expression patterns of Survivin and Smac proteins in the two types of tissues (Figure 3). Survivin protein was mainly localized in the cytoplasm and nucleus of fibroblasts in pectoral keloid tissues, showing obvious brown-yellow staining, with a positive expression rate of 75.0%. In contrast, Survivin protein was weakly expressed in normal skin tissues with only a small number of positive cells, and the positive expression rate was only 25.0%.

Smac protein was predominantly expressed in the cytoplasm of epithelial cells in normal skin tissues, presenting strong brown-yellow staining with a high positive expression rate of 80.0%, while its expression was significantly reduced in pectoral keloid tissues with a positive expression rate of only 20.0%. The differences in the positive expression rates of Survivin and Smac proteins between pectoral keloid tissues and normal skin tissues were both statistically significant (P<0.05) (Table 3, Table 4).

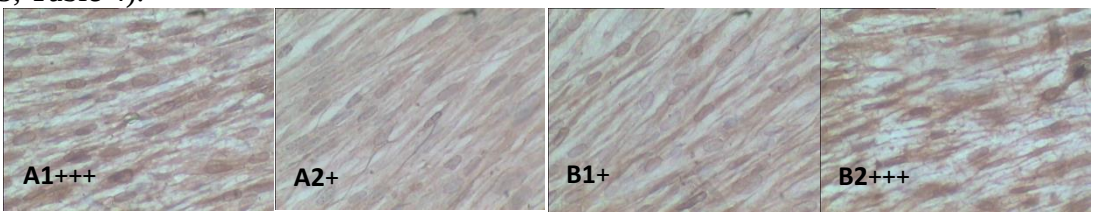

Figure 3 Expression of Survivin and Smac proteins in two types of tissues (IHC staining, ×400).

A: Survivin in pectoral keloid tissue; B: Survivin in normal skin tissue; C: Smac in pectoral keloid tissue; D: Smac in normal skin tissue

Table 3 Number of positive Survivin expression cases in two tissues.

Group	number	-	+	++	+++	positive rate(%)
Keloid	20	5	3	4	8	75*
normal skin	20	15	3	2	0	25

*Compared with normal skin, p<0.05

Table 4 Number of positive Smac expression cases in two tissues.

Group	number	-	+	++	+++	positive rate(%)
Keloid	20	16	2	2	0	20*
normal skin	20	4	3	5	8	80

*Compared with normal skin, p<0.05

3.3 Correlation between Survivin and Smac Protein Expressions in Pectoral Keloid Tissues

Spearman's rank correlation analysis was performed to explore the correlation between Survivin and Smac protein expressions in pectoral keloid tissues, and the results showed that there was a significant negative correlation between the two proteins (r=-0.334, P<0.01), indicating that the higher the expression of Survivin protein, the lower the expression of Smac protein in pectoral keloid tissues (Table 5).

Table 5 Correlation analysis of Survivin and Smac protein expressions in pectoral keloid tissues (n).

Survivin	Smac		Total	Spearman correlation coefficient	P
	-	+			
-	2	2	4	r = -0.334	P<0.01
+	14	2	16		
Total	16	4	20		

4. Discussion

Keloid is a benign fibroproliferative lesion caused by an abnormal and excessive wound healing response of the skin, characterized by excessive collagen deposition by fibroblasts and progressive invasive growth into the surrounding normal tissues beyond the original injury site [5]. Essentially, keloid is a special type of pathological scar, and even regarded as a benign skin tumor induced by the unregulated hyperproliferation of dermal connective tissue. Its typical clinicopathological features include abnormally active metabolism, uncontrolled proliferation and impaired apoptosis of dermal fibroblasts [6].Clinically, keloid shares numerous similarities with malignant tumors, such as invasive growth pattern, local recurrence and resistance to conventional treatment. Keloids have a distinct predilection for the pectoral region, perineum, earlobes and other skin sites with high skin tension, among which the pectoral region is the most common site. At present, the clinical treatment of pectoral keloids mainly includes surgical resection, local drug injection, radiotherapy and laser therapy, but the overall therapeutic effect is unsatisfactory with a high postoperative recurrence rate, which is mainly attributed to the unclear molecular pathogenesis of keloids.

In recent years, it has been increasingly recognized that the imbalance between fibroblast proliferation and apoptosis is the core molecular mechanism underlying keloid formation [7]. Relevant research has confirmed that keloid fibroblasts lack physiological programmed cell death and continuously secrete extracellular matrix components such as collagen, leading to the persistent growth and invasive expansion of keloid lesions [8]. Accumulating studies have indicated that cytokines related to cell proliferation and apoptosis-associated proteins play an important regulatory role in the pathogenesis of keloids, and keloid formation may be associated with the resistance of fibroblasts to physiological apoptosis, which is similar to the anti-apoptotic characteristics of malignant tumor cells.

Survivin, a member of the inhibitor of apoptosis protein (IAP) family and the first identified IAP molecule, is a key anti-apoptotic gene that is highly expressed in embryonic stem cells and actively proliferating somatic cells [9], but is barely expressed in differentiated and mature normal adult tissues [10]. Survivin exerts dual biological functions of inhibiting cell apoptosis and regulating cell cycle progression, and is regarded as a core regulator of cell proliferation and apoptosis [11]. In addition, *Survivin* is frequently overexpressed in a variety of malignant tumors, and its overexpression is closely associated with the self-renewal, proliferation and anti-apoptotic ability of

cancer stem cells. The upregulation of Survivin can protect tumor cells from apoptosis and autophagy induced by various stimuli, thereby promoting tumor progression and metastasis [12,13].A large number of studies have confirmed that *Survivin* is widely expressed in most malignant tumor tissues, and its expression level is closely correlated with tumor stage, lymph node metastasis and poor prognosis, making it a research hotspot in tumor molecular biology and targeted therapy [14-17]. Given the similar biological characteristics between keloids and malignant tumors, our research team and other relevant studies have found that the *Survivin* gene is significantly overexpressed in keloid tissues. Existing studies have demonstrated that the overexpression of Survivin in keloid fibroblasts can inhibit mitochondrial and death receptor-mediated apoptotic pathways, leading to the inhibition of fibroblast apoptosis and the continuous proliferation and expansion of keloid lesions [18], which is consistent with the results of the present study that Survivin is highly expressed in pectoral keloid tissues.

Smac (Second mitochondria-derived activator of Caspase), also known as Diablo, is one of the newly discovered pro-apoptotic molecules, and is the only protein currently found to bind to and inhibit the activity of multiple members of the IAP family [19]. Smac exerts its pro-apoptotic effect mainly by interacting with IAP proteins through the downstream signaling pathways of the mitochondrial apoptosis pathway and death receptor pathway, thereby relieving the inhibitory effect of IAPs on Caspase family proteins and activating the apoptotic cascade reaction, which plays a crucial role in the regulation of cell apoptosis [20].

The human *Smac* gene is located on chromosome 12, and the Smac protein is synthesized in the cytoplasm and then transported to the mitochondria, where it is cleaved by mitochondrial signal peptidases to form the mature and biologically active Smac molecule containing 184 amino acids. X-ray crystallography studies have shown that Smac binds to the surface groove of the baculovirus IAP repeat (BIR) domain of IAP family proteins through its N-terminal four amino acid motif (alanine-valine-proline-isoleucine), thereby blocking the interaction between IAPs and Caspase-3, Caspase-7 and Caspase-9, and ultimately activating the apoptotic signaling pathway.Smac is widely expressed in various normal human tissues, but its expression is significantly reduced or even absent in most malignant tumors, and the expression level varies greatly among different types of tumors [21], suggesting that the downregulation of Smac may be an important molecular event in tumorigenesis and progression by enhancing the anti-apoptotic ability of tumor cells. However, few studies have reported the expression pattern and regulatory role of Smac in the occurrence and development of pectoral keloids. In the present study, we found that the mRNA and protein expression levels of Smac were significantly downregulated in pectoral keloid tissues compared with normal skin tissues, which was consistent with the expression pattern of Smac in malignant tumors.

Both Survivin and Smac are key regulatory molecules of cell proliferation and apoptosis, and their expressions are abnormally regulated in pectoral keloid tissues. Further correlation analysis showed a significant negative correlation between Survivin and Smac protein expressions in pectoral keloid tissues, suggesting that there may be an antagonistic or negative feedback regulatory relationship between Survivin and Smac in the regulation of fibroblast proliferation and apoptosis during the formation and development of pectoral keloids. The overexpression of Survivin and the downregulation of Smac may jointly disrupt the balance of the proliferation-apoptosis signal network of keloid fibroblasts, leading to the excessive proliferation and impaired apoptosis of fibroblasts, and ultimately promoting the formation and progression of pectoral keloids.

5. Conclusion

The present study confirmed that Survivin is significantly overexpressed and Smac is markedly

downregulated in pectoral keloid tissues, and there is a significant negative correlation between their protein expressions. The overexpression of Survivin and the downregulation of Smac may play crucial roles in the proliferation-apoptosis signal transduction network of keloid fibroblasts, and both molecules may be involved in the occurrence and progression of pectoral keloids by regulating the balance of fibroblast proliferation and apoptosis. This study provides a new molecular perspective for further exploring the pathogenesis of pectoral keloids, and Survivin and Smac may serve as potential molecular targets for the clinical prevention and targeted therapy of pectoral keloids.

This study has certain limitations: first, the sample size is relatively small (20 cases), and more large-sample and multi-center studies are needed to verify the research results; second, this study only explored the expression and correlation of Survivin and Smac in pectoral keloid tissues, and the specific molecular mechanism by which Survivin and Smac interact and regulate the proliferation and apoptosis of keloid fibroblasts remains to be further explored in subsequent *in vitro* and *in vivo* experiments.

References

[1] Zheng XF, He RL, Huang TY, et al. Efficacy of autologous keloid skin grafting combined with local drug injection in the treatment of giant pectoral keloids[J]. Chinese Journal of Dermatovenereology, 2021,35(7):820-824. (in Chinese)

[2] Wu ML, Wang R, Zheng XN, et al. Effect of metformin on proliferation and apoptosis of human keloid fibroblasts and its underlying mechanism[J]. Chinese Journal of Burns and Wound Repair, 2025,41(4):355-363. (in Chinese)

[3] Zhang J, Wang D, Xu KY, et al. Expressions of Survivin and Smac in ovarian cancer tissues and their clinical significance[J]. Practical Journal of Cancer, 2025,40(7):1093-1095,1104. (in Chinese)

[4] Liu JY, Quan LL, Chen XX. Expressions of FBXW7, Smac and Survivin in ovarian cancer tissues and their correlation with clinicopathological features[J]. Chinese Journal of Practical Medicine, 2021,48(6):19-22. (in Chinese)

[5] Ogawa R. The most current algorithms for the treatment and prevention of hypertrophic scars and keloids: a 2020 update of the algorithms published 10 years ago[J]. Plastic and Reconstructive Surgery, 2022,149(1):79-94.

[6] Cohen AJ, Nikbakht N, Uitto J. Keloid disorder: genetic basis, gene expression profiles, and immunological modulation of the fibrotic processes in the skin[J]. Cold Spring Harbor Perspectives in Biology, 2023,15(7):a041245.

[7] Erlendsson AM, Rosenberg LK, Lerche CM, et al. A one-time pneumatic jet-injection of 5-fluorouracil and triamcinolone acetonide for the treatment of hypertrophic scars: A blinded randomized controlled trial[J]. Lasers in Surgery and Medicine, 2022,54(5):663-671.

[8] Frech FS, Hernandez L, Urbonas R, et al. Hypertrophic scars and keloids: advances in treatment and review of established therapies[J]. American Journal of Clinical Dermatology, 2023,24(2):225-245.

[9] Wang Q, Greene MI. Survivin as a therapeutic target for the treatment of human cancer[J]. Cancers (Basel), 2024,16(9):1705.

[10] Rohayem J, Diestlkoetter P, Weigle B, et al. Antibody response to the tumor-associated inhibitor of apoptosis protein survivin in cancer patients[J]. Cancer Research, 2000,60(7):1815-1817.

[11] Zhao ZS, Ding C, Huang PT, et al. Expressions of PLK1, MYH9 and Smac in keloid tissues and their clinical significance[J]. Chinese Journal of Health Care Medicine, 2025,27(1):131-135. (in Chinese)

[12] Li FK, Gu XY, Zhu YL, et al. Mechanism of Huoxue Jiedu Runzao Decoction on regulating the expression of Smac in submandibular gland cells of mice with Sjögren's syndrome[J]. Shaanxi Journal of Traditional Chinese Medicine, 2023,44(6):693-698. (in Chinese)

[13] Albadari N, Li W. Survivin small molecule inhibitors: recent advances and challenges[J]. Molecules, 2023,28(3):1376.

[14] Mai RH, Wei XM, Yang YW. Expression of Survivin in patients with lung adenocarcinoma and its prognostic significance[J]. Chinese Journal of Experimental Surgery, 2025,42(9):1850-1852. (in Chinese)

[15] Lu DF, Mu YM, Chen XL. Expression of serum pyroptosis-related factors Caspase-3, Survivin, Bax and Bcl-2 in cervical cancer and their involvement in invasion and metastasis[J]. Medical Research and War Trauma Treatment, 2025,38(10):1061-1066. (in Chinese)

[16] Liang HT, Zheng WP. Expressions of C-erbB-2, Ki67 and Survivin in breast cancer tissues and their correlation with clinicopathological features and prognosis[J]. Chinese Journal of Laboratory Diagnosis, 2025,29(6):621-625. (in Chinese)

[17] Mei SS, Tian SW, Duan YL, et al. Expressions of SIRT2, P65 and Survivin in breast cancer tissues and their clinical significance[J]. Journal of Guizhou Medical University, 2024,49(6):819-825. (in Chinese)
[18] Liu YH, Li J, Wang N, et al. Experimental design of Survivin gene silencing inducing apoptosis of cervical cancer cells by RNA interference[J]. Research and Exploration in Laboratory, 2023,42(9):146-150. (in Chinese)
[19] Albadari N, Li W. Survivin small molecule inhibitors: recent advances and challenges[J]. Molecules, 2023,28(3):1376.
[20] Miao QZ, Fan M, Yuan J, et al. Verification of the target role of Survivin (BIRC5) in targeted therapy of keloids by network pharmacology and experimental validation[J]. Chinese Journal of Aesthetic and Plastic Surgery, 2024,35(3):167-178. (in Chinese)
[21] Pandey SK, Paul A, Shteinfer-Kuzmine A, et al. SMAC/Diablo controls proliferation of cancer cells by regulating phosphatidylethanolamine synthesis[J]. Molecular Oncology, 2021,15(11):3037-3061.