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Mechanism of Astrin in head and neck squamous cell carcinoma

Jian Wang[1], Changjian Liu[1], Minghui Wei[2*]

[1] Department of Head and Neck Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100021, China
[2] Department of Head and Neck Surgery, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital & Shenzhen Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Shenzhen, 518116, China

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ABSTRACT

Head and neck squamous cell carcinoma(HNSCC) is a malignant epidermal tumor that seriously threatens human life and health. The main factors affecting the death of patients are local recurrence and lymph node metastasis. Astrin antibody is the basic component of the mitotic spindle required for normal chromosome separation and later development. There are few domestic studies on the mechanism of Astrin in HNSCC. Based on this, this article is studying Astrin in HNSCC. The expression and function of Astrin, and analyze its correlation with clinical pathological parameters and prognosis of patients, and further explore the relevant mechanisms involved in the progression of Astrin in HNSCC. In this experiment, the real-time fluorescent quantitative polymerase chain reaction (PCR) method was used to detect the expression of the Astrin antibody in HNSCC cell lines A and B. Secondly, this article will focus on high metastatic HNSCC cells B. Divided into five groups (blank control group, overexpression positive group, overexpression negative control group, expression suppression positive group, expression suppression negative control group), using real-time fluorescent quantitative PCR technology to detect the expression of Astrin in each group, and then speculate the mechanism of Astrin in HNSCC. Experiments have shown that Astrin is expressed in A and B cells, but its expression in B is significantly higher than its expression in A, and the difference is statistically significant (P<0.001). This shows that the inhibition of Astrin expression has a significant anti-tumor effect and that Astrin plays an important role in the occurrence and development of tumors. It is expected to provide new ideas and reference basis for exploring new therapeutic strategies for targeted therapy of HNSCC.

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Introduction

Squamous cell carcinoma of the head and neck is the world's sixth most common malignant tumor. Its survival rate has not improved significantly in the past few years, and lymph node metastasis is also one of the most important prognostic factors closely related to patients' poor long-term survival rate. It is clear that miRNAs play an important regulatory role in cell life activities such as cell proliferation, differentiation and apoptosis. For head and neck tumors, surgery damages large defects and even affects organ function, and serious side effects caused by radiotherapy often affect patients' quality of life. In the occurrence and development of HNSCC, many oncogenes and tumor suppressor genes play a key role in it, which is helpful for the early diagnosis and treatment strategy formulation and prognosis evaluation of patients with head and neck malignancies, especially HNSCC. It is expected to improve the survival rate of patients (1-3).

Research on the treatment of HNSCC in foreign countries is much earlier than that in China, and the discovery of the Astrin antibody is also earlier than in China, and the development and update of HNSCC treatment technology is fast. The treatment methods and methods of HNSCC have been greatly improved and developed. It is believed that the use of Astrin antibody treatment will become an important breakthrough in the near future. Zhang HD found that miR-17-5p and miR-20a negatively regulate the translation of cyclin D1, and inhibit cells from entering the S phase, thereby inhibiting the proliferation of breast cancer cells and acting as tumor suppressor genes (1). Thavarajah R evaluated the effect of miR-20a on the invasion and migration of oral squamous cell carcinoma cells through CCK-8, Transwell and scratch experiments and found that the expression of miR-20a was down-regulated; after up-regulating the expression of HPV-16E7, the expression of miR-20a increased (2). Azimi studied the role of miR-20a in oral squamous cell carcinoma and found that HPV16E7 inhibited the proliferation, invasion and metastasis of oral squamous cell carcinoma by up-regulating the expression of miR-20a (3).

The use of Astrin antibody to treat HNSCC originated in Western countries. Compared with Western countries, our country's HNSCC treatment technology started late and its development is relatively slow. With the continuous development of science and technology and the maturity of biomaterials, the prevention of local recurrence and regional lymph node metastasis after our country's treat-

* Corresponding author. Email: huazhunpin580323@163.com

ment of HNSCC has become increasingly mature. Warnakulasuriya S proposed that the mechanism of miR-20a is mainly through up-regulating or down-regulating the expression of miR-20a in tumor cells, and then observing the changes in the biological behavior of tumor cells, and then evaluating the relationship between miR-20a and tumor development (4). Liu Y cultured cell lines of head and neck tumors in vitro, and used PCR to determine the infection status of the cells and then grouped them, and irradiated the positive and negative tumor cell lines in a test tube (5). Lakshmanaperumal AS cultured cervical cancer cell lines and head and neck squamous cell cancer cell lines in vitro, and used the antiviral drug cidofovir to reduce the E6/E7 protein at the transcription level and found that it induces cyclin-dependent kinase inhibition in tumor cell lines accumulation of agents (6).

In this paper, by detecting the expression of Astrin in HNSCC cells and clinical specimens, analyzing the relationship between its expression level and relevant clinicopathological parameters and patient survival rate, revealing the expression and clinical significance of Astrin in the occurrence and development of HNSCC, lay the foundation for further study of Astrin's functions and biological effects in vivo and in vitro. At the same time, further, evaluate the imaging data of patients with related HNSCC and unrelated HNSCC after Astrin antibody treatment, calculate the degree of tumor regression of the two before and after treatment, and further perform tumor regression degree classification to compare the two the difference in sensitivity of Astrin antibody therapy provides new ideas and reference for future clinical treatment options for HNSCC.

As the main treatment for patients with HNSCC, radiotherapy has achieved great success in the treatment of early nasopharyngeal carcinoma. However, conventional fractional radiotherapy is not satisfactory in terms of local control rate and survival rate of patients with advanced HNSCC, so radiotherapy many doctors in the world have changed the traditional conventional treatment methods and use unconventional segmentation treatment. Hyperfractionated radiotherapy increases the number of radiotherapy divisions under the premise that the total radiotherapy dose remains unchanged and shortens the radiotherapy time, thereby improving the control rate of local lesions (7-8). The dose-dependence of radiotherapy in normal tissues is greater than that of early responding tissues such as tumors. Increasing the number of radiotherapy divisions while reducing the division dose can give tumor cells a relatively high dose and reduce normal tissue radiation damage.

Radiotherapy is one of the main treatment methods for HNSCC. The fundamental purpose of precise radiotherapy is to increase the dose in the target area while giving the greatest protection to surrounding tissues and organs. Applying techniques such as cone beam tomography and CT simulation three-dimensional planning can help implement precise positioning during radiotherapy to better take advantage of the highly conformable dose of intensity-modulated radiation therapy. Early diagnosis of malignant tumors, precise positioning during radiotherapy and prognostic analysis of patients all rely on advanced imaging equipment. With the development of technology, imaging technology will play an increasingly important role in targeted radiotherapy (9-10).

The main purpose of image preprocessing is to suppress the influence of image speckles on ultrasound images, improve the quality of ultrasound images during the ultrasound-guided needle puncture process, that is, speckle noise, and reduce the ultrasonic imaging system's ability to distinguish between puncture needles and soft tissues, which affected the diagnosis of physicians during percutaneous puncture surgery (11-12).

Ultrasound images have high requirements for edge detail and are non-stationary signal, so the traditional Fourier transform-based signal denoising method can no longer meet the requirements (13-14). Ultrasonic speckle suppression and denoising methods can be roughly divided into spatial domain local statistical filtering, anisotropic diffusion filtering and filtering based on wavelet transform.

Since the filtering denoising effect based on wavelet transform is superior to Kuan filtering, SRAD filtering, Gamma/MAP filtering, Wiener filtering, enhanced Frost filtering, Lee filtering and other standard speckle removal techniques on ultrasound images, the wavelet transform based Filter transformation to remove speckles in ultrasound images (15-16).

The wavelet domain threshold denoising algorithm can select wavelet denoising thresholds at different scales, and then use this threshold to directly or indirectly process the wavelet transform coefficients, especially the wavelet coefficients corresponding to noise, to achieve the purpose of denoising or suppressing noise (19-20). The function of the wavelet threshold function is to remove the wavelet transform coefficients with small values, and to retain or shrink the wavelet transform coefficients with large values. From this, it can be known that it is very important to select the appropriate wavelet domain value function and wavelet denoising threshold (21-22).

Materials and Methods

Experimental design of the mechanism of Astrin in HNSCC

Test Subject

In this experiment, the HNSCC cell lines A and B cultured in a hospital were selected. A was derived from the primary tumor of an HNSCC patient, and B was derived from the lymph node metastasis of the same HNSCC patient. Therefore, B is considered to be a cell line with high metastatic ability, and A is a cell line with low metastatic ability. This article first grouped the cells according to different cell lines (A group and B group), and detected the difference in Astrin expression between the two groups of cells; secondly, this article divided the high-metastatic HNSCC B into five groups (Blank control group, overexpression positive group, overexpression negative control group, expression suppression positive group, expression suppression negative control group), using real-time fluorescent quantitative PCR technology to detect the expression of Astrin in each group. From the differential expression of Astrin in HNSCC cells, the differential expression of Astrin in highly metastatic HNSCC cells, the effect of Astrin on the proliferation of highly metastatic HNSCC cells, and the apoptosis ability of Astrin on highly metastatic HNSCC cells. The influence of Astrin, the influence of Astrin on the migration ability of highly metastatic HNSCC cells, and the influence of Astrin on the invasion

ability of highly metastatic HNSCC cells are analyzed in six aspects.

Experimental Method

Astrin expression in HNSCC

Take out an A and a B cell from the liquid nitrogen irrigation. After the liquid nitrogen evaporates, place them in a 37-degree constant temperature water bath for rapid dissolution. Add the lysed cells to a 15ml centrifuge tube containing 9ml of the medium, centrifuge at 800rpm for 3min, discard the supernatant, add 2ml of complete medium to the centrifuge tube, use a pipette to blow evenly into a single cell suspension, and then inoculate it into the culture flask. Place it in an incubator at 37°C and 5% CO2. The A and B cells in the culture flask were collected separately, and all RNA was extracted after centrifugation, and the RNA concentration was determined by PCR.

Cell transfection and PCR detection after transfection

Choose high-metastasis B cells in good condition for laying 6-well plates, divide the experiment into five groups, and mark the groups on the 6-well plate. After plating, place the plate in a 37°C, 5% CO2 incubator for 24h. After 24h, perform no treatment, overexpression positive transfection, overexpression negative transfection, expression suppression positive transfection, expression suppression negative transfection operation, and then continue to culture for 48h, harvest cells from time to time, and do PCR to detect Astrin after transfection express the situation.

Establish model evaluation index system

The evaluation index is a specific evaluation item determined according to some evaluation goals, which can reflect some basic characteristics of the evaluation object. The index is specific and measurable, and it is the observation point of the goal. Definite conclusions can be drawn through actual observation of objects. Generally speaking, the evaluation index system includes three levels of evaluation indexes: they are the relationship between gradual decomposition and refinement. Among them, the first-level evaluation indicators and the second-level evaluation indicators are relatively abstract and cannot be used as a direct basis for evaluation. The third-level evaluation indicators should be specific, measurable and behavior-oriented and can be used as a direct basis for teaching evaluation.

Statistical processing

Statistical analysis was performed with SPSS 13.0 statistical software. The significance test of difference was performed by one-way analysis of variance, the difference between the two groups was tested by LSD-t, and the PCR results of Astrin expression in cells were performed by group t-test. $P<0.05$ is considered significant and statistically significant.

Results and Discussion

Evaluation index system based on index reliability testing

Here we carry out a reliability analysis on each index of each analysis object, and the results are shown in Table 1.

It can be seen from Figure 1 that the effect of Astrin on the proliferation of highly metastatic HNSCC cells, the effect of Astrin on the apoptotic ability of highly metastatic HNSCC cells, the effect of Astrin on the migration ability of highly metastatic HNSCC cells, and the effect of Astrin on the migration ability of highly metastatic HNSCC cells. The influence of the invasion ability of metastatic HNSCC cells the data obtained by various indicators have a very good effect on the impact of this experiment ($\alpha>0.8$). The differential expression of Astrin in HNSCC cells and Astrin in the highly metastatic head and neck the data obtained from the differential expression of various indicators in squamous cell carcinoma cells has an acceptable impact on this experiment ($\alpha>0.7$), which illustrates the six selected in this article when studying the mechanism of Astrin in HNSCC. The indicators are reasonable, which provides a basis for subsequent experiments.

Based on inspection data

Differential expression of Astrin in HNSCC

The PCR method was used to detect the expression of Astrin in low metastatic HNSCC A and high metastatic HNSCC B. The results are shown in Table 2.

From Figure 2 we can see that Astrin is expressed in both high metastatic HNSCC B and HNSCC A, but its ex-

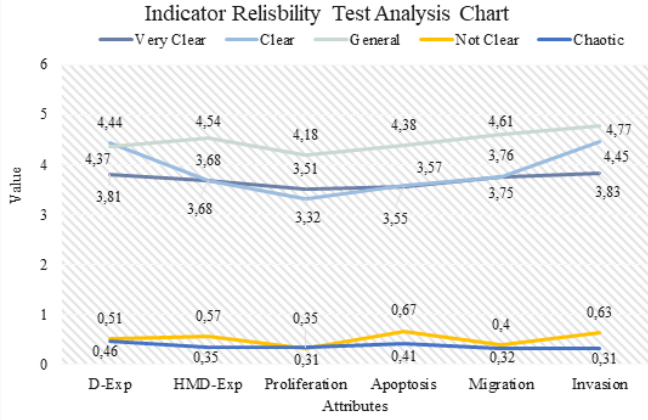

Figure 1. Indicator reliability test analysis chart.

Table 1. Data sheet of evaluation index system for index reliability testing.

	Very Clear	Clear	General	Not Clear	Chaotic	Alpha
Differential Expression	3.81	4.44	4.37	0.51	0.46	0.7754
High Metastatic Differential Expression	3.68	3.68	4.54	0.57	0.35	0.7319
Cell Proliferation	3.51	3.32	4.18	0.31	0.35	0.8328
Apoptosis	3.55	3.57	4.38	0.67	0.41	0.8361
Cell Migration	3.76	3.75	4.61	0.40	0.32	0.8576
Cell Invasion	3.83	4.45	4.77	0.63	0.31	0.8194

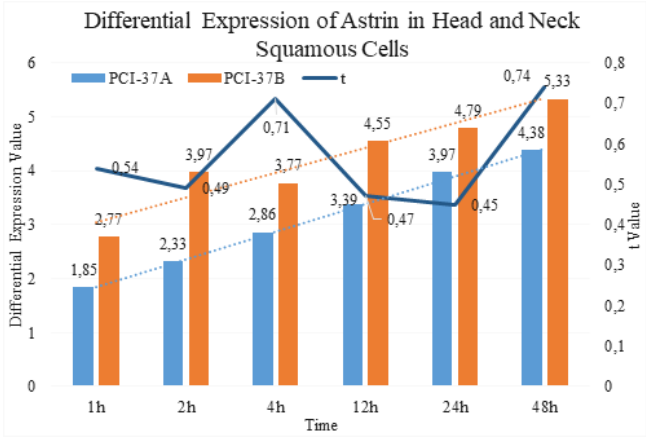

Figure 2. Analysis of differential expression of Astrin in head and neck squamous cells.

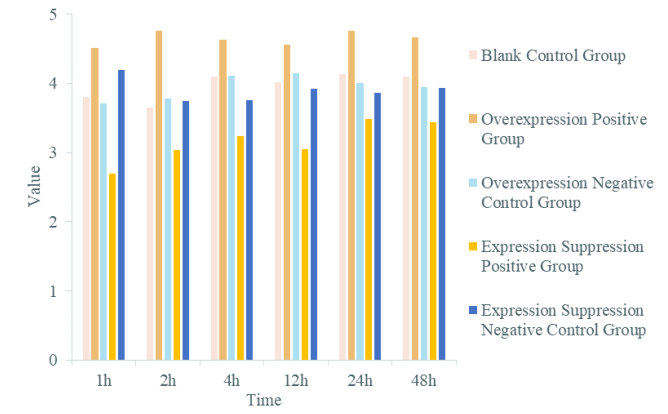

Figure 3. Analysis of the expression of Astrin by PCR after transfection.

pression in high metastatic HNSCC B is higher than that of HNSCC B. Of squamous cell carcinoma cells, the difference was statistically significant (P<0.05). At the same time, because A came from the primary tumor of HNSCC patients, B came from the same HNSCC patients' lymph node metastases. This also proves that B is a cell line with high metastatic ability, while A is a cell line with low metastatic ability.

Differential expression of Astrin in highly metastatic HNSCC

Through transient transfection technology, the overexpression vector, inhibitor and blank vector were respectively transfected into B cells. The experiment was divided into five groups, namely blank control group, overexpression positive group, overexpression negative control group, and expression suppression positive group, expression suppression negative control group, the results are shown in Table 3.

From Figure 3, we can see that the expression of Astrin in the expression suppression positive group was significantly lower than that in the expression suppression negative control group and the blank control group. The results were statistically significant and the difference was significant (P<0.05); the expression suppression negative control group and the blank control group Compared with the control group, there was no difference in the expression of Astrin, showing no difference (P>0.05). It shows that the overexpression plasmid vector we constructed can increase the expression of Astrin; the constructed Astrin inhibitor can inhibit the expression of Astrin, and the transfection is effective.

Effect of Astrin on the proliferation of highly metastatic HNSCC

PCR method was used to detect the effect on the proliferation of HNSCC B. The experiment was divided into five groups, namely blank control group, overexpression positive group, overexpression negative control group, expression suppression positive group, and expression suppression negative control group, each group was measured at 0, 24, 48, 72, 96 hours after transfection Table 4 shows the OD value of the cells.

From Figure 4, we can see that the OD values of each group are basically the same at 0h. On the whole, the differences in cell proliferation in each group were obvious, and the differences in cell proliferation at each time point were also statistically significant. The cell proliferation

Table 2. Astrin differential expression data table in HNSCC.

Time	A	B	t	P
1h	1.85	2.77	0.54	<0.001
2h	2.33	3.97	0.49	<0.001
4h	2.86	3.77	0.71	<0.001
12h	3.39	4.55	0.47	<0.001
24h	3.97	4.79	0.45	<0.001
48h	4.38	5.33	0.74	<0.001

Table 3. Astrin differential expression data table in highly metastatic HNSCC.

	Blank Control Group	Overexpression Positive Group	Overexpression Negative Control Group	Expression Suppression Positive Group	Expression Suppression Negative Control Group
1h	3.80	4.51	3.71	2.70	4.19
2h	3.65	4.76	3.78	3.04	3.74
4h	4.10	4.63	4.11	3.24	3.76
12h	4.02	4.56	4.15	3.05	3.92
24h	4.13	4.76	4.01	3.49	3.86
48h	4.10	4.67	3.95	3.44	3.93
P	0.976	0.001	0.854	0.005	0.987

Table 4. Effect of high metastatic HNSCC cell proliferation.

	Blank Control Group	Overexpression Positive Group	Overexpression Negative Control Group	Expression Suppression Positive Group	Expression Suppression Negative Control Group
0h	1.09	1.07	1.14	1.06	1.17
24h	2.44	3.21	2.67	2.22	2.51
48h	2.97	3.86	3.22	2.84	3.07
72h	3.22	3.93	3.44	3.14	3.56
96h	4.21	4.67	4.29	3.29	4.28
P	0.173	<0.001	0.217	<0.001	0.163

ability of the overexpression positive group was significantly higher than that of the overexpression negative control group and the blank control group (P<0.05); the cell proliferation ability of the inhibition positive group was significantly lower than that of the expression inhibition negative control group and the blank control group (P<0.05), and the difference was statistically significant. This shows that B cell proliferation ability is enhanced after overexpression of Astrin, and B cell proliferation ability is reduced after inhibiting Astrin expression.

Effect of Astrin on the apoptotic ability of highly metastatic HNSCC

The PCR method was used to detect the effect on the apoptosis of HNSCC cells B. The experiment was divided into five groups, namely blank control group, overexpression positive group, overexpression negative control group, expression suppression positive group, and expression suppression negative control group, each group was measured at 0, 24, 48, 72, 96 hours after transfection the number of apoptotic cells and the results are shown in Tables 5 and 6.

From Figure 5, we can see that the expression of Astrin is up-regulated, and the early apoptosis of HNSCC cells B is inhibited; when the expression of Astrin is reduced, the early apoptosis of HNSCC cells B is increased. Comparing the experimental group with the control group, P<0.05, which is statistically significant, and the difference is significant; while the negative control group and the blank control group, P>0.05, which is not statistically significant, indicating that there is no difference between the groups.

Effect of Astrin on the migration ability of highly metastatic HNSCC

The effect of Astrin on the migration ability of head

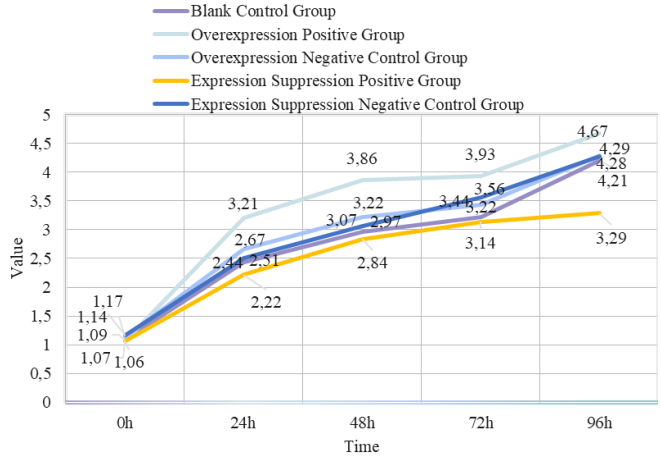

Figure 4. The effect of Astrin on the proliferation of HNSCC.

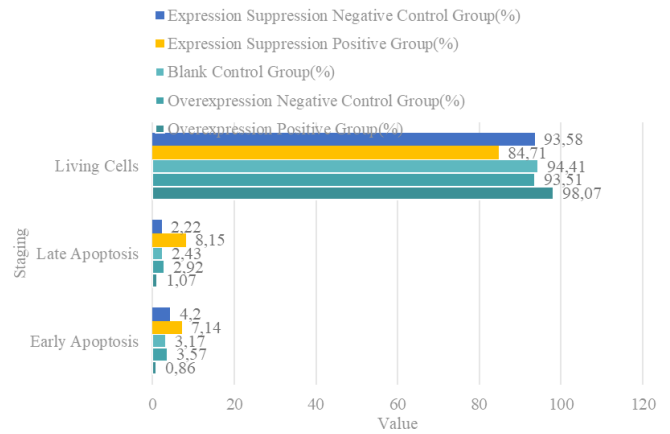

Figure 5. Effect of Astrin on Apoptosis of HNSCC.

Table 5. After Astrin overexpression, cell apoptosis in each group.

Staging	Overexpression Positive Group (%)	Overexpression Negative Control Group (%)	Blank Control Group (%)
Early Apoptosis	0.86	3.57	3.17
Late Apoptosis	1.07	2.92	2.43
Living Cells	98.07	93.51	94.41

Table 6. After the inhibition of Astrin expression, the apoptosis of each group.

Staging	Expression Suppression Positive Group (%)	Expression Suppression Negative Control Group (%)	Blank Control Group (%)
Early Apoptosis	7.14	4.20	3.17
Late Apoptosis	8.15	2.22	2.43
Living Cells	84.71	93.58	94.41

and neck squamous cell carcinoma cell B was studied by PCR method. The number of cells passing through the cell membrane reflects the level of cell migration ability. After transfection, the number of cells passing through the cell was calculated, and the result is shown in Figure 6.

From Figure 6, we can see that the overexpression positive group, overexpression negative control group, and blank control group are compared in pairs, and statistical analysis is performed. The result shows that overexpression negative control group=blank control group<overexpression positive group, that is, overexpression. After Astrin, the number of cells passing through the chamber was significantly more than that of the negative control and the blank control group, and there was no significant difference between the negative control group and the blank control group (P>0.05). It shows that overexpression of Astrin can up-regulate the migration ability of B cells (P<0.05); the same reason can show that inhibiting Astrin expression can down-regulate the migration ability of B cells (P<0.05).

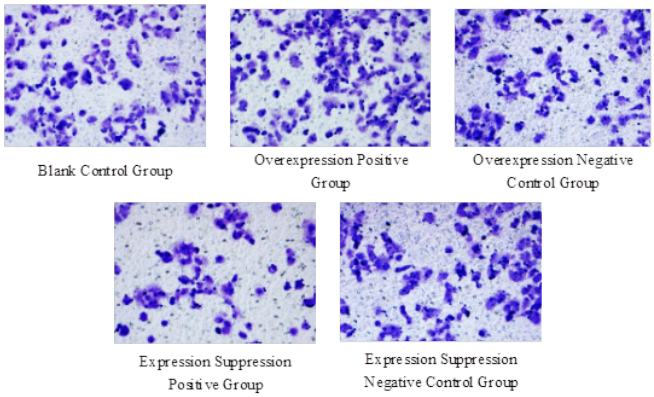

Figure 6. The effect of Astrin on the migration ability of HNSCC. (https://image.baidu.com/)

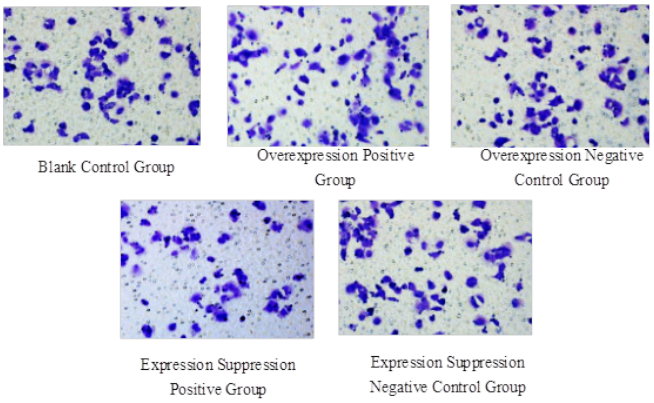

Figure 7. Effect of Astrin on the invasive ability of HNSCC. (https://image.baidu.com/)

Effect of Astrin on the invasion ability of highly metastatic HNSCC

The effect of Astrin on the invasion ability of head and neck squamous cell carcinoma B was studied by PCR method. The cells passing through the Matrigel glue reflect the level of cell invasion. The results are shown in Figure 7.

From Figure 7 we can see that the overexpression positive group, the overexpression negative control group and the blank control group are compared. The result is that the overexpression negative control group=blank control group<the overexpression positive group, that is, the overexpression vector is transfected The number of B cells passing through Matrigel gel was significantly more than that of the other two groups of cells. It shows that overexpression of Astrin can up-regulate the invasion ability of B cells (P<0.05); the same reason can show that inhibiting Astrin expression can down-regulate the invasion ability of B cells (P<0.05). In this regard, there are already similar reports (23-25).

The expression of Astrin in the high-metastatic HNSCC cell B was higher than that in the low-metastatic HNSCC cell A. Astrin can promote the proliferation, migration and invasion of HNSCC cells, and inhibit the apoptosis of HNSCC cells. The expression of Astrin in the overexpression positive group was significantly higher than that in the overexpression negative control group and the blank control group, and the results were statistically significant and the difference was significant (P<0.05); the expression of Astrin in the expression suppression positive group was significantly lower than the expression suppression negative control group compared with the blank control group, the results are statistically significant and the difference is significant (P<0.05), indicating that the overexpression plasmid vector we constructed can increase the expression of Astrin; the constructed Astrin inhibitor can inhibit the expression of Astrin, and the transfection is effective.

Astrin is abnormally highly expressed in HNSCC and has important clinical significance. Therefore, this paper uses PCR in vitro to study the biological functions of Astrin in tumorigenesis and development. Astrin can significantly inhibit the proliferation, migration and invasion of HNSCC cells and enhance the sensitivity to chemotherapeutic drugs. Inhibition of Astrin expression has a significant anti-tumor effect, indicating that Astrin plays an important role in the development of tumors and is expected to be a target for exploration of new treatment strategies for HNSCC providing new ideas and reference basis.

Astrin is highly expressed in patients with HNSCC, showing its tumor-promoting effect. In order to better study the biological functions of Astrin, this article studied its effect on the proliferation, invasion, metastasis and monoclonal formation ability of HNSCC cell lines A and B in vitro. In this paper, PCR and linear regression analysis proved that miRNAs and Astrin in HNSCC tissues are obviously negatively correlated, and the expression level of Astrin in HNSCC cells transfected with miRNAs was significantly reduced.

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Interest conflict

The authors declare that they have no conflict of interest.

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