Cancer and Tumor Review

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ABSTRACT
Purpose: (1) To investigate the expression of CaSR in papillary thyroid carcinoma, thyroid benign lesion and normal thyroid cells by immunohistochemistry and to analyze the relationship between CaSR and papillary thyroid carcinoma. (2) To study the difference of the expression of thyroid papillary carcinoma between calcification group and thyroid papillary carcinoma without calcification and the difference of calcification between thyroid papillary carcinoma and benign thyroid lesions and to analyze its significance. (3) To investigate the expression characteristics of CaSR in blood stasis syndrome group and non-blood stasis syndrome group and to analyze the correlation between CaSR and TCM blood gall blood stasis syndrome. Methods: Thirty patients (thyroid papillary carcinoma and 40 cases of thyroid benign tumor) were treated with MaxvisionTM2 / HRP immunohistochemical two-step method to investigate the effect of CaSR on thyroid papillary carcinoma, thyroid benign lesion and normal thyroid tissue. All data were analyzed by SPSS 17.0 using nonparametric test, P <0.05 for the difference was statistically significant. Results: The expression of CaSR in thyroid papillary carcinoma and the positive expression of CaSR in thyroid benign lesion were statistically significant. (3) CaSR in thyroid papillary carcinoma was significantly higher than that in CaSR (P <0.05) and the positive expression of CaSR in the calcification group of thyroid papillary carcinoma was higher than that in benign thyroid calcification group, the difference was statistically significant. (3) The expression of CaSR in thyroid papillary carcinoma was significantly higher than that in thyroid papillary carcinoma. There was a significant difference in the positive expression of CaSR between blood stasis syndrome group and non-blood stasis syndrome group (P <0.05). Conclusion: (1) CaSR in normal thyroid tissue in a small amount or no expression in papillary thyroid carcinoma and thyroid benign lesions in the expression of thyroid papillary carcinoma in the high expression of: (2) CaSR in the thyroid papillary carcinoma of the calcification group (P <0.05). In conclusion, CaSR may play a key role in the calcification of thyroid papillary carcinoma; (3) CaSR may play an important role in the calcification of thyroid papillary carcinoma. The positive expression of blood stasis syndrome group was higher than that of non-blood stasis syndrome group which indicated that CaSR might be correlated with Chinese medicine gall blood stasis syndrome.

KEYWORDS: CaSR; Thyroid cancer; Calcification; Immunohistochemistry; Blood stasis syndrome

Preface

Thyroid cancer in the traditional Chinese medicine is known as the ‘stone gall’ and the cause is due to lack of righteousness, evils virtual invasion, gathered in the meridians, organs, leading to qi stagnation, phlegm coagulation, blood stasis and other pathological changes. The modern pathology of thyroid cancer is the organization of hyperplasia and degeneration, increased blood around the tumor, blood flow, pathological tissue material exchange increased, which from the micro-prompted the presence of blood stasis. Tumor is a systemic disease, Chinese medicine blood stasis and tumor development and metastasis have a close relationship, blood circulation is an important role in the treatment of cancer. CaSR as a possible participatory factor in the development of thyroid cancer which may be associated with the stone gall blood stasis there is a certain correlation.

In this study, the role of CaSR in the pathology of thyroid carcinoma and the mechanism of calcification of thyroid carcinoma were analyzed by immunohistochemical method. The role of CaSR in the pathogenesis of thyroid carcinoma was analyzed by studying the relationship between CaSR expression in thyroid papillary carcinoma.

Clinical research

1. Materials and methods

1.1. Clinical specimens

Selected from May 2011 to November 2011, Fujian Provincial Hospital, the basic surgery by surgery in the frozen confirmed thyroid tissue paraffin specimens in 60 cases and by two pathologists for benign and malignant identification
including thyroid papillary carcinoma 40 cases of benign thyroid lesions in 20 cases (including nodular goiter and adenoma lesions). No other treatment before surgery except for drug treatment which are the initial operation. Preoperative thyroid ultrasound or CT examination were done

1.2. Diagnostic criteria

Thyroid cancer and thyroid benign lesions are mainly based on intraoperative and postoperative pathology.

Chinese medicine gall blood stasis syndrome diagnosis criteria [3]: According to the 2002 version of ‘Chinese medicine new drug clinical research guidelines’, as follows:

Subcutaneous ecchymosis, disease product, from the blood of the blood, dark purple tongue or ecchymosis, petechia, tongue pulse rough, pulse astringent, no veins or Shen string, chord late

Secondary disease: skin disorder, limb numbness or hemiplegia, insanity, manic, forgetfulness, local sensory abnormalities, trauma history, history of surgery and history of abortion.

With blood stasis syndrome 2, or the main symptoms of 1, secondary disease 2, you can diagnose.

1.3. Case grouping

(1) During the study period, some of the patients admitted to the preoperative Chinese medicine data collection, the use of hope, smell, ask, cut four diagnostic ginseng, record the relevant symptoms and signs by two senior Chinese medicine practitioners according to the above blood stasis syndrome. The data of patients with postoperative pathology were recorded and divided into blood stasis syndrome group and non-blood stasis syndrome group.

(2) Postoperative pathological diagnosis of sand bodies combined with preoperative thyroid ultrasonography, CT examination prompted calcification. Both were unified into calcification group (due to the essence of sand is the formation of calcification, it is a group). Thyroidectomy after the pathology of benign and malignant lesions is divided into thyroid papillary carcinoma of the calcification group, thyroid papillary carcinoma without calcification group and benign thyroid calcification group.

1.4. Main reagents

Anti-human CaSR polyclonal antibody / Calcium Sensing Receptor, two-step immunohistochemical reagent / ready-to-use MaxvisionTM2 / HRP kit, concentrated EDTA antigen repair buffer, liquid DAB enzyme substrate reagent kit, PBS Buffer, poly-L-lysine anti-off tablets were purchased from Fujian Mai new biotechnology development company. Other reagents include anhydrous ethanol, xylene, hematoxylin and turpentine for the sale of pure products which are provided by the Fujian Provincial Hospital of Pathology.

1.5. Main instrument

Paraffin slices, refrigerator, thermostat oven, electric thermostat oven automatic dehydration machine, induction cooker, pressure cooker, optical microscope, photographic microscope, graphic analysis box, slide, dyeing tank, moisturizing incubator box high temperature plastic slices Fujian Provincial Hospital of Pathology provided.

1.6. Experimental methods

40 cases of papillary thyroid carcinoma were taken 4um slices of thickness, of which a slice for the immunohistochemical staining of CaSR and the other one for random extraction. The PBS negative pairs of 20 cases of benign thyroid lesions are selected from the corresponding normal tissue wax block 10 cases with each one were taken 4um thickness of the slice 1. Store the oven at 60 °C for at least 3 hours but not more than 24 hours long.

Line maxvisionTM2 / HRP immunohistochemical staining, the steps are as follows:

1. Paraffin section dewaxing, hydration will be sliced in turpentine 15min, xylene 10min, 100% alcohol 5min, 95% alcohol 5min, 85% alcohol 5min, dewaxing, gradient alcohol, hydration. Tap water rinse.

2. The slices washed with PBS 3min × 3 times.

3. Repair the antigen will be concentrated EDTA antigen repair buffer in a pressure cooker, heated to boiling, the dewaxed hydrated tissue slices into the boiling buffer, continue to heat to the jet, 2min after taking the pressure cooker, in the Water under the cooling, room temperature.

4. Washed with PBS 3min × 3 times.
5. Dropping 3% hydrogen peroxide 50ul, need to completely cover the slice area, incubated at room temperature for 10min, to block the activity of endogenous peroxidase.

6. The slices washed with PBS 3min × 3 times.

7. Remove the PBS, sliced on the diluted to 1: 100 concentration of the first antibody 50ul, 4 ℃ refrigerator overnight.

8. The slices washed with PBS 3min × 3 times.

9. Remove the PBS, each slice on the use of MaxvisionTM2 / HRP reagent 50ul, need to completely cover the tissue section area, incubated at room temperature for 15min.

10. The slices were rinsed with PBS for 3 min x 3 times.

11. Remove the PBS, sliced on the freshly prepared enhanced DAB color reagent color. Microscopic observation for 5 minutes to control the degree of color development.

12. Tap water rinse to terminate the color, hematoxylin dyeing, washing. PBS rinse back to blue.

13. Gradient alcohol dehydration, xylene transparent, neutral gum seal.

Replace the primary antibody with PBS as a negative control for the positive expression of CaSR. The procedure is the same as above.

1.7. Determination of results

The expression of CaSR in the experimental group and the control group was observed by microscopy and compared with the control group. Cells appear in the cytoplasm above the background stained brown granules stained as positive cells. In each tissue slice, select 5 high power field (× 400) camera camera and enter the computer storage, using HMIAS. 2000 color pathology analysis system, semi-quantitative analysis [4]: After dyeing, optical microscope at high magnification per field count 200 nucleated cells, a total of 5 visual field. Where cytoplasmic brownish are CaSR positive cells. (15% ~ 20%), expressed as +: flake distribution (20% ~ 50%), expressed as ++; around the positive cells, the positive cells ≥ 15% positive expression, Glands tight cloth (50% to 80% and above), counted as +++.

All counts were assessed by an experienced 2-day physician.

1.8. Statistical analysis

All data were analyzed by SPSS 17.0, using nonparametric test of grade data, P <0.05 for the difference was statistically significant.

2. Results

2.1. Immunohistochemical staining

Under the light microscope, thyroid tissue was observed to appear brownish brown granules in the cytoplasm, and its color intensity was higher than that of the background nonspecific staining, and CaSR immunohistochemical positive cells were determined. (Figure 2), CaSR in thyroid cancer in patients with thyroid cancer (Figure 2, Figure 3, Figure 4, Figure 5); CaSR in thyroid papillary carcinoma cells positive (Figure 2, Figure 3); positive cells stained in the cytoplasm, the distribution was dense brown or brown granules, in the thyroid papillary carcinoma of the cancer cells expressed significantly.

![Figure 1](immunohistochemical staining, x 100, PBS alternative primary antibody negative control)
2.2. Statistical analysis

Table 1. CaSR in thyroid cancer (TC), thyroid benign lesions (BTL), thyroid normal tissue (NT) expression

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<td>4</td>
<td>7</td>
<td>10</td>
<td>19</td>
<td>40</td>
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<tr>
<td>BTL</td>
<td>12</td>
<td>4</td>
<td>3</td>
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<tr>
<td>NT</td>
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<td>2</td>
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Note: The Kruskal-Wallis H nonparametric rank test with multiple samples was used as the following: a total of 40 patients in the TC group, the average rank of 46.41; the BTL Group 20 cases, the average rank of 23.33; NT group 10 cases, the average rank of 16.2. Chi-square statistic is 29.935, the degree of freedom is 2, \( P = 0.000 \); according to \( \alpha = 0.05 \) level, statistically significant, can be considered thyroid cancer, thyroid benign lesions and thyroid normal tissue CaSR receptor expression is generally difference.

Note b: Further application of Wilcoxon rank sum test for thyroid cancer, thyroid benign lesions and normal tumor thyroid tissue comparison, the results are as follows:

TC group and NT group, TC group of 40 cases, the average rank of 29.73, the rank of the sum of 189.00, NT group of 10 cases, the average rank of 8.60, the rank of the sum of 86.00. Mann-Whitney U statistic is 31.000; \( Z = -4.278 \), bilateral test \( P = 0.000 \); according to \( \alpha = 0.05 \) level, statistically significant, can be considered a difference between the two.

TC group and BTL group, TC group of 40 cases, the average rank of 37.19, the rank of the sum of 1917.00, BTL group of 20 cases, the average rank of 17.13, the rank of the sum of 342.5. Mann-Whitney U statistic is 132.500; \( Z = -4.278 \), bilateral test \( P = 0.000 \); according to \( \alpha = 0.05 \) level, statistically significant, can be considered a difference between the two.
-4.355, bilateral test $P = 0.000$; according to $\alpha = 0.05$ level, statistically significant, can be considered between the two differences.

BTL group and NT group, BTL group, 20 cases, the average rank of 16.70, the rank of the sum of 334.00, NT group of 10 cases, the average rank of 13.10, the rank of the sum of 131.00. Mann-Whitney U statistic was 76.000; $Z = -1.266$, bilateral test $P = 0.205$; according to $\alpha = 0.05$ level, no statistically significant, can be considered no difference between the two.

### Table 2. CaSR in thyroid cancer (TC) calcification group and non-calcified group expression

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<td>9</td>
<td>19</td>
<td>30</td>
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<tr>
<td>Non-calcification group</td>
<td>4</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>10</td>
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</table>

Note: a non-parametric rank test with two independent samples, a total of 30 cases of calcification and calcification between the TC calcification group and the calcification group, with an average order of 25.12, a rank of 753.50, no calcification group 10 cases, the average ranking of 6.65, the rank of the sum of 66.50. Mann-Whitney U statistic was 11.500; $Z = -4.634$, bilateral test $P = 0.000$; according to $\alpha = 0.05$ level, statistically significant.

### Table 3. Expression of CaSR in thyroid carcinoma (TC) and thyroid benign lesion (BTL) calcification

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<tr>
<td>TC</td>
<td>0</td>
<td>2</td>
<td>9</td>
<td>19</td>
<td>30</td>
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<tr>
<td>BTL</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>7</td>
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Note: The non-parametric rank test of two independent samples was used. There were 30 cases of TC calcification and BTL calcification and TC calcification. The average rank was 22.30, the rank was 669.00, the BTL calcification group A total of 7 cases, the average ranking of 4.86, the rank of the sum of 34.00. Mann-Whitney U statistic was 6.000; $Z = -4.187$, bilateral test $P = 0.000$; according to $\alpha = 0.05$ level, statistically significant.

### Table 4. Expression of CaSR in thyroid carcinoma (TC) blood stasis syndrome group and non-blood stasis syndrome group

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<td>2</td>
<td>4</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>Non-blood stasis syndrome</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>15</td>
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Note: a non-parametric rank test with two independent samples, 25 cases of blood stasis syndrome group and blood stasis syndrome group, 25 cases of blood stasis syndrome group, average order of 25.70, 642.50, non-blood stasis syndrome group of 15 cases, the average rank of 11.83, the rank of the sum of 177.50. Mann-Whitney U statistic was 57.500; $Z = -3.891$, bilateral test $P = 0.000$; according to $\alpha = 0.05$ level, statistically significant.

### 3. Discussion

#### 3.1. Expression of CaSR in Thyroid Papillary Carcinoma

Thyroid cancer is a common surgical disease. In recent years, the incidence of a significant increase in the trend of epidemiological studies [5] showed: the incidence of differentiated thyroid cancer had increased the proportion of patients with early thyroid cancer and thyroid papillary carcinoma than the rise of the current domestic thyroid cancer clinical epidemiology of the three main features. On the other hand, because of its changing biological behavior and pathological process of slow and occult, there are diagnosis difficulty especially for small cancer and other lesions. It is prone to missed diagnosis, misdiagnosis, as well as delayed treatment or over-treatment. Meanwhile, ultrasound exploration for thyroid nodular calcification has been widely used in the diagnosis of thyroid cancer, thyroid calcification and thyroid cancer, especially papillary carcinoma have a clear relationship.

Ultrasoundography has become an important means of preoperative examination of thyroid disease and calcification especially microcalcification which is one of the specific signs of thyroid cancer. A number of studies have shown that thyroid calcification of thyroid cancer diagnosis is highly specific to the most obvious micro-calcification. Khoo et al. [6] reported that the calcification rate of thyroid malignancy was much higher than that of benign thyroid disease and the difference was statistically significant. Consorti et al. [7] also reported that the degree of specificity of simple calcification for thyroid cancer For 83% to 90% and papillary carcinoma of the diagnostic specificity is as high as 93% to 95%, thyroid cancer in the pathological diagnosis, 40-50% of the cases have the presence of sand, whether in the lymph nodes or Thyroid surrounding tissue, found that the presence of sand particles have suggested the possibility of occult thyroid cancer. Qin Qian Miao et al [8] found that almost all of the sand in the papillary thyroid can be found in the preoperative examination of the microcalcifications can basically reflect the pathology of the sand. It is caused
by the tip of the papillary infiltration of calcium deposition and cell necrosis and formation, hence the diagnosis of malignant nodules have a higher specificity. In fact, the incidence of calcification in the incidence of thyroid cancer is between 50% -75% [9]. The incidence of papillary carcinoma may be higher in this group of experimental papillary thyroid carcinoma in 40 cases of which 30 cases of calcification, calcification Rate of 75% and this is basically similar.

CaSR is a key component in the calcium balance system, not only in maintaining the body calcium ion steady state and other metal ions but also play a key role in the steady play and participate in regulating cell differentiation, value, apoptosis, gene expression, calcium channel opening [10]. CaSR can cause tumor malignancy and changes in biological characteristics in different tissues and the expression level is quite different. Sanders JL et al [11] study: CaSR in normal breast tissue and breast cancer were expressed in the high metastatic, especially in bone metastases in breast cancer increased significantly at the cell level is also true, which indicates that CaSR and tumor malignancy and changes in biological characteristics are closely related in which case it has carcinogenic properties. Liao J et al [12] found that with the increase in Ca2+ prostate cancer, its proliferation changes were also found to have a high expression of CaSR. In contrast, Chakraborty S et al. [16] found that colon cancer and parathyroid cancer often showed a decrease or absence of CaSR expression. CaSR activation inhibited cell proliferation, suggesting that CaSR in these malignant cells play a role of tumor suppressor gene. Keiichi Hizaki et al [13] used RT-PCR and immunohistochemistry to analyze the expression of CaSR in colon cancer cell lines and found that the expression of CASR gene and protein in cancer tissues was significantly down-regulated, CASR methylation was detected in colorectal cancer 69% and 90% of lymph node metastasis were significantly associated with the decrease of CASR expression. The results showed that the inactivation of CASR played an important role in the development and progression of colorectal cancer. CASR in a variety of tumors are expressed, and calcium metabolism is closely related.

The expression of CaSR in thyroid papillary carcinoma was significantly different from that in thyroid papillary carcinoma and thyroid benign lesion and normal thyroid tissue and the positive expression of CaSR in thyroid papillary carcinoma was significantly different from that in normal thyroid tissue. There was no significant difference in the expression of CaSR between thyroid papillary carcinoma and thyroid benign lesion and thyroid normal tissue but there was no significant difference between thyroid benign lesion and normal thyroid tissue. Thyroid benign lesions are mostly thyroid nodular swelling including thyroid normal tissue between the cells caused by small atypia and some contain some cases of adenoma-like cases, cell shape slightly larger and some are small cancer which cannot be exclude or contain calcification so there are still some expression. The positive expression rate of CaSR in thyroid papillary carcinoma was 90%, and there was a significant difference between thyroid papillary carcinoma and thyroid benign lesion and thyroid normal tissue which indicated that CaSR was highly specific for thyroid papillary carcinoma, CaSR and thyroid nipple. The development of cancer has a very close relationship. On the other hand, the positive expression of CaSR in calcification group of thyroid papillary carcinoma was significantly higher than that in thyroid papillary carcinoma without calcification (P <0.05). The positive expression of CaSR in thyroid carcinoma calcification group was significantly higher than that in thyroid benign lesion (P <0.05), the difference was statistically significant, suggesting that CaSR may play a key role in the calcification of thyroid papillary carcinoma which is similar to calcification in the highly specificity of thyroid papillary carcinoma. The presence of calcified foci in papillary carcinoma is the same as the high expression of CaSR in thyroid cancer which is associated with Ca2+ transduction metabolism in combination with colorectal cancer, breast cancer bone metastases, etc. [14,15] CaSR is likely to be involved. The occurrence and development of thyroid cancer, and calcification has a close relationship. The reasons for the formation of malignant calcification, there are two main points of view,(1) Firstly, it may be thyroid cancer due to the rapid growth of malignant tumor cells, tumor blood vessels and fibrous tissue proliferation quickly and unbalanced, so that the tip of the nipple or even progressive (2) It may also be some of the substances secreted by the tumor itself, such as glycoproteins and mucopolysaccharides, leading to calcification [16]. At present, some studies have questioned the view of the former that the formation of sand is not secondary to tumor necrosis, such as Cameron et al. [17] that the sand particles are released from intact tumor cells to local metabolites secondary to calcification The According to the results of this immunohistochemistry, CaSR in papillary thyroid carcinoma in the strong expression, and its calcification is closely related, we believe that the formation of sand is very likely due to tumor cells caused by their own secretion of substances. The essence of calcification is the formation of calcification. In this study, the cases of calcification in the pathology were attributed to the calcification group, and the calcification group was used as an effective supplement to preoperative color Doppler ultrasonography. The proportion of calcification group in papillary thyroid carcinoma was higher, Also confirmed from the side of the thyroid papillary carcinoma has a relatively high calcification rate.

Tumor is associated with a variety of genes and a variety of factors, CaSR on the role of the tumor also involves a number of Gang Su, its role in the tumor mechanism is not very clear, now that CaSR may be through the G proteinc-PLC-IP3 Mediated intracellular calcium overload leads to mitochondrial damage, thereby activating downstream Caspase-3-induced apoptosis. CaSR activation causes calcium (Ca2+ ) increase in the main mechanism of endoplasmic reticulum or sarcoplasmic reticulum Ca2+ release. In most cases, activation of CaSR is mediated by a G-protein-mediated second messenger system (eg. activation of the PLC-IP3 pathway, facilitation of calcium release in the calcium pool; DAG activation of PKC, via calcium storage-induced calcium channels, Calcium influx), leading to rapid increase in Ca2+ [18]. The mitogen-activated protein kinase (MAPK) and tyrosine kinase may also play an important
role in CaSR signaling [19]. With the gradual disclosure of the study, it may be possible to find a new entry point for clinical treatment.

3.2. Correlation between CaSR and Chinese Herbal Medicine and Blood Stasis Syndrome

Ming Chen Gong Gong in the ‘surgical authentic’ said ‘wife slimming disease, non-yin and yang is qi swollen, is the five blood stasis phlegm stagnation.’ Qing Qi Qi in the ‘surgery Dacheng’ also said “the five internal organs fire turbidity, blood stagnation, each have a sense.” Qing Dynasty Zou Yue “surgical authentic is thin tumor more than six evil, camp health qi stagnation.” These instructions showed that thyroid tumors and blood stasis is closely related.

Western medicine name ‘thyroid cancer’ in the motherland medicine is called stone gall, ‘three because of extreme disease syndrome theory? Gall tumor syndrome’ by the type of edema, color is divided into gas, blood, tendons, meat. Five, said: ‘hard cannot move, the name of stone gall’. The development of stone gall and emotional, diet, soil and water and other closely related to the cause, the basic pathogenesis is: qi stagnation, phlegm coagulation, blood stasis in the neck before the end. ‘Medical gold Kam’ treatment of gall disease name ‘seaweed Yuhu Tang’ is for the phlegm stasis blood of the card, the rule of law to ‘qi and blood circulation, phlegm Xiaoling’, the side of angelica, Chuanxiong, Blood stasis of the top grade, which can achieve a certain effect and stone gall blood stasis in the understanding of the relationship.

Modern medical research that: the blood of patients with tumor concentration, sticky, poly, coagulation hypercoagulable state, tumor blood stasis [20] through the tumor occurrence, proliferation, invasion and metastasis of different pathological stages. Famous scholar Chen Keji that: tumor and blood stasis is closely related to the main manifestations of hemorheology, platelet function, coagulation, inflammation and connective tissue metabolism, microcirculation, vasoactive factors, hemodynamics, tissue support and so on Changes in close correlation, in recent years, this research is also increasing, such as Hu Qingfu et al. [21] observed blood stasis type malignant tumor patients with erythrocyte membrane micro-viscosity was significantly higher than healthy people, resulting in microcirculation disorders, and easy to form micro thrombus.

Molecular biology, the expression factor and the increase in blood stasis, such as a large number of literature [22,23] that VEGF and a variety of tumor blood stasis has a significant correlation, Zhang Bin, Xu Zhihui [24] also found that VEGF has anti-ischemia-reperfusion-induced apoptosis, the mechanism may be through inhibition of CaSR activity, thereby reducing the pro-apoptotic protein Bax and increased anti-apoptotic protein Bel2 to achieve, in view of VEGF and blood stasis between the positive correlation, There was a negative correlation between VEGF and CaSR, and CaSR may be associated with blood stasis syndrome. On the other hand: Chinese medicine that cancer, calcification are attributed to ‘Zhengjia accumulation’, and ‘Zhengjia accumulation’ and blood stasis syndrome inseparable.

Immunohistochemistry showed that the positive expression of CaSR in thyroid carcinoma group and non-blood stasis syndrome group was statistically significant (P <0.05), CaSR in thyroid cancer group Positive expression was significantly higher than non-blood stasis syndrome group, suggesting that CaSR may be associated with Chinese medicine gall blood stasis. CaSR is likely to be involved in the formation of blood stasis syndrome, combined with the previously thought that CaSR is likely to be the secretory substance of the tumor itself, CaSR may play a role in the formation of blood stasis in the process of promoting the formation of calcification Blood stasis syndrome formation, and may be thyroid cancer blood stasis one of the material basis. Blood stasis is a pathological product, to a certain extent, is the cause, blood stasis after the formation of, but also increase the expression of CaSR, which is CaSR in thyroid cancer in the high expression of the characteristics of performance. At present, the diagnostic criteria of blood stasis syndrome of Chinese gallst is still being explored. In the diagnosis standard of blood stasis syndrome of gastric cancer and colorectal cancer, there are a large number of molecular biology test indicators such as P53, c-erbB-2, VEGF and so on , And is expected to judge the condition and prognosis of molecular indicators, the role of blood stasis in the diagnosis.

3.3. Significance of CaSR in diagnosis and treatment of Chinese and western medicine

As with all malignant tumors, accurate diagnosis before surgery is an important factor in the correct treatment due to the domestic fine needle aspiration cytology (FNAC) diagnosis of the level and the lack of popularity, is the differentiation of thyroid cancer. The overall level of diagnosis is lower than the advanced level of foreign advanced medical reasons. Thyroid papillary carcinoma in thyroid cancer in the highest proportion of a type is more prone to lymph node metastasis. Ultrasound diagnosis, especially the combination of ultrasound technology and needle aspiration technology as a diagnostic method will be used as a differentiation of thyroid cancer diagnosis of important development direction. If CaSR can be specifically applied to the thyroid papillary carcinoma in needle aspiration technology, because of its positive expression in thyroid cancer, combined with calcification of thyroid cancer and its high specificity and calcium metabolism may exist, will be beneficial Improve the early diagnosis of thyroid cancer.
Expression and significance of CaSR in papillary thyroid carcinoma and its correlation with Chinese medicine gall blood stasis syndrome

With the progress of molecular biology, CaSR agonists have been experimentally used [25,26] such as in parathyroid disease, CaSR agonists can rapidly and dose-dependently reduce PTH secretion, thereby inhibiting parathyroid cell proliferation and Reduce blood phosphorus to maintain calcium and phosphorus balance, the treatment process can prevent hypocalcemia and other side effects. The development of CaSR agonists makes it possible to inhibit the secretion of PTH, which avoids the presence of side effects such as hypercalcemia and is of new hope for the treatment of primary and secondary HPT patients, independent of elevated serum calcium concentration and inhibition of PTH secretion. Molostvov et al [27] also found that CaSR in chronic kidney disease in patients with vascular calcification play a key role. They used neomycin (CaSR agonists), MEK1 inhibitors, PLC inhibitors and transfected CaSR-siRNA, etc., to stimulate CaSR can lead to MEK1 / ERK1, and PLC pathway activation and cell proliferation up. CaSR antagonist research, whether it can avoid some patients such as thyroid microsurgery surgery, such as the use of CaSR antagonist for local injection of tumors to treat thyroid cancer, thyroid cancer will be a clinical treatment to bring some help. The combination of Chinese medicine and the diagnosis of Western medicine has not yet been related to the study and its research with Chinese medicine gall blood stasis. It also can provide a basis for it.

4. Conclusions

(1) CaSR is expressed in normal thyroid tissue, or is expressed in thyroid papillary carcinoma and thyroid benign lesion, and is expressed in the tissues of thyroid papillary carcinoma.

(2) The positive expression of CaSR in thyroid papillary carcinoma was higher than that in calcification group, and there was a significant difference between calcification group and thyroid benign lesion, suggesting that CaSR may be calcified in thyroid papillary carcinoma Play a key role.

(3) The positive expression of CaSR in thyroid cancer group was significantly higher than that in non-blood stasis syndrome group, suggesting that CaSR may be related to Chinese medicine gall blood stasis syndrome, and may be the basis of blood stasis syndrome one.

(4) In this study, the expression and significance of CaSR in papillary thyroid carcinoma were discussed, and the relationship between CaSR and thyroid gingival blood stasis syndrome was discussed. However, due to the experimental study, the study time, There are still many deficiencies, such as thyroid benign disease sample cases are too few, thyroid cancer cases of follicular myeloid carcinoma, lack of CaSR in different stages of thyroid cancer and its metastasis in-depth study, calcification Further classification (microcalcification, calcification, peripheral calcification, isolated calcification spots), and Chinese medicine gall blood stasis syndrome, such as the severity of light and so did not further explore. In the future, we can further study and increase the number of samples to arrive at more objective conclusions and use them in clinical practice.

References