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# The Expression and Clinical Significance of IL-4 and IL-13 in Papillary Thyroid Carcinoma

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**Abstract:** Papillary thyroid carcinoma (PTC) is one of the most common thyroid tumors in clinic. The incidence of papillary thyroid carcinoma is increasing year by year, especially in Cangzhou area, which brings great physical and mental pain to patients. *Object*: To explore the expression and clinical significance of interleukin-4 (IL-4) and interleukin-13 (IL-13) in the tissues and serum of patients with papillary thyroid carcinoma (PTC). *Method*: 120 cases of PTC patients were randomly selected as the experimental group, who underwent radical mastectomy at the Thyroid and Breast Surgery Department of Cangzhou Central Hospital from January 2018 to April 2019, and the PTC tissues and their adjacent tissues and serum samples were collected. 120 healthy people were matched 1:1 as the control group in the hospital physical examination center during the same period, according to the gender, age and body mass index of the experimental group, and serum samples were collected. The immunohisto chemical SP method is adopted to test the expression of IL-4 and IL-13 in the tissues, and the ELISA is adopted to test the serum levels of IL-4 and IL-13. Analyze the relationship between IL-4 and IL-13 expression and clinicopathological characteristics in PTC. *Result*: It was significantly higher with the positive expression rate of IL-4 and IL-13 in PTC tissues than that in adjacent tissues ($P<0.05$), and it was a significant positive correlation between IL-4 and IL-13 expressed in PTC tissues ($r=0.375$, $P=0.002$); It was significantly higher in the serum levels of IL-4 and IL-13 in PTC patients, than that in healthy subjects ($P<0.05$), and it was a significant positive correlation between IL-4 and IL-13 expressed in the serum of PTC patients ($r=0.381$, $P<0.01$); The expression of IL-4 and IL-13 was related to the maximum tumor diameter, TNM stage, degree of differentiation, and lymphatic metastasis in PTC ($P<0.05$). *Conclusion*: IL-4 and IL-13 were highly expressed in PTC, and the expression level may become a reference indicator for predicting the occurrence and development of PTC.

**Keywords:** Papillary Thyroid Carcinoma, Interleukin-4, Interleukin-13, Clinical Significance

## 1. Introduction

Thyroid cancer (TC) is one of the most common malignant tumors in the head and neck and endocrine system. Its incidence has been increasing year by year in recent years. The continuous emergence of new cases has attracted great attention from the global medical community, despite the fact that there are improved diagnosis and treatment methods and the overall mortality rate has not increased significantly. Thyroid cancer can be divided into thyroid follicular carcinoma, papillary thyroid carcinoma, medullary thyroid carcinoma, anaplastic thyroid carcinoma according to histological morphology [1]. Papillary thyroid carcinoma (PTC) is one of the most common thyroid tumors in clinical

practice, accounting for about 80%-85% of all thyroid cancers [2]. The occurrence, development and prognosis of papillary thyroid carcinoma are affected by many factors such as the patient's age, gender, environmental factors, genetic factors, histopathological types, lymph node metastasis, clinical staging, immunohistochemical factors, among which cellular immune function disorders plays an important role in its occurrence and development [3, 4]. Helper T (Th) cells play an important role in the immune response process. They are mainly divided into two types, Th1 cell subgroup and Th2 cell subgroup. Among them, Th1 cells secrete cytokines such as interferon-gamma (IFN-γ), which participate in cellular immune response, and play a key role in tumor occurrence and anti-tumor immunity; Th2 cells secrete IL-4, IL-13 and other cytokines, and mediate fluid immune responses by stimulating B lymphocytes to produce immunoglobulins [5-7]. Th1 and Th2 cells maintain dynamic balance to ensure the normal immune function of the body under normal circumstances. However, recent studies have shown that it is very likely to break the balance between Th1/Th2 cells and make Th2 cells dominate, resulting in an unbalanced immune response during tumor occurrence and development [8, 9]. Cytokines are not only involved in the differentiation and proliferation of immune cells, but are also closely related to the growth, reproduction and metabolic regulation of a variety of cells in the body. Some cytokines can promote host anti-tumor immunity, and some can also promote tumor growth and proliferation. Recent studies have found that Interleukin-4 (IL-4) and Interleukin-13 (IL-13) secreted by the cells may be involved in the occurrence and development of PTC mediated by Th1/Th2 imbalance [10]. The purpose of this study is to study the expression of IL-4 and IL-13 in PTC and its clinical significance, which is of great significance for guiding treatment and judging prognosis. According to different prognostic factors, appropriate individualized comprehensive treatment plans are selected in order to maximize the benefits of patients.

# 2. Materials and Methods

### *2.1. Materials*

120 cases of PTC patients were randomly selected as the experimental group, who received radical mastectomy at the Thyroid and Breast Surgery Department of Cangzhou Central Hospital from January 2018 to April 2019. Among them, 90 were women and 30 were men, aged 18 to 70 years old, with an average age of (45.29±4.42) years old, and an average body mass index (Body mass index, BMI) of (27.76±1.31) kg/m$^2$. 69 patients were older than 45 years old, 51 patients were younger than or equal to 45 years old; 49 cases were larger than 2 cm and 71 cases were less than or equal to 2 cmin terms of the largest tumor diameter; 58 cases were single and 62 cases were multiple casesin terms of the number of lesions; 62 cases were in stage I-II, and 58 cases were in stage III-IV in terms of TNM staging; 34 cases were low, 53 cases were medium, and 33 cases were highin terms of the degree of differentiation; 46 cases had lymphatic metastasis, 74 cases did not. 120 healthy people served as the control group, matched 1:1 to the physical examination center of the hospital in the same period, according to the gender, age and BMI of the experimental group. Among them, 90 were females and 30 were males, aged from 18 to 70 years old, with an average age of (46.12±4.48) years and an average BMI of (28.23±1.35) kg/m$^2$.

### *2.2. Inclusion and Exclusion Criteria*

#### *2.2.1. Inclusion Criteria*

Inclusion criteria of study subjects: (1) All patients were between 18 and 80 years old; (2) All patients were pathologically confirmed to be papillary thyroid carcinoma and were primary [11]; (3) All patients did not receive radiotherapy, chemotherapy or other related treatments before enrollment; (4) All patients were New-onset patients; (5) All patients have complete clinical and follow-up data; (6) All patients have informed consent and signed an informed consent form.

Inclusion criteria for the control group: (1) All patients have been excluded from immune diseases, malignant tumors and other related diseases; (2) All patients have no history of thyroid disease or surgery. (3) The research complied with the regulations of the hospital ethics committee, and the subjects signed the informed consent form.

#### *2.2.2. Exclusion Criteria*

Exclusion criteria: (1) Combined with other malignant tumors; (2) Recurrent papillary thyroid carcinoma; (3) With other autoimmune or infectious diseases; (4) Insufficiency of important organs.

### *2.3. Methods*

#### *2.3.1. Sample Collection*

Tissue samples: Select PTC tissues that have been surgically removed and adjacent tissues that are greater than or equal to 2 cm from the edge of the tumor, freeze them in liquid nitrogen, and store them in a refrigerator at -80°C for later use.

Serum samples: Take 5 mL of peripheral venous blood from the experimental group and the control group in the fasting state in the morning, centrifuge at 3500 r/min for 10 min, take the supernatant, and store it in a refrigerator at -80°C for later use.

#### *2.3.2. Determination of IL-4 and IL-13 in Tissues*

Frozen tissues were taken, fixed with 4% paraformaldehyde for 24 hours, followed by decalcification, dehydration, transparency, wax immersion, embedding, and a microtome to prepare slices with a thickness of about 3μm. Then dewax and hydrate in sequence, place in 3% hydrogen peroxide solution at room temperature for 10 minutes to inactivate endogenous enzymes; rinse with distilled water 3 times, place in sodium citrate solution, and incubate at room temperature for 20 minutes to restore antigen. Rinse 3 times with PBS solution, add 5% fetal bovine serum dropwise, at room temperature for 10 minutes to block antibodies. Drop IL-4 antibody

(American Affinity company, product number AF5142), IL-13 antibody (American Affinity company, product number DF6813) with a dilution ratio of 1:300, incubate overnight at 4°C, and use PBS as a negative control group. Rinse 3 times with PBS solution for 2 minutes each time, add dropwise HRP-labeled goat anti-rabbit IgG antibody (Affinity, USA, item number S0001) with a dilution ratio of 1:100, reaction at room temperature for 30 minutes. Rinse 3 times with PBS solution for 2 minutes each time, use DAB color reagent kit (Beijing Yita Biotechnology Company, Item No. YT8204) for reaction. Counterstain with hematoxylin for 2 minutes after rinsing with distilled water, then sequentially dehydrate, transparent, and mount the slides with neutral gum, then randomly select 5 high-power fields (×400) to observe the number of cells and the degree of staining under the microscope.

It is negative if the number of stained cells is less than 10% or unstained, otherwise it is positive, and the positive expression rate is calculated.

#### *2.3.3. Determination of IL-4 and IL-13 in Serum*

Serum IL-4 and IL-13 levels were determined, using double antibody sandwich enzyme-linked immunosorbent assay, and operating in strict accordance with the instructions. All kits were purchased from Hebei Jincan Medical Equipment Sales Company, and all use the same batch number.

### *2.4. Statistical Analysis*

The SPSS19.0 software is used for date analysis and processing. The measurement data conforming to the normal distribution are represented by (±s), the two groups are compared by independent sample t-test, and the three groups are compared by one-way analysis of variance. Counting data is expressed by frequency or composition ratio. The chi-square exact probability method is used when the total number of cases is less than 40 or the minimum theoretical frequency is less than 1; the chi-square correction method is used when the total number of cases is greater than or equal to 40 and the minimum theoretical frequency is 1 to 5; the chi-square non-correction method is used when the total number of cases is greater than or equal to 40 and the minimum theoretical frequency is greater than 5. The correlation was analyzed by Pearson. The difference is statistically significant with $P<0.05$.

## 3. Results

### *3.1. Comparison of the Expression of IL-4 and IL-13 in PTC Tissues and Adjacent Tissues*

The positive expression rates of IL-4 and IL-13 were 93.33 and 88.33 respectively in PTC tissues and the positive expression rates of IL-4 and IL-13 were 30.00 and 35.00respectively in adjacent tissues. The positive expression rates of IL-4 and IL-13 in PTC tissues were significantly higher than those in adjacent tissues ($P<0.05$). Correlation analysis showed that the expression of IL-4 and IL-13 in PTC tissues was significantly positively correlated ($r=0.375$, $P=0.002$). (Tables 1, 2).

***Table 1.*** *Comparison of IL-4 and IL-13 levels in PTC Tissues and Adjacent Tissues n/%.*

| Group | n | IL-4 | | IL-13 | |
|---|---|---|---|---|---|
| | | - | +~+++ | - | +~+++ |
| PTC tissues | 120 | 8/6.67 | 112/93.33 | 14/11.67 | 106/88.33 |
| Adjacent tissues | 120 | 84/70.00 | 36/30.00 | 78/65.00 | 42/35.00 |
| $\chi^2$ | | 101.810 | | 72.197 | |
| $P$ | | <0.01 | | <0.01 | |

***Table 2.*** *Correlation of IL-4 and IL-13 Expression in PTC Tissues.*

| IL-13 | IL-4 | | Total |
|---|---|---|---|
| | - | +~+++ | |
| - | 4 | 10 | 14 |
| +~+++ | 4 | 102 | 106 |
| Total | 8 | 112 | 120 |

### *3.2. Comparison of Serum IL-4 and IL-13 Levels Between the Two Groups of Subjects*

Serum IL-4 and IL-13 levels were significantly higher in PTC patients, compared with healthy subjects ($P<0.05$); and correlation analysis showed that the expression of IL-4 and IL-13 was significantly positively correlated in PTC patients serum ($r=0.381$, $P<0.01$). (Table 3, Figure 1).

***Table 3.*** *Comparison of serum IL-4 and IL-13 levels between the two groups (±s).*

| Group | n | IL-4 (pg/mL) | IL-13 (pg/mL) |
|---|---|---|---|
| Test group | 120 | 6.38±1.15 | 8.94±1.23 |
| Control group | 120 | 3.35±1.12 | 4.36±1.18 |
| $t$ | | 20.677 | 29.435 |
| $P$ | | <0.01 | <0.01 |

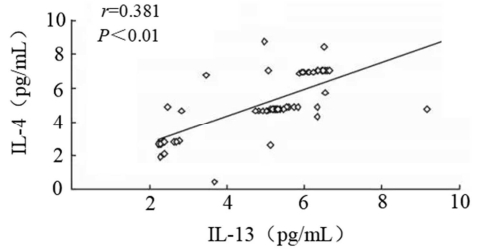


***Figure 1.*** *Correlation of serum IL-4 and IL-13 levels in PTC patients.*

### *3.3. The Relationship BetweenIL-4 Levels in PTC and Clinicopathological Characteristics*

The expression of IL-4 in serum and tissues was related to the maximum tumor diameter, TNM stage, degree of differentiation, and lymphatic metastasis in PTC ($P<0.05$). There was no significant difference in serum and tissue IL-4 expression in terms of age, gender, and number of lesions ($P>0.05$). (Table 4).

***Table 4.*** *Relationship between IL-4 Levels in PTC and clinicopathological characteristics.*

| Feature | n | Tissue IL-4 levels | | *P* | Serum IL-4 levels (pg/mL) | *P* |
|---|---|---|---|---|---|---|
| | | - | +~+++ | | | |
| Age | | | | 0.076 | | 0.383 |
| >45years | 69 | 7 | 62 | | 5.82±0.51 | |
| ≤45years | 51 | 1 | 50 | | 5.79±0.48 | |
| Gender | | | | 0.398 | | 0.379 |
| Male | 30 | 3 | 27 | | 5.93±0.47 | |
| Female | 90 | 5 | 85 | | 5.96±0.45 | |
| Maximum tumor diameter | | | | 0.015 | | <0.01 |
| >2cm | 49 | 0 | 49 | | 7.11±0.23 | |
| ≤2cm | 71 | 8 | 63 | | 5.28±0.25 | |
| Number of lesions | | | | 0.922 | | 0.095 |
| Single | 58 | 4 | 54 | | 5.36±0.31 | |
| Multiple | 62 | 4 | 58 | | 5.39±0.28 | |
| TNM staging | | | | 0.036 | | <0.01 |
| Stage I~II | 62 | 7 | 55 | | 5.14±0.31 | |
| Stage III~IV | 58 | 1 | 57 | | 6.92±0.33 | |
| Differentiation | | | | <0.01 | | <0.01 |
| Low | 34 | 6 | 28 | | 4.22±0.23 | |
| Middle | 53 | 2 | 51 | | 6.39±0.25 | |
| High | 33 | 0 | 33 | | 7.01±0.24 | |
| Lymphaticmetastasis | | | | <0.01 | | <0.01 |
| Yes | 46 | 1 | 45 | | 6.96±0.25 | |
| No | 74 | 7 | 67 | | 4.72±0.28 | |

### *3.4. The Relationship BetweenIL-13 Levels in PTC and Clinicopathological Characteristics*

The expression of IL-13 in serum and tissues was related to the maximum tumor diameter, TNM stage, degree of differentiation, and lymphatic metastasis in PTC ($P<0.05$). There was no significant difference in serum and tissue IL-13 expression in terms of age, gender, and number of lesions ($P>0.05$). (Table 5).

***Table 5.*** *Relationship between IL-13 Levels in PTC and clinicopathological characteristics.*

| Feature | n | Tissue IL-13 levels | | *P* | Serum IL-13 levels (pg/mL) | *P* |
|---|---|---|---|---|---|---|
| | | - | +~+++ | | | |
| Age | | | | 0.977 | | 0.520 |
| >45years | 69 | 8 | 61 | | 7.38±0.52 | |
| ≤45years | 51 | 6 | 45 | | 7.32±0.48 | |
| Gender | | | | 0.101 | | 0.662 |
| Male | 30 | 6 | 24 | | 7.25±0.51 | |
| Female | 90 | 8 | 82 | | 7.29±0.47 | |
| Maximum tumor diameter | | | | <0.01 | | <0.01 |
| >2cm | 49 | 3 | 46 | | 8.33±0.62 | |
| ≤2cm | 71 | 11 | 60 | | 6.27±0.59 | |
| Number of lesions | | | | 0.894 | | 0.768 |
| Single | 58 | 7 | 51 | | 7.21±0.54 | |
| Multiple | 62 | 7 | 55 | | 7.18±0.56 | |
| TNM staging | | | | 0.032 | | <0.01 |
| Stage I~II | 62 | 11 | 51 | | 6.39±0.35 | |
| Stage III~IV | 58 | 3 | 55 | | 9.38±0.32 | |
| Differentiation | | | | <0.01 | | <0.01 |
| Low | 34 | 7 | 27 | | 6.29±0.38 | |
| Middle | 53 | 4 | 49 | | 7.83±0.44 | |
| High | 33 | 3 | 30 | | 9.41±0.47 | |
| Lymphaticmetastasis | | | | 0.049 | | <0.01 |
| Yes | 46 | 2 | 44 | | 8.82±0.17 | |
| No | 74 | 12 | 62 | | 6.91±0.25 | |

## 4. Discussions

### *4.1. Research Background*

In recent years, the molecular biology research of thyroid cancer has made great progress with the deepening of tumor molecular biology research and the development of modern biochemical and pathological techniques. There are also new understandings about the changes in other products such as matrix proteins and their enzymes, telomerase and cytokines, which are related to the occurrence, development and metastasis of thyroid cancer, in addition to having a deeper understanding of the role of related oncogenes and tumor

suppressor genes in the pathogenesis. Thyroid cancer ranks the first among head and neck tumors in the world, with more women than men, and papillary thyroid cancer (PTC) is the most common [12]. It is currently not clear about the etiology and pathogenesis of papillary thyroid carcinoma. Among many possible mechanisms, changes in the body's immune system are closely related to PTC, and cytokines play an important role [13, 14]. At present, the types of cytokines used clinically are limited and their side effects are large. Therefore, the combined application of cytokines can not only enhance its anti-tumor effect, but also reduce its side effects, which has broad application prospects [15].

### *4.2. PTC and IL-4*

Interleukin-4 (IL-4) is a factor in the T cell culture supernatant discovered by Howard et al. in 1982, which promotes the proliferation of B cells. It was first named B cell growth factor 1, and later renamed interleukin-4. IL-4 is a cytokine with a variety of biological functions, mainly secreted by Th2 cells, but also by eosinophils, basophils and mast cells.

IL-4 can promote its occurrence and development in the inflammatory response characterized by Th2 as a characteristic cytokine of Th2 cells. IL-4 can activate B cells in the allergic inflammatory response induced by allergen stimulation. It can de-inhibit the B cell receptor (BcR) by reducing the expression of receptors that have inhibitory effects on B cells and eliminating the inhibitory B cell effects mediated by cD22FcγII, and finally activate B cells and mediate the humoral immune response. Th2 cells and the IL-4/IL-4R secreted by them can induce M2-type polarization of macrophages through the JAK/STAT6 signaling pathway during the occurrence and development of tumors [16]. Studies have found that macrophages in the tumor microenvironment (tumor micro environment, TME), that is, tumor-associated macrophages (tumor associated macrophages, TAMs) also secrete IL-4 and other cytokines, which not only lose the ability to kill cancer cells, but are also an important force for cells in tumor tissues to exert paracrine effects to promote tumor growth and promote lymphatic and angiogenesis [17]. IL-4 can also bind to cancer cell surface receptors, activate the JAK1/STATA6 signaling pathway, and then affect the differentiation and function of inflammatory cells around the tumor, and ultimately cause tumor immune escape, trigger tumor cell proliferation and metastasis [18].

Studies have found that a variety of tumor cells can secrete IL-4 and express IL-4R in addition to increased levels of IL-4 during parasite infection and hypersensitivity reactions [19]. In breast cancer, high levels of IL-4R are expressed on the surface of breast cancer cells and IL-4 can bind to IL-4R on the surface of tumor cells to activate the JAK1/STAT6 signaling pathway [20]. Todaro et al. further found that IL-4/IL-4R can up-regulate the anti-apoptotic proteins PED, c FLIP, Bcl-xl and Bcl-2 in cancer cells, thereby making cancer cells resistant to apoptosis-inducing ligand (TRAIL) or apoptosis caused by other drugs, and ultimately promote the growth of cancer cells [21]. Many scholars believed that IL-4/IL-4R could inhibit the growth of colon cancer in the 20th century [22]. However, more and more data support it to promote the development of colon cancer in the 21st century. Koller et al. found that the surface of human colon adenocarcinoma cells highly expresses IL-4Rα, and IL-4/IL-4R significantly enhances the proliferation ability of cancer cells in a dose-dependent manner [23]. IL-4/IL-4R up-regulates the expression of cFLIP and Bcl-xL, making cancer cells resistant to drug-induced apoptosis in primary prostate cancer [24]. Lee et al. found that IL-4/IL-4R increases the sensitivity of AR in prostate cell carcinoma so that it can be activated by very low concentrations of androgens [25]. IL-4/IL-4R can increase the dephosphorylated form of Rbp in gastric cancer cells and block cells in the G0/G1 phase.

In this study, IL-4 levels were measured in the tissues and serum samples of PTC patients and found that the positive expression rate of IL-4 in PTC tissues (93.33%) was significantly higher than that of adjacent tissues (30.00%), in line with the results of previous studies [10], and The serum IL-4 level of PTC patients was significantly higher than that of healthy subjects, indicating that IL-4 is highly expressed in PTC, and the up-regulation of IL-4 expression may be involved in the occurrence of PTC. Further analysis revealed that IL-4 expression is related to tumor maximum diameter, TNM stage, degree of differentiation, and lymphatic metastasis in PTC. It indicates that the up-regulation of IL-4 expression may be involved in the progress of PTC, and the regulation of IL-4 may have a reversal effect on tumor immune escape, which needs to be explored in future studies.

### *4.3. PTC and IL-13*

IL-13 is a cellular immune regulatory factor mainly produced by activated Th2 cells. It was originally named p600 protein and later officially named IL-13. Scholars at home and abroad have done a lot of research on the structure, biological characteristics, mechanism of action, and clinical application of IL-13. Studies have found that the biological activities of IL-13 mainly include: 1. IL-13 can chemo attract monocytes and macrophages, extend their survival time in vitro, and induce their secretion of inflammatory factors, which ultimately promotes inflammation; 2. Enhance the ability of NK cells to produce IFN-γ, and induce B lymphocytes to produce Ig G and Ig E, thus playing a key role in inducing lymphokine-activated killer cell activity and Th1-type cellular immunity [26-28].

IL-13 is involved in the occurrence and development of fibrosis, allergic diseases, inflammation and tumors. Tumor development is often accompanied by Th2 cytokine-related fibrosis and inflammation. Studies have found that IL-13 has the function of promoting inflammation and immune regulation [29]. Studies pointed out that the expression level of IL-13 was significantly increased in various tumor tissues and peripheral blood such as leukemia, Hodgkin’s lymphoma, breast cancer and lung cancer [30, 31]. IL-13 is an important regulator of cell proliferation in acute myeloid leukemia (AML). The expression of IL-13 is higher in patients with

AML and the co-culture of AML cells with IL-13 can increase cell proliferation, compared with normal people. IL-13 is highly expressed in Hodgkin's lymphoma, which is closely related to its poor prognosis. The human breast cancer stromal microenvironment can present IL-13-related inflammation and fibrosis, which will promote the development of breast cancer [32]. The abnormal activity of breast stromal fibroblasts mediated by IL-13 will lead to malignant selection of breast epithelial cells. In lung cancer, IL-13 can promote tumor growth by inhibiting the body's immune monitoring effect on tumors. And it can almost completely inhibit tumor recurrence when using a IL-13 Rα2 fusion protein (IL-13Rα2-Fc) that inhibits the function of IL-13 to treat this malignant tumor model. Recent studies have shown that: Abnormal expression of IL-13 plays an important role in the pathogenesis of cancer, and is closely related to the occurrence, development, metastasis and prognosis of a variety of clinical malignancies [33]. IL-13 has different roles in different tumors. Liu Rui et al. pointed out: IL-13 is highly expressed in malignant tumors such as colon cancer and pancreatic cancer, and IL-13 can promote the proliferation of prostate cancer and pancreatic cancer cells [10]. Another study found: IL-13 can inhibit breast cancer proliferation [34]. Studies have also pointed out that IL-13 can inhibit the growth of lung cancer tumors, and its anti-tumor effect is reflected in promoting the activation of tumor suppressor genes and inhibiting tumor angiogenesis [35]. This reflects the duality of IL-13 in the occurrence and development of tumors [36, 37]. Wei Qing et al. found that the positive expression rate of IL-13 in PTC was 93.75%, which was significantly higher than that of adjacent tissues (8.75%) [38]. Liu Rui et al. found that the positive expression rate of IL-13 in PTC was 90.81%, which was significantly higher than that of adjacent tissues (41.08%) [10]. In this study, the expression of IL-13 in PTC tissue and its adjacent tissues was also detected by immunohistochemical SP staining, and it was found that the positive expression rate of IL-13 in PTC tissues (88.33%) was significantly higher than that of adjacent tissues (35.00%), in line with previous research results [10, 37]. And the serum IL-13 level of PTC patients was significantly higher than that of healthy subjects. IL-13 expression is related to the maximum tumor diameter, TNM stage, degree of differentiation, and lymphatic metastasis. It is also concluded that the up-regulation of IL-13 expression is involved in PTC The process of occurrence and development.

# 5. Conclusion

A small proportion of patients still have a poor prognosis although the vast majority of papillary thyroid cancers are considered "indolent" tumors. During the occurrence and development of papillary thyroid carcinoma, the positive expression rates of IL-4 and IL-13 in PTC tissue were significantly higher than those in adjacent tissues, and the expression of IL-4 and IL-13 in PTC tissue was significantly positively correlated; the serum levels of IL-4 and IL-13 in PTC patients were significantly higher than those in healthy subjects. The expression of IL-4 and IL-13 in the serum of patients with PTC was significantly positively correlated; in PTC, the expression of IL-4 and IL-13 was correlated with the maximum tumor diameter, TNM staging, degree of differentiation, lymphatic metastasis. Therefore, the expression level of IL-4 and IL-13 may become a reference indicator for predicting the occurrence and development of PTC. Clinically, an appropriate individualized comprehensive treatment plan can be selected according to the changes in the expression levels of IL-4 and IL-13 to reduce the morbidity as much as possible, increase the cure rate, and prolong the survival period.

The results of this study still need to be validated by a better-designed clinical cohort study with a larger sample size due to the limitations of methodology and sample size, although this study proved that IL-4 and IL-13 are highly expressed in PTC serum and tissues. This research only stays at the phenomenon level. In the next step, we need to further study the specific reasons for the imbalance of Th1/Th2 cytokines in tumor tissues, transformation rules, and specific biological effects in the development and development of tumors.

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