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Retraction

Retracted: Two Potential Biomarkers for the Diagnosis and Prognosis of Laryngeal Carcinoma: CCL20 and IL-17A

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

(1) Discrepancies in scope
(2) Discrepancies in the description of the research reported
(3) Discrepancies between the availability of data and the research described
(4) Inappropriate citations
(5) Incoherent, meaningless and/or irrelevant content included in the article
(6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their agreement or disagreement to this retraction. We have kept a record of any response received.

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[1] Y. Teng, H. He, H. Wang et al., "Two Potential Biomarkers for the Diagnosis and Prognosis of Laryngeal Carcinoma: CCL20 and IL-17A," *Wireless Communications and Mobile Computing*, vol. 2022, Article ID 2148240, 6 pages, 2022.

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Research Article

Two Potential Biomarkers for the Diagnosis and Prognosis of Laryngeal Carcinoma: CCL20 and IL-17A

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This study is to uncover the possibilities of CCL20 and IL-17A to be potential hallmarks for laryngeal carcinoma. Relative levels of CCL20 and IL-17A in laryngeal carcinoma tissues were detected by quantitative real-time polymerase chain reaction (qRT-PCR). Correlation between CCL20 and IL-17A was analyzed by Pearson correlation test. Receiver operating characteristic (ROC) curves were depicted for assessing diagnostic values of CCL20 and IL-17A in laryngeal carcinoma. In addition, 98 laryngeal carcinoma patients were followed up for 5 years. Their follow-up data were utilized for assessing prognostic values of CCL20 and IL-17A. CCL20 and IL-17A were upregulated in laryngeal carcinoma tissues than those of normal ones. ROC curves identified diagnostic values of CCL20 (AUC = 0.9719, cutoff value = 4.86, sensitivity = 98.98%, specificity = 87.76%) and IL-17A (AUC = 0.7965, cutoff value = 3.39, sensitivity = 71.31%, specificity = 71.52%) in laryngeal carcinoma. Worse prognosis was observed in laryngeal carcinoma patients expressing high level of CCL20 or IL-17A. CCL20 and IL-17A are upregulated in laryngeal carcinoma tissues, which are unfavorable factors for the prognosis of laryngeal carcinoma. CCL20 and IL-17A are promising hallmarks of laryngeal carcinoma.

1. Introduction

Laryngeal carcinoma is one of the highly invasive malignant tumors originating from head and neck, accounting for 2.4% of malignant tumors annually [1]. Unhealthy lifestyle, external environment, genetic factors, and HPV (human papillomavirus) infection are all risk factors for laryngeal carcinoma [2]. Great strides have been made on surgical procedures, chemotherapy, and radiotherapy for laryngeal carcinoma. However, detective rate of early-stage laryngeal carcinoma is low because of insidious symptoms [3, 4]. It is necessary and urgent to search for effective hallmarks for diagnosing laryngeal carcinoma as early as possible.

CCL20 is a newly discovered chemokine belonging to the CC subfamily. The primary structure of its mature body has two forms, which can participate in the directed migratory process of immune cells by binding to corresponding receptors. CCL20 is of significance in the development of autoimmune diseases, tumors, infectious diseases, and inflammatory diseases [5]. A relevant study has confirmed the accelerative effects of CCL20 on proliferative and migratory abilities in human pancreatic cancer cell line COLO-357 [6]. Lu et al. [7] have shown that CCL20 can promote the progression of laryngeal carcinoma.

IL-17 cytokine family contains six members, namely, IL-17A, IL-17B, IL-17C, IL-17D, IL-17E, and IL-17F. IL-17A (also known as IL-17) is the most representative member of the IL-17 family [8]. IL-17A is mainly secreted by T helper cell 17 and, sometimes, neutrophils, eosinophils, and mononuclear macrophages [9–11]. Yang et al. [12] and Xiang et al.

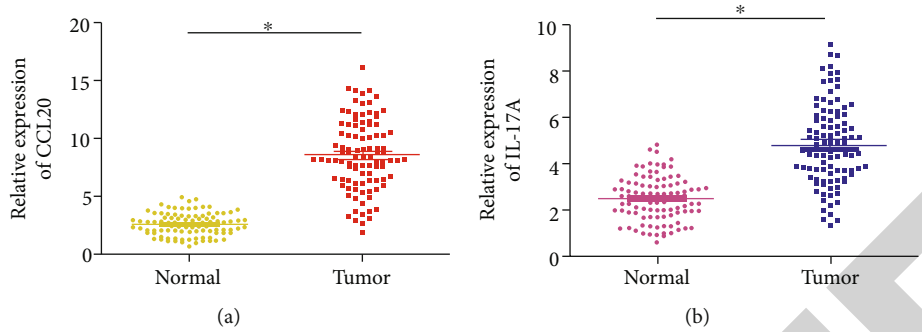

Figure 1: (a) CCL20 and (b) IL-17A were upregulated in 98 cases of laryngeal carcinoma tissues.

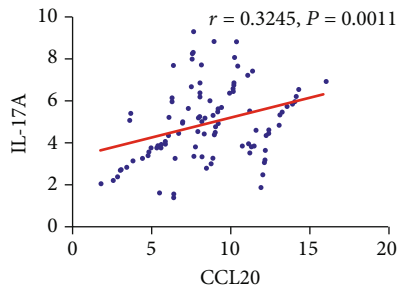

Figure 2: Correlation between expression levels of CCL20 and IL-17A in laryngeal carcinoma tissues. A positive correlation between expression levels of CCL20 and IL-17A in laryngeal carcinoma tissues.

[13] have shown that IL-17RA, the IL-17A receptor, is expressed in both cancer stem cells and cancer tissues. Exogenous IL-17A and IL-17A in cancer cells directly stimulate proliferation ability in cancer [14]. It is reported that IL-17A is upregulated in laryngeal carcinoma [15]. In colorectal cancer, CCL20 and IL-17 are synergistically utilized as biological hallmarks for diagnosing and predicting the prognosis of colorectal cancer [16]. In this paper, we mainly explore the diagnostic and prognostic potentials of CCL20 and IL-17A in laryngeal carcinoma. Our findings provide new directions in therapeutic strategies of laryngeal carcinoma.

2. Materials and Methods

2.1. Sample Collection. Laryngeal carcinoma tissues and normal ones were collected from 98 laryngeal carcinoma patients admitted in the Department of Otorhinolaryngology and Head and Neck Surgery, Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine, and Chaoyang Central Hospital, from April 2016 to December 2018. Follow-up data of every enrolled subject were collected. Patients and their families in this study have been fully informed. This study was approved by the Ethics Committee of Affiliated Hangzhou First People's Hospital, Zhejiang University School of Medicine.

2.2. Quantitative Real-Time Polymerase Chain Reaction (qRT-PCR). TRIzol (Invitrogen, Carlsbad, CA, USA) was utilized for isolating RNA from laryngeal tissues. RNA was reversely transcribed into complementary deoxyribose nucleic acid (cDNA) using PrimeScript RT Reagent (TaKaRa, Otsu, Japan) and applied for qRT-PCR. Glyceraldehyde 3-phosphate dehydrogenase (GAPDH) was the internal reference. Primer sequences were as follows: CCL20 forward: 5′-AGCAGCAAGCAACTACGACT-3′, reverse: 5′-TCTTAGGCTGAGGAGGTTCA-3′; IL-17A forward: 5′-TCCCACGAAATCCAGGATGC-3′, reverse: 5′-GGATGTTCAGGTTGACCATCAC-3′; GAPDH forward: 5′-TGAAGGTCGGAGTCAACGG-3′, reverse: 5′-CCTGGAAGATGGTGATGCG-3′.

2.3. Follow-Up. Postoperative follow-up was conducted in every laryngeal carcinoma patient by clinical review or telephone once every three months in the first year and once every six months till 2018 year. Death of patient was the end point of follow-up.

2.4. Statistical Analysis. Statistical Product and Service Solutions (SPSS) 22.0 (IBM, Armonk, NY, USA) was used for data analyses. Differences between two groups were compared by the *t*-test. Correlation between CCL20 and IL-17A was analyzed by the Pearson correlation test. Diagnostic potentials of CCL20 and IL-17A were assessed by depicting receiver operating characteristic (ROC) curves. Their prognostic values were evaluated by the Kaplan-Meier method, followed by log-rank test for comparing differences between two curves. $P < 0.05$ was considered as statistically significant.

3. Results

3.1. Upregulation of CCL20 and IL-17A in Laryngeal Carcinoma. Compared with normal tissues, CCL20 (Figure 1(a)) and IL-17A (Figure 1(b)) were upregulated in 98 cases of laryngeal carcinoma tissues. CCL20 and IL-17A may be involved in the progression of laryngeal carcinoma.

3.2. Correlation between Expression Levels of CCL20 and IL-17A in Laryngeal Carcinoma Tissues. Correlation between expression levels of CCL20 and IL-17A in laryngeal carcinoma tissues was analyzed by the Pearson correlation test. A positive correlation between CCL20 and IL-17A in

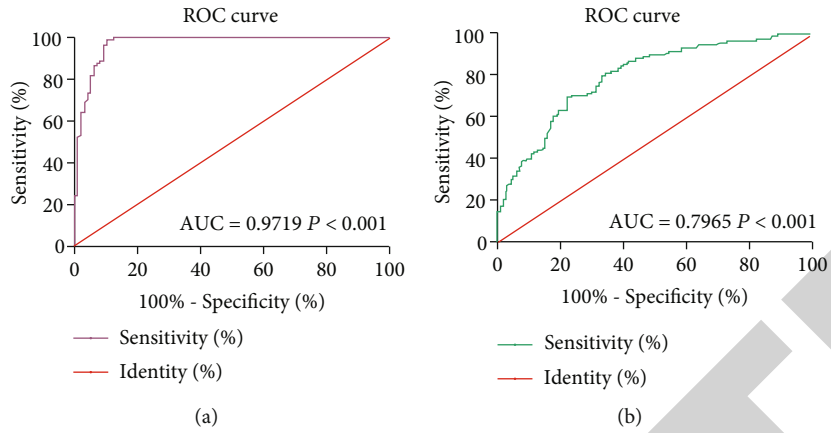

Figure 3: Diagnostic potentials of CCL20 and IL-17A in laryngeal carcinoma. ROC curves identified diagnostic values of (a) CCL20 (AUC = 0.9719, cutoff value = 4.86, sensitivity = 98.98%, specificity = 87.76%) and (b) IL-17A (AUC = 0.7965, cutoff value = 3.39, sensitivity = 71.31%, specificity = 71.52%) in laryngeal carcinoma.

laryngeal carcinoma, finally, was identified ($r = 0.3245$, $P = 0.0011$) (Figure 2).

3.3. Diagnostic Potentials of CCL20 and IL-17A in Laryngeal Carcinoma. Differential expressions of CCL20 and IL-17A in laryngeal carcinoma tissues and normal ones indicated their potentials to be diagnostic hallmarks. Here, ROC curves identified diagnostic values of CCL20 (AUC = 0.9719, cutoff value = 4.86, sensitivity = 98.98%, specificity = 87.76%) (Figure 3(a)) and IL-17A (AUC = 0.7965, cutoff value = 3.39, sensitivity = 71.31%, specificity = 71.52%) (Figure 3(b)) in laryngeal carcinoma. Thus, CCL20 and IL-17A were promising diagnostic hallmarks for laryngeal carcinoma.

3.4. Influences of CCL20 and IL-17A on Survival of Laryngeal Carcinoma Patients. Based on the cutoff value of CCL20 in 98 enrolled laryngeal carcinoma patients, they were assigned into high-level and low-level groups. Through collecting 5-year follow-up data of enrolled patients, Kaplan-Meier curves revealed worse survival in laryngeal carcinoma patients of the high-level group compared to those of the low-level group (HR = 13.73, $P < 0.001$) (Figure 4(a)). In a similar way, worse prognosis was observed in laryngeal carcinoma patients expressing high level of IL-17A (HR = 10.45, $P = 0.0012$) (Figure 4(b)). Moreover, overall survival was lower in laryngeal carcinoma patients with both high levels of CCL20 and IL-17A compared with those expressing both low levels (HR = 14.55, $P = 0.0022$) (Figure 4(c)). As a result, CCL20 and IL-17A were unfavorable to the prognosis of laryngeal carcinoma.

4. Discussion

Laryngeal carcinoma is a common malignancy in the regions of ears, throat, and nose. The mortality and incidence of laryngeal carcinoma present increased trends annually [17]. The majority of laryngeal carcinoma patients in the early stage could be recovered or even cured after active treatment. However, most laryngeal carcinoma patients are diagnosed in advanced stage (about 70%) owing to atypical symptoms, leading to poor prognosis and high mortality [18]. Meanwhile, high rates of metastases and recurrence severely restrict clinical outcomes of laryngeal carcinoma as well. The 5-year survival of advanced laryngeal carcinoma is as low as 50% [19].

Human CCL20 locates on chromatin 2q35-36, containing 4 exons and 3 introns [20]. In 1997, Hieshima et al. [21] first found that biological functions of CCL20 are closely linked to one α helix and three β-pleated sheets in its structure. CCL20 is expressed in liver tissue, skin keratinocytes, etc. [22]. CCL20 is of significance in the physiological barrier composition and inflammatory response of the corresponding sites [23]. Studies have shown that CCL20 is highly expressed in hepatocellular carcinoma [24]. In laryngeal carcinoma, CCL20 stimulates tumor cells to proliferate and metastasize [7]. Consistently, our findings uncovered the upregulated CCL20 in laryngeal carcinoma tissues, which was an unfavorable factor for the prognosis. Furthermore, its diagnostic value was identified.

IL-17 is a cytokine mainly secreted by CD4+ T lymphocytes, monocytes, etc. It is critical in natural immunity and host defense, participating in immune regulation and tumor cell growth [25]. As a crucial regulator in immune surveillance, IL-17 triggers angiogenesis and tumor growth in the tumor microenvironment [26]. In many types of tumors, IL-17 is upregulated [27, 28]. IL-17A is a member of the IL-17 family, which is of significance in inflammatory diseases and allergic diseases [29, 30]. Besides, IL-17A is involved in the occurrence and progression of tumors as well [31, 32]. Here, IL-17A was found to be upregulated in laryngeal carcinoma tissues and predicted a poor prognosis.

Wang et al. [17] suggested that CCL20 and IL-17A are effective diagnostic hallmarks for early-stage colorectal carcinoma. High levels of CCL20 and IL-17A predict worse survival in colorectal carcinoma patients, which could be served as independent prognostic factors. Our findings uncovered worse survival in laryngeal carcinoma patients

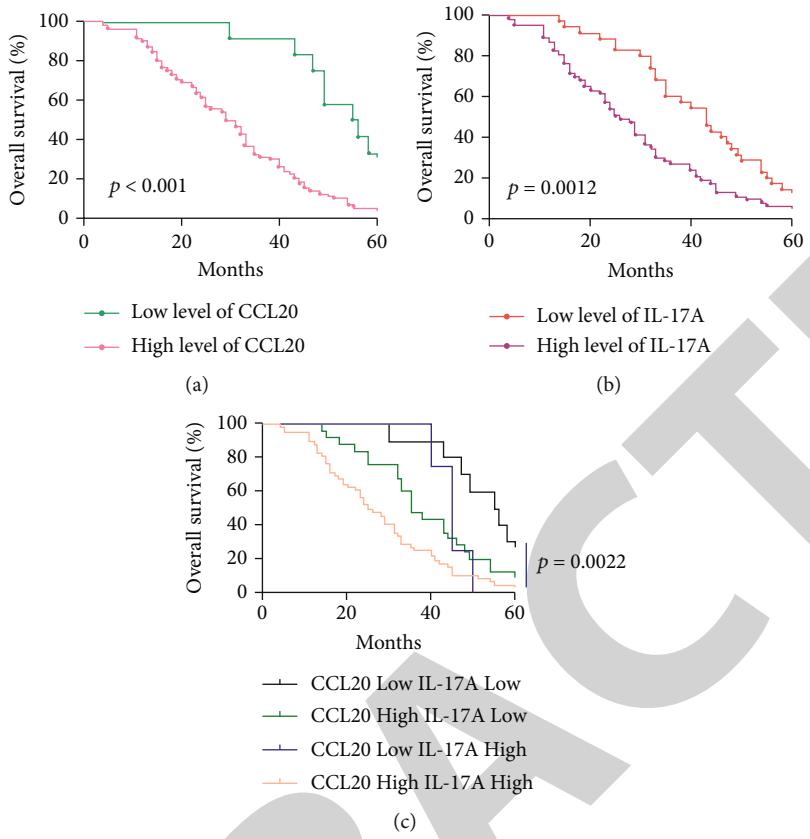

Figure 4: Influences of CCL20 and IL-17A on survival of laryngeal carcinoma patients. (a) Worse survival in laryngeal carcinoma patients expressing high level of CCL20 than those expressing low level of CCL20 (HR = 13.73, $P < 0.001$). (b) Worse survival in laryngeal carcinoma patients expressing high level of IL-17A than those expressing low level of IL-17A (HR = 10.45, $P = 0.0012$). (c) Worse survival in laryngeal carcinoma patients expressing both high levels of CCL20 and IL-17A than those expressing both low levels of CCL20 and IL-17A (HR = 14.55, $P = 0.0022$).

expressing both high levels of CCL20 and IL-17A. Based on these data, we believed that synergistic detection of CCL20 and IL-17A levels is effective and sensitive for predicting the prognosis of laryngeal carcinoma.

5. Conclusions

CCL20 and IL-17A are upregulated in laryngeal carcinoma tissues, which are positively correlated and unfavorable to the prognosis of laryngeal carcinoma. CCL20 and IL-17A are promising candidates of laryngeal carcinoma hallmarks.

Data Availability

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declared no conflict of interest.

Authors' Contributions

YT, HH, and HW designed the study and performed the experiments; YLu and XW collected the data; YLi and ZL analyzed the data; YT, HH, and HW prepared the manuscript. All authors read and approved the final manuscript. Yaoshu Teng, Hanyi He, and Hongmei Wang contributed equally to this work.

Acknowledgments

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