Combined detection of inflammatory proteins is beneficial for diagnosing the papillary thyroid carcinoma and nodular goiter

Yongqin Pan[1#], Mingxi Xu[1#], Tsz Hong Chong[1], Siping Xie[2], Kunsong Huang[1], Guanghao Wang[1], Yuhua Ma[1], Jinyi Li[1], Wah Yang [3*]

[1]Department of Thyroid Surgery, The First Affiliated Hospital of Jinan University, Guangzhou 510632, China
[2]Medical Record Room, The First Affiliated Hospital of Jinan University, Guangzhou 510632, China
[3]Department of Metabolic and Bariatric Surgery, The First Affiliated Hospital of Jinan University, Guangzhou 510632, China

Papillary thyroid carcinoma

	incidence rates	mortality rates
Male	10.1/100,000	0.5/100,000
Female	3/100,000	0.3/100,000

(*Margherita P et al., 2022*)

Fine-needle aspiration cytology (FNAC) and imaging examinations are commonly used diagnostic tools for PTC in clinical practice. **However, it is an invasive procedure that carries the risk of severe complications and has a non-diagnostic rate of about 10%−20%.**

(*Güven G et al., 2017*)

There is a positive correlation between chronic inflammation and the increased risk of thyroid cancer, which has attracted increasing attention as the main culprit mechanism of thyroid cancer occurrence
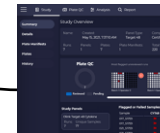
(*Loredana P et al., 2017*)

Proximity extension assay

Pre-Amplification

Amplification and Detection
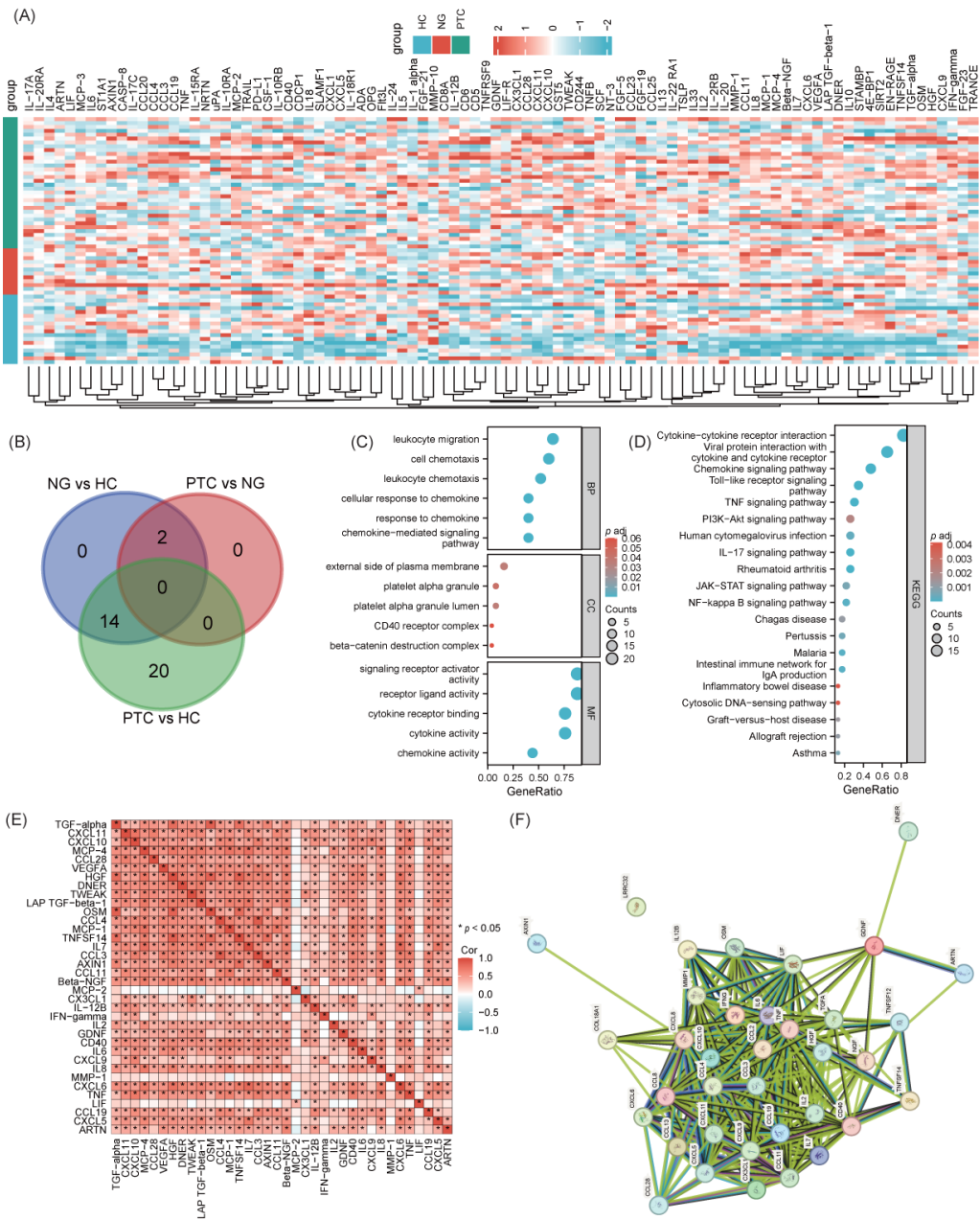
Analysis
(NPX signature software)

(*Erika A et al., 2014*)

Highlights

- **Total 36 differentially expressed inflammatory proteins were found among PTC, nodular goiter, and healthy control.**

- **TGF-α + CXCL11 exhibited promising diagnostic capabilities in distinguishing nodular goiter from healthy control.**

- **TGF-α + CXCL11 exhibited promising diagnostic capabilities in distinguishing PTC from healthy control.**

- **GDNF + CXCL5 + ARTN demonstrated optimal diagnostic effectiveness in distinguishing PTC from nodular goiter.**

- **The combination derived from the LASSO algorithm outperforms logistic regression, albeit with a higher number of proteins.**

1. Differences of inflammatory protein among healthy control, nodular goiter, and PTC

(1) A comparison revealed 16 differentially expressed inflammatory proteins between healthy control and nodular goiter, 34 differentially expressed inflammatory proteins between healthy control and PTC, and 2 differentially expressed inflammatory proteins between nodular goiter and PTC.

(2) The Venn diagram illustrates the intersection of the three groups, revealing 36 differentially expressed inflammatory proteins.

2. Inflammatory biomarkers of different proteins were investigated for diagnosing nodular goiter from healthy control, diagnosing PTC from the healthy control, and diagnosing PTC from nodular goiter
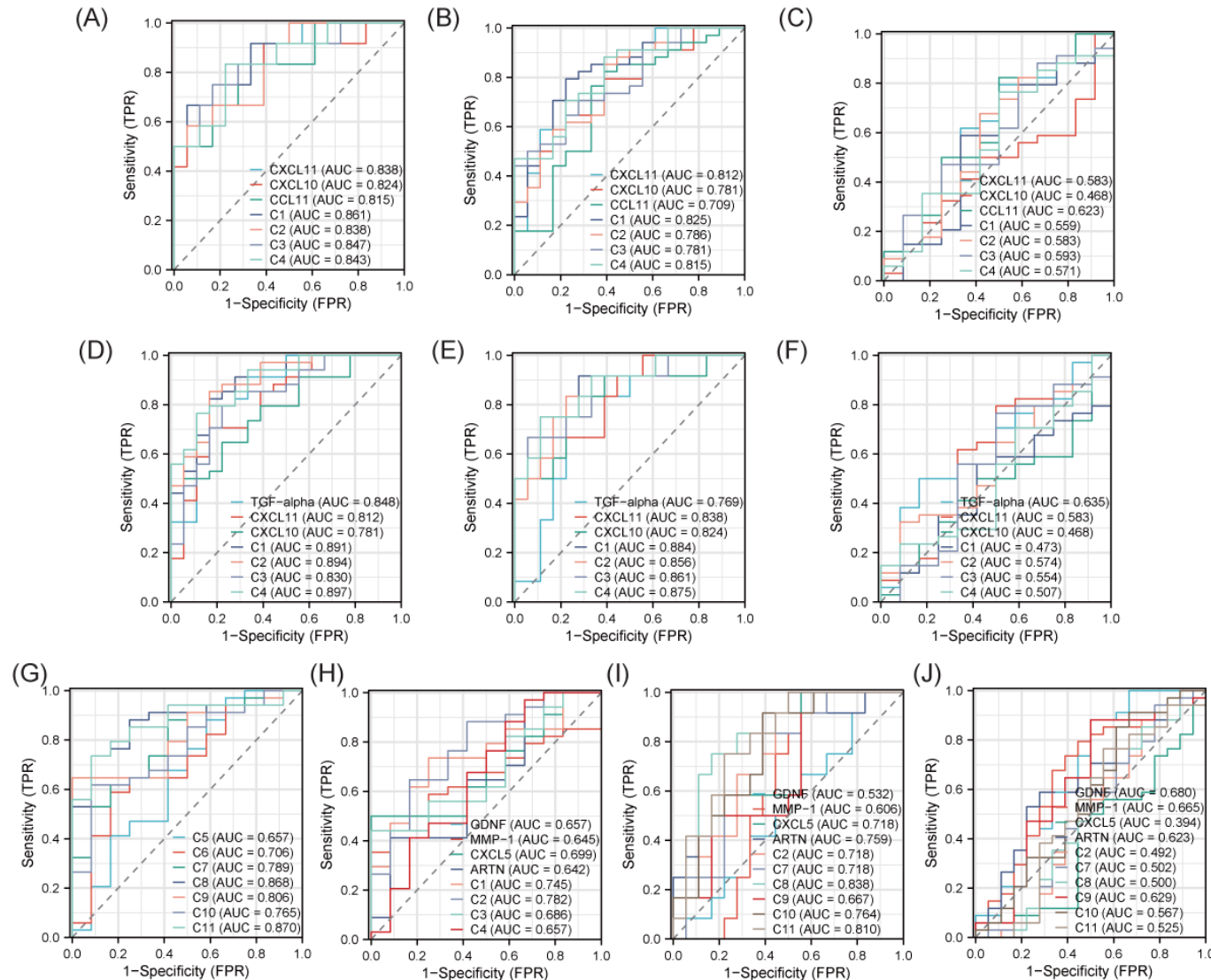
(1) **TGF-α + CXCL11 exhibited promising diagnostic capabilities in distinguishing nodular goiter from healthy control (AUC = 0.88).**

(2) **TGF-α + CXCL11 exhibited promising diagnostic capabilities in distinguishing PTC from healthy control (AUC = 0.89).**

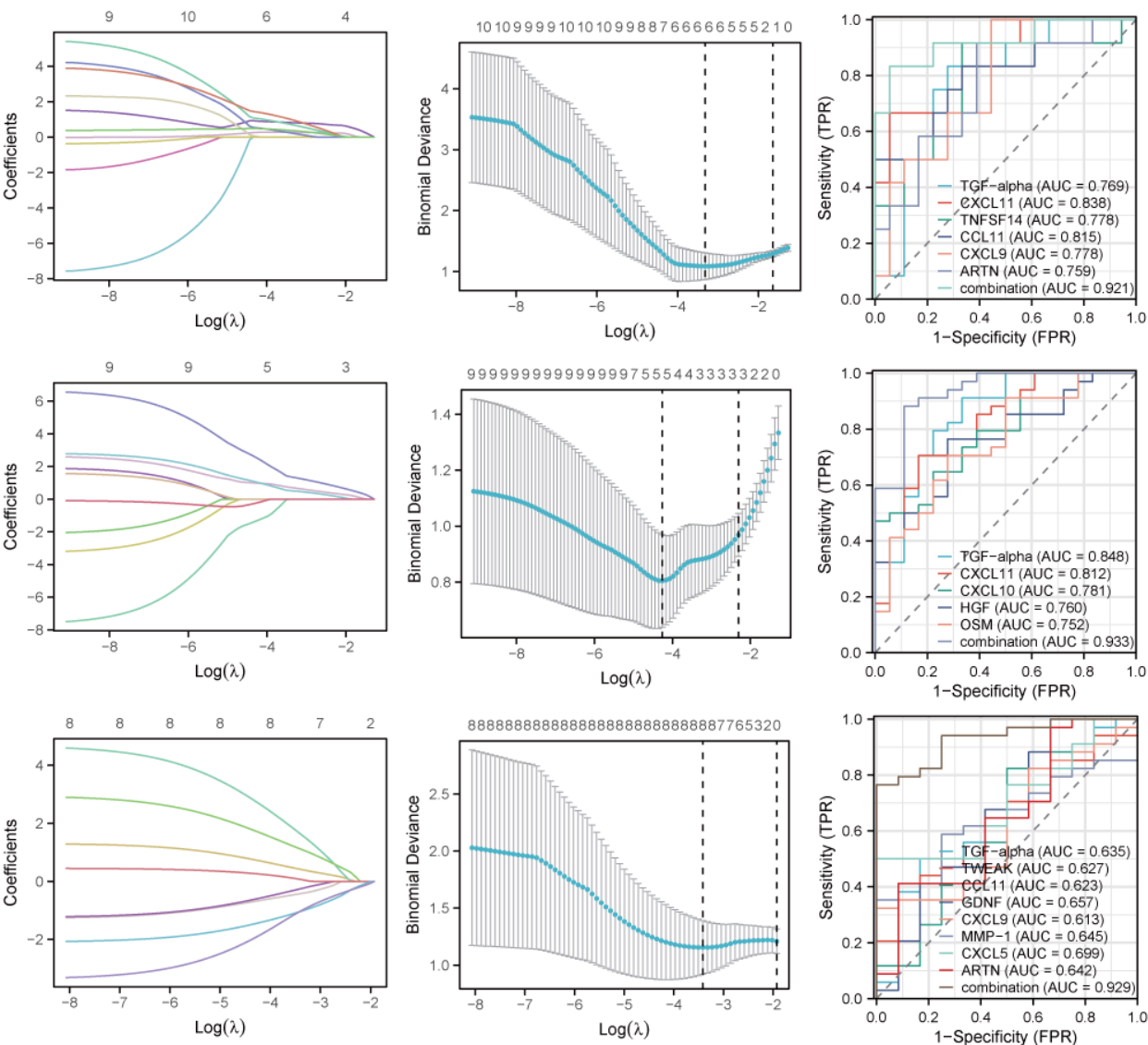(3) **GDNF + CXCL5 + ARTN exhibited promising diagnostic capabilities in distinguishing PTC from nodular goiter (AUC = 0.87).**

3. **A diagnostic marker for thyroid cancer was developed using the the least absolute shrinkage and selection operator (LASSO) algorithm**


(1) The combination of TGF-alpha, CXCL11, TNFSF14, CCL11, CXCL9, and ARTN exhibited promising diagnostic capabilities in distinguishing nodular goiter from healthy control (AUC = 0.92).

(2) The combination of TGF-alpha, CXCL11, CXCL10, HGF, and OSM exhibited promising diagnostic capabilities in distinguishing PTC from healthy control (AUC = 0.93).

(3) The combination of TGF-alpha, TWEAK, CCL11, GDNF, CXCL9, MMP-1, CXCL5, and ARTN exhibited promising diagnostic capabilities in distinguishing PTC from nodular goiter (AUC = 0.93).

4. The expression of main differences in inflammatory protein
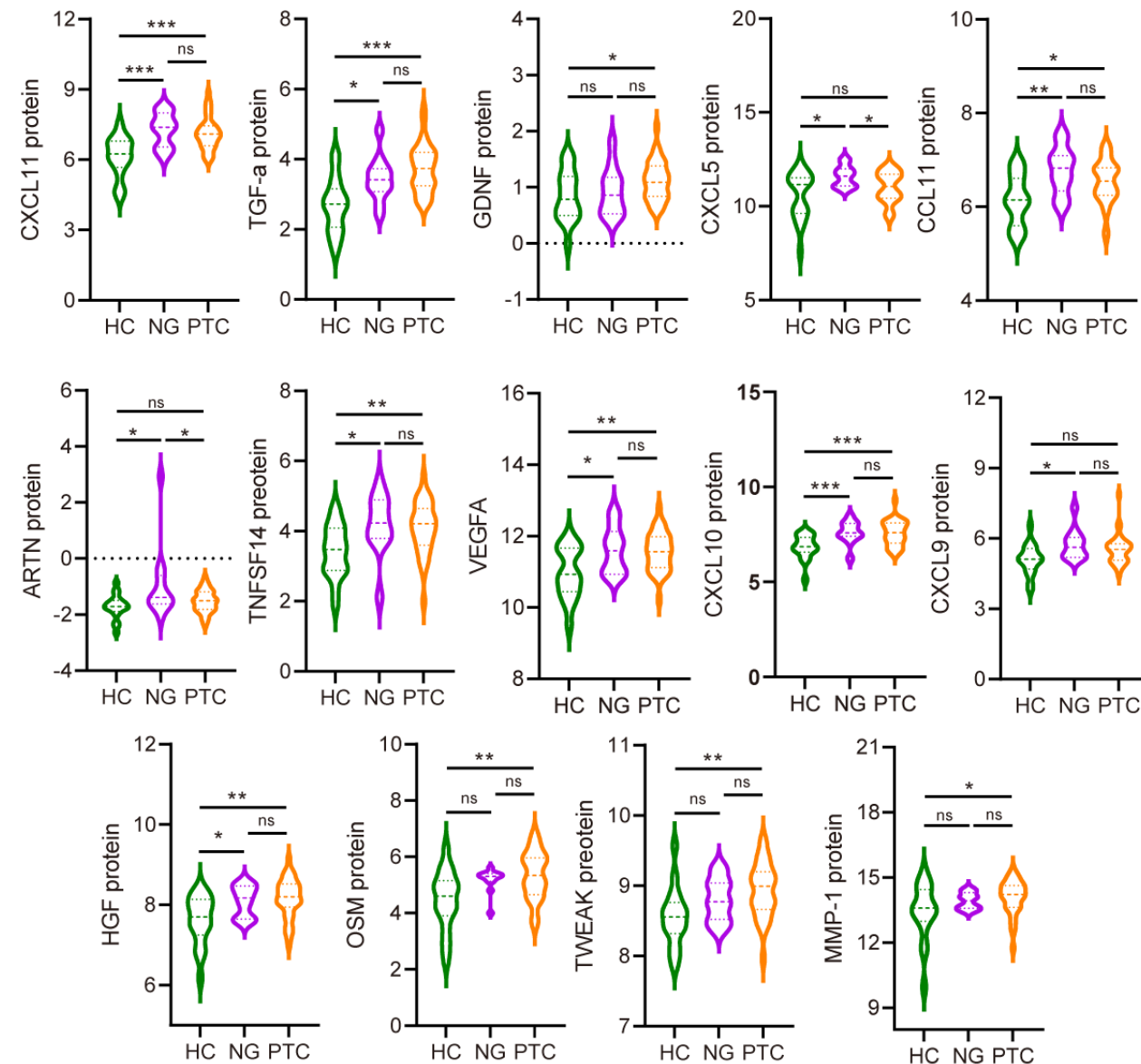
(1) nodular goiter exhibited significant elevations in the proteins CXCL11, TGF-α, CXCL5, ARTN, TNFSF14, CCL11, VEGFA, CXCL10, CXCL9, and HGF, compared to the healthy control group.

(2) Similarly, PTC demonstrated significant elevations in the proteins CXCL11, TGF-α, GDNF, TNFSF14, CCL11, VEGFA, CXCL10, OSM, TWEAK, and MMP-1.

(3) Additionally, CXCL5 and ARTN proteins experienced notable decreases in the PTC group compared to the nodular goiter group.

Summary

❑ This study offers potential biomarkers for distinguishing between PTC and nodular goiter in clinical practice, thereby aiding in developing treatment strategies and mitigating overtreatment.

❑ Furthermore, compared to logistic regression, the results from the LASSO algorithm demonstrate better diagnostic efficacy, albeit requiring more protein combinations. This implies that while the LASSO algorithm yields superior diagnostic outcomes, it also entails higher costs. Therefore, further research is needed to strike a balance between diagnostic accuracy and healthcare expenditure.

Yongqin Pan, Mingxi Xu, Tsz Hong Chong, Siping Xie, Kunsong Huang, Guanghao Wang, Yuhua Ma, Jinyi Li, Wah Yang. 2024. Combined detection of inflammatory proteins is beneficial for diagnosing the papillary thyroid carcinoma and nodular goiter. *iMetaOmics* 1: e14. https://doi.org/10.1002/imo2.14

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