

Proteomics Profile in Encapsulated Follicular Patterned Thyroid Neoplasms

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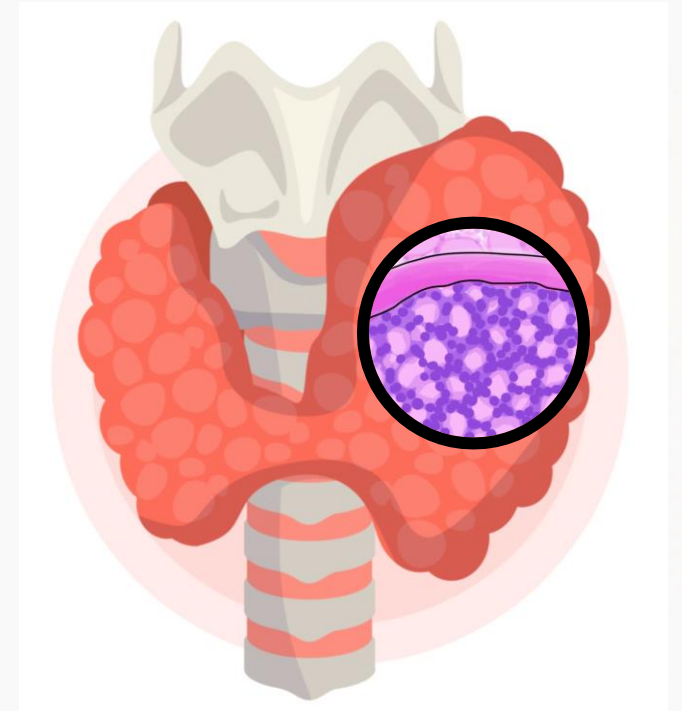
Poster 12

Disclosure of Relevant Financial Relationships

I have no financial relationship to disclose

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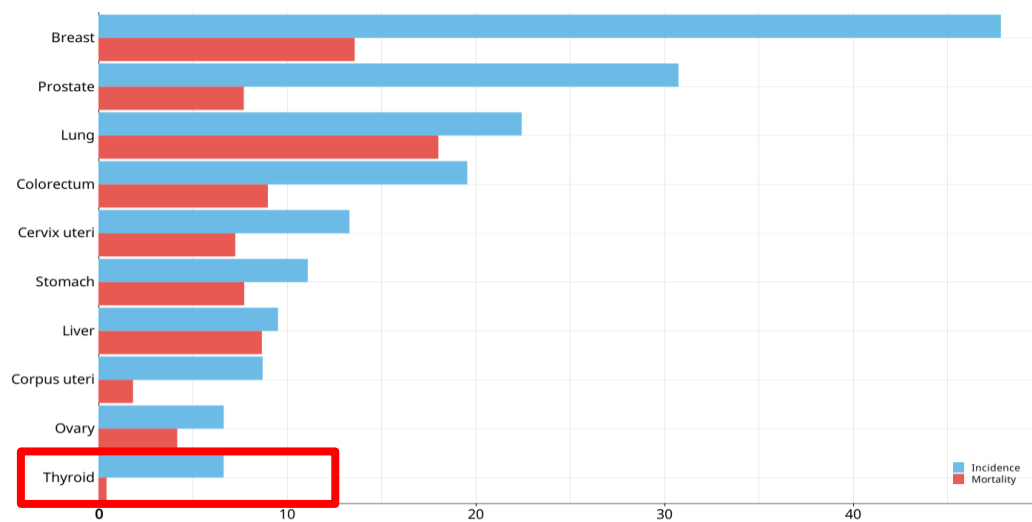
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INTRODUCTION

Incidence and mortality rate of thyroid cancer (Globocan 2020)

Estimated age-standardized incidence and mortality rates (World) in 2020, World, both sexes, all ages (excl. NMSC)

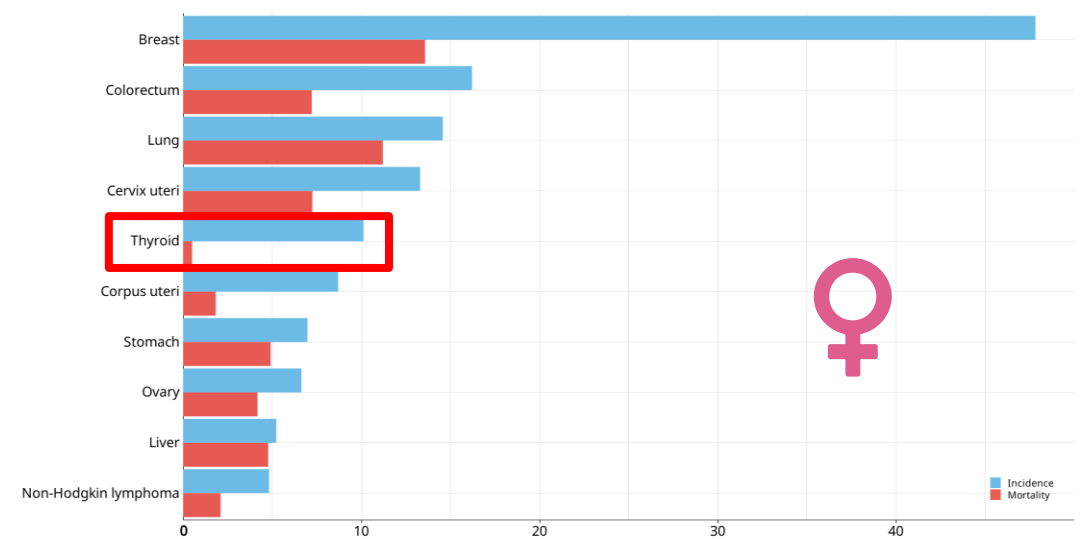


Data source: Globocan 2020
Graph production: Global Cancer Observatory (<http://gco.iarc.fr>)

ASR (World) per 100 000

International Agency for Research on Cancer
World Health Organization

Estimated age-standardized incidence and mortality rates (World) in 2020, World, females, all ages (excl. NMSC)



Data source: Globocan 2020
Graph production: Global Cancer Observatory (<http://gco.iarc.fr>)

ASR (World) per 100 000

International Agency for Research on Cancer
World Health Organization

INTRODUCTION

WHO Classification of Endocrine and Neuroendocrine Tumors 2022

Developmental abnormalities

1. Thyroglossal duct cyst
2. Other congenital thyroid abnormalities

Follicular cell-derived neoplasms

1. Benign tumors
 - a. Thyroid follicular nodular disease
 - b. Follicular adenoma
 - c. Follicular adenoma with papillary architecture
 - d. Oncocytic adenoma of the thyroid
2. Low-risk neoplasms
 - a. Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
 - b. Thyroid tumors of uncertain malignant potential
 - c. Hyalinizing trabecular tumor
3. Malignant neoplasms
 - a. Follicular thyroid carcinoma
 - b. Invasive encapsulated follicular variant papillary carcinoma
 - c. Papillary thyroid carcinoma
 - d. Oncocytic carcinoma of the thyroid
 - e. Follicular-derived carcinomas, high-grade
 - i. Differentiated high-grade thyroid carcinoma
 - ii. Poorly differentiated thyroid carcinoma
 - f. Anaplastic follicular cell-derived thyroid carcinoma

Thyroid C-cell-derived carcinoma

1. Medullary thyroid carcinoma

Mixed medullary and follicular cell-derived carcinomas

Salivary gland-type carcinomas of the thyroid

1. Mucoepidermoid carcinoma of the thyroid
2. Secretory carcinoma of salivary gland type

Thyroid tumors of uncertain histogenesis

1. Sclerosing mucoepidermoid carcinoma with eosinophilia
2. Cribriform morular thyroid carcinoma

Thymic tumors within the thyroid

1. Thymoma family
2. Spindle epithelial tumor with thymus-like elements
3. Thymic carcinoma family

Embryonal thyroid neoplasms

1. Thyroblastoma

ENCAPSULATED FOLlicULAR-PATTERNED THYROID TUMORS (EFPTTs)

Benign:

- Follicular adenoma (FA)

Borderline (Low-risk neoplasms):

- Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)

- Follicular tumor of uncertain malignant potential (FT-UMP)

- Well-differentiated tumor of uncertain malignant potential (WDT-UMP)

Malignant:

- Invasive encapsulated follicular variant papillary carcinoma (IEFVPTC)

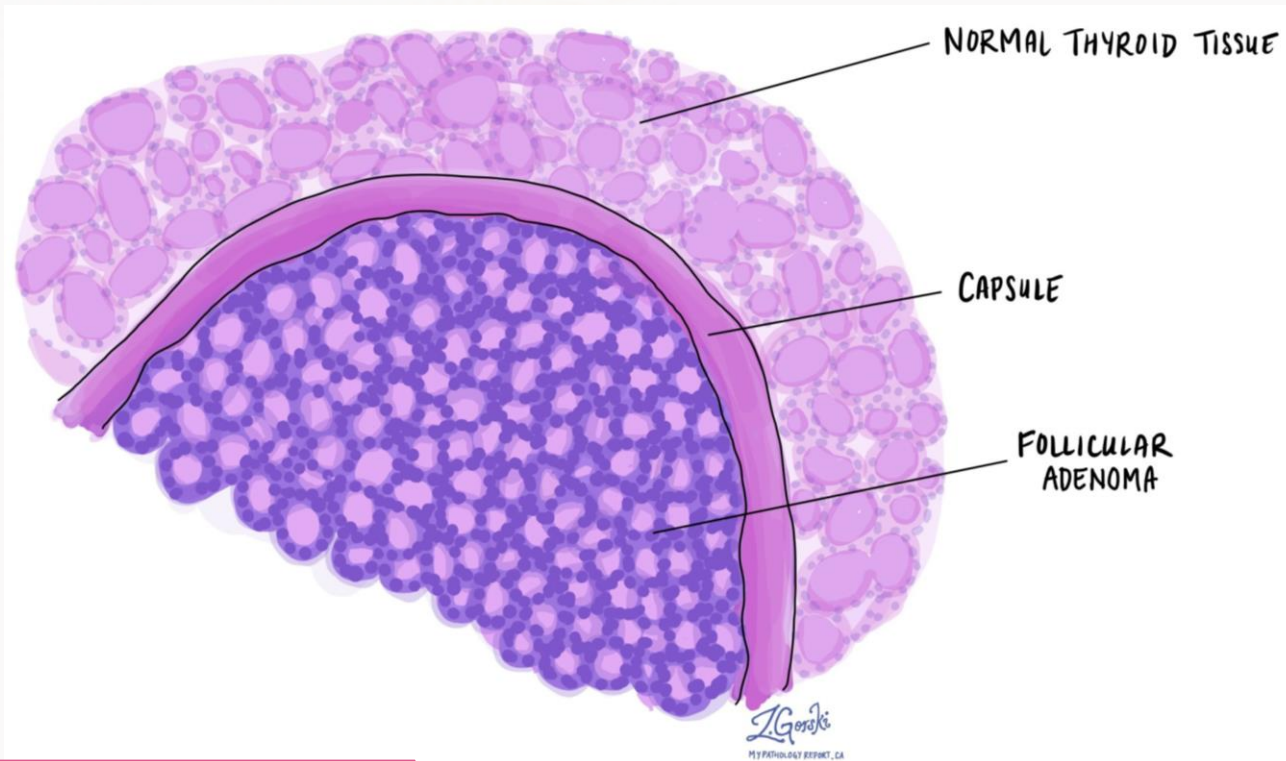
- Follicular carcinoma (FTC)

INTRODUCTION



INTRODUCTION

Similarity



Difference

Capsular/ vascular invasion

Nuclear features of PTC

EFPTTs:

FA

NIFTP

FT-UMP

WDT-UMP

FTC

IEFVPTC

INTRODUCTION

*Sharing the same molecular characteristics → can not determine the type of tumor

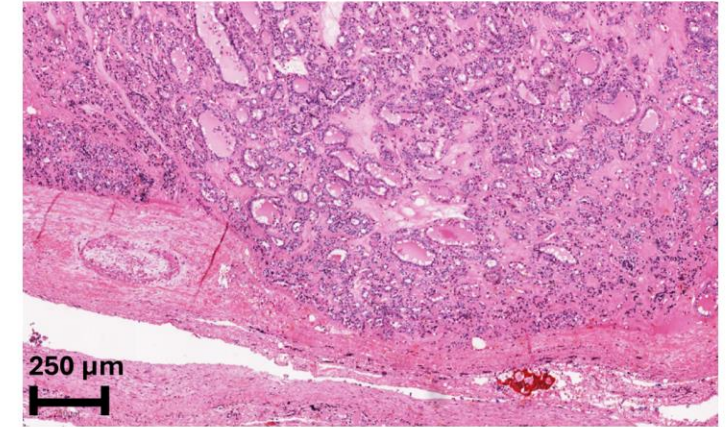
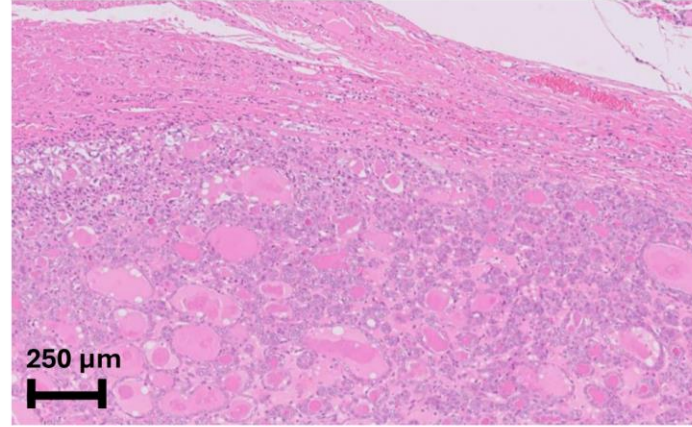
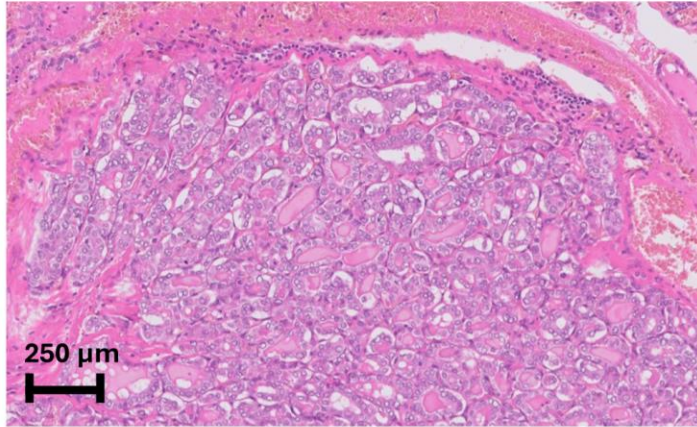
	FA	FT-UMP	WDT-UMP	NIFTP	IEFVPTC
Category	Benign	Low-risk	Low-risk	Low-risk	Malignant
RAS mutation	up to 20%	up to 20%	up to 20%	up to 60%	up to 70%
BRAFK601E, EIF1AX, EZH1, DICER1, PTEN, or TSHR mutations	<10%	<10%	<10%	<10%	<10%
PAX8::PPARG	<10%	<10%	Rare	up to 30%	up to 40%
THADA fusions	<10%	Not determined	Not determined	up to 30%	<5%
BRAF, RET, NTRK, or ALK fusions	Not found	Not found	Not found	Not found	Rare
BRAF V600E	Absent	Absent	Absent	Absent	Infrequent

IEFVPTC

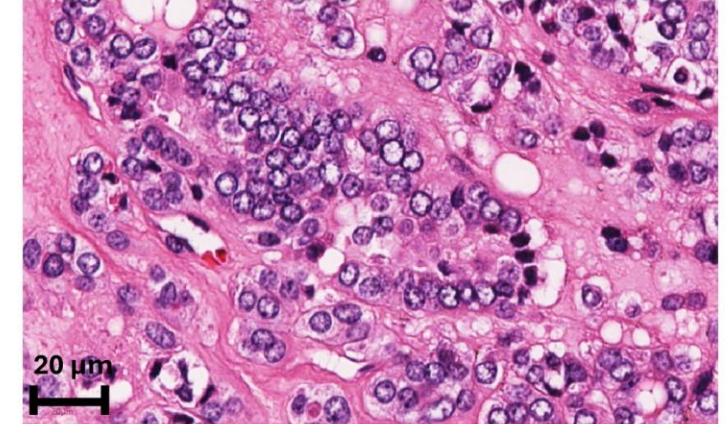
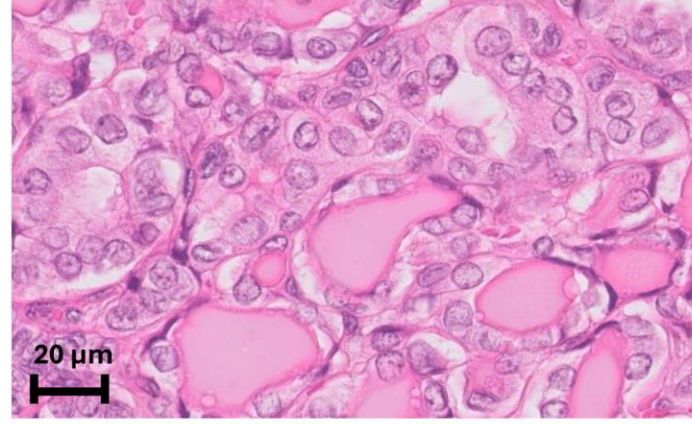
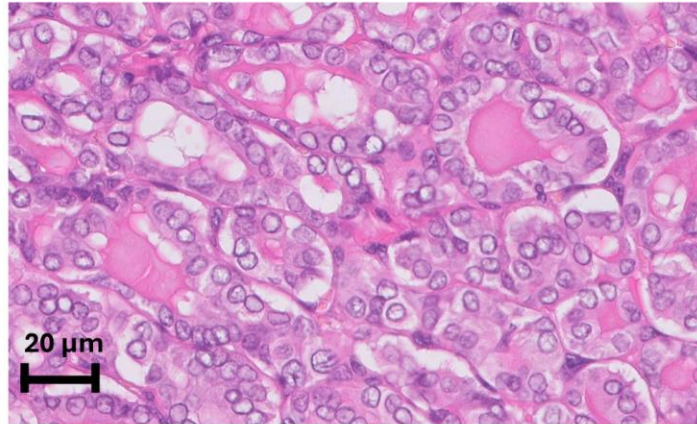
NIFTP

WDT-UMP

100x



400x



- Malignant
- Thyroidectomy
- Excision of central neck lymph nodes
- Radioiodine therapy
- TSH suppression with l-thyroxine

- Borderline tumor
- Thyroid lobectomy
- Closed surveillance

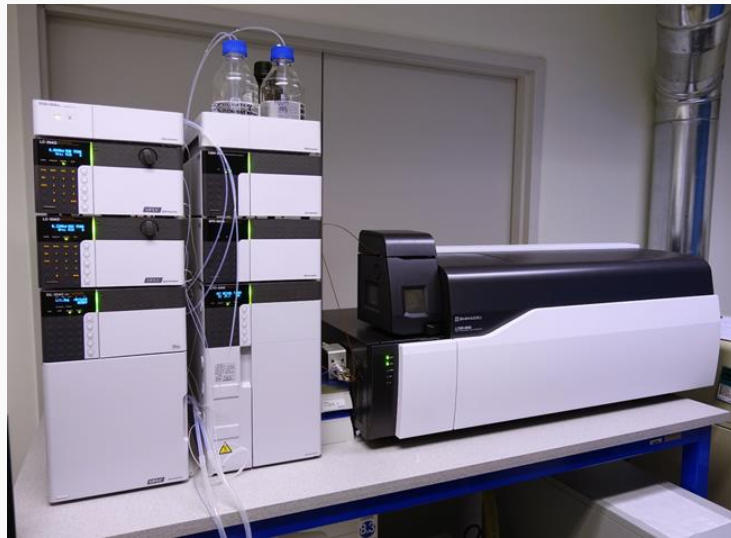
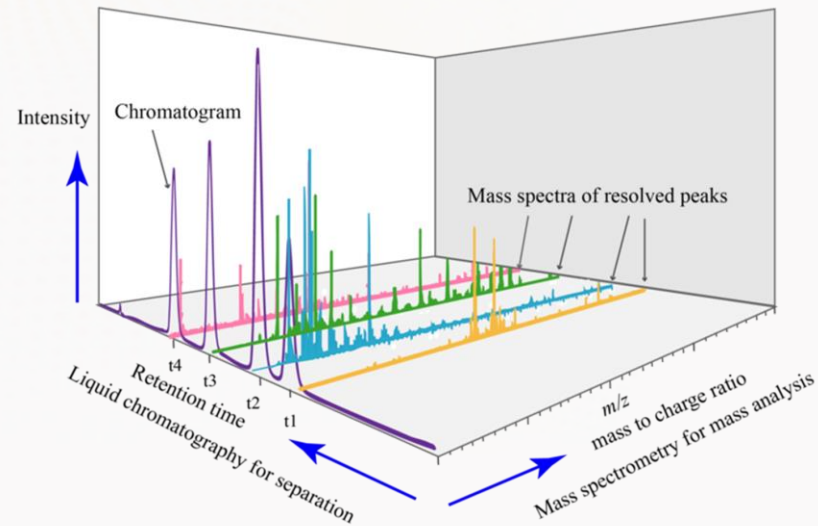
- Borderline tumor
- Thyroid lobectomy
- Clinical & radiologic surveillance

Invasive encapsulated follicular variant papillary carcinoma (**IEFVPTC**)

Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (**NIFTP**)

Well-differentiated tumor of uncertain malignant potential (**WDT-UMP**)

INTRODUCTION



Liquid chromatography (LC) tandem mass spectrometry (MS/MS) is an analytical chemistry technique that combines the physical separation capabilities of liquid chromatography (or HPLC) with the mass analysis capabilities of mass spectrometry (MS)

A beneficial, robust, and sensitive procedure used for a wide variety of small molecules

Advantages

Large number of molecules can be detected

Differentiate tumor subtypes, tumor stage, or degree of metastasis, prognosis

Aichler M, et, al. Laboratory Investigation. 2015.

STUDY OBJECTIVES

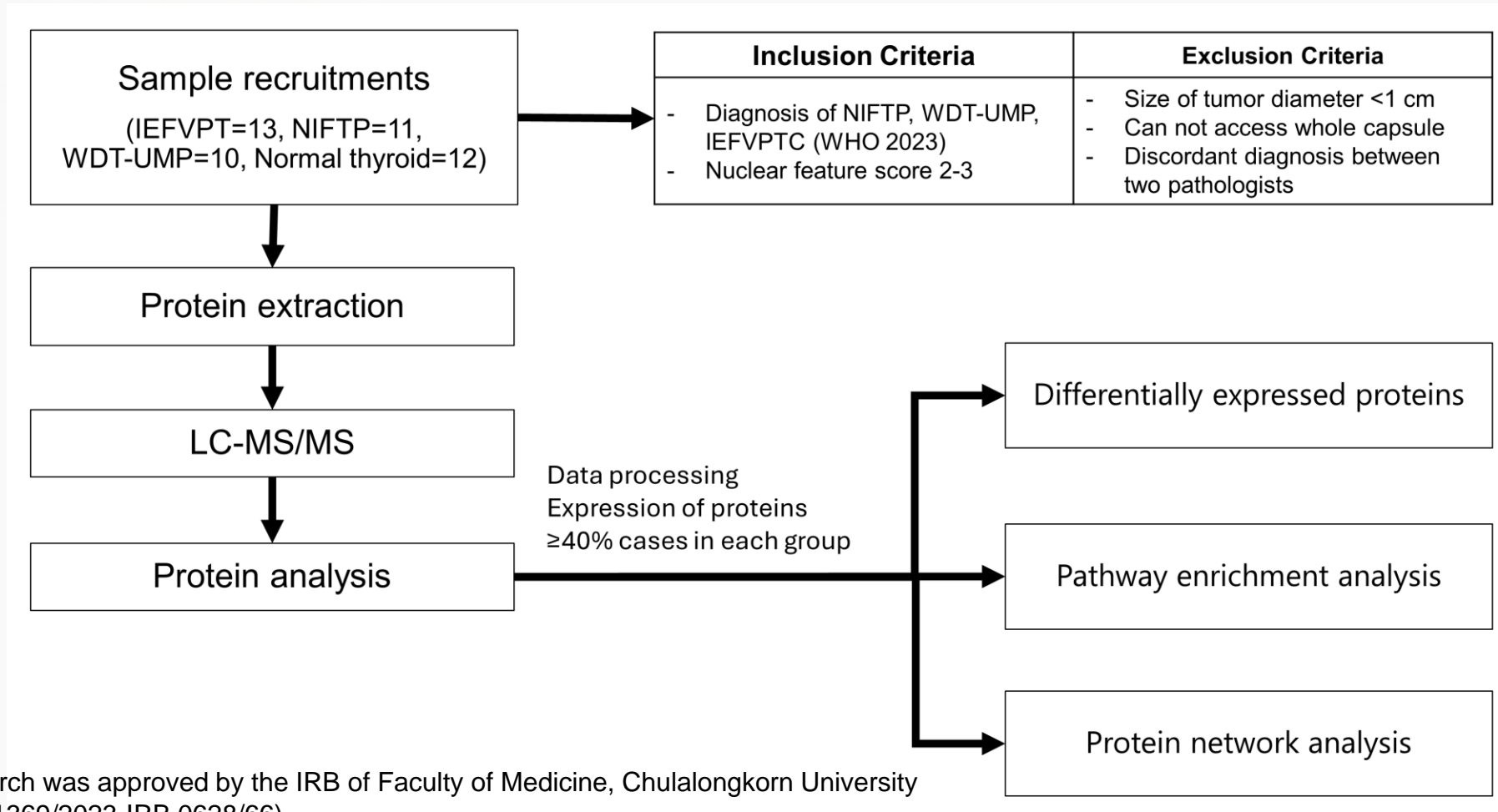


Investigate the distinct proteins among NIFTP, WDT-UMP, IEFVPTC



Discover biological pathway through proteomic analysis

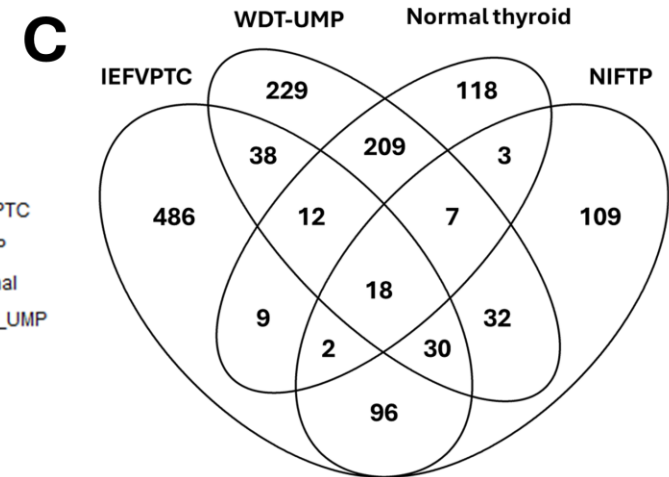
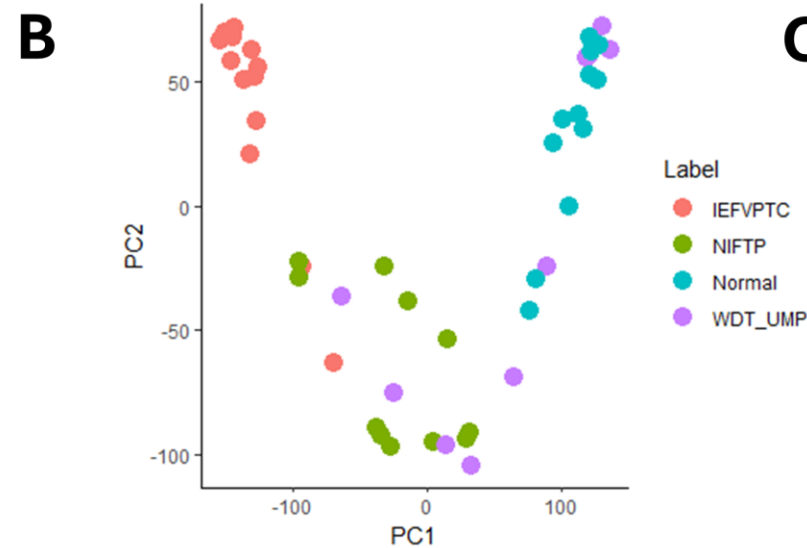
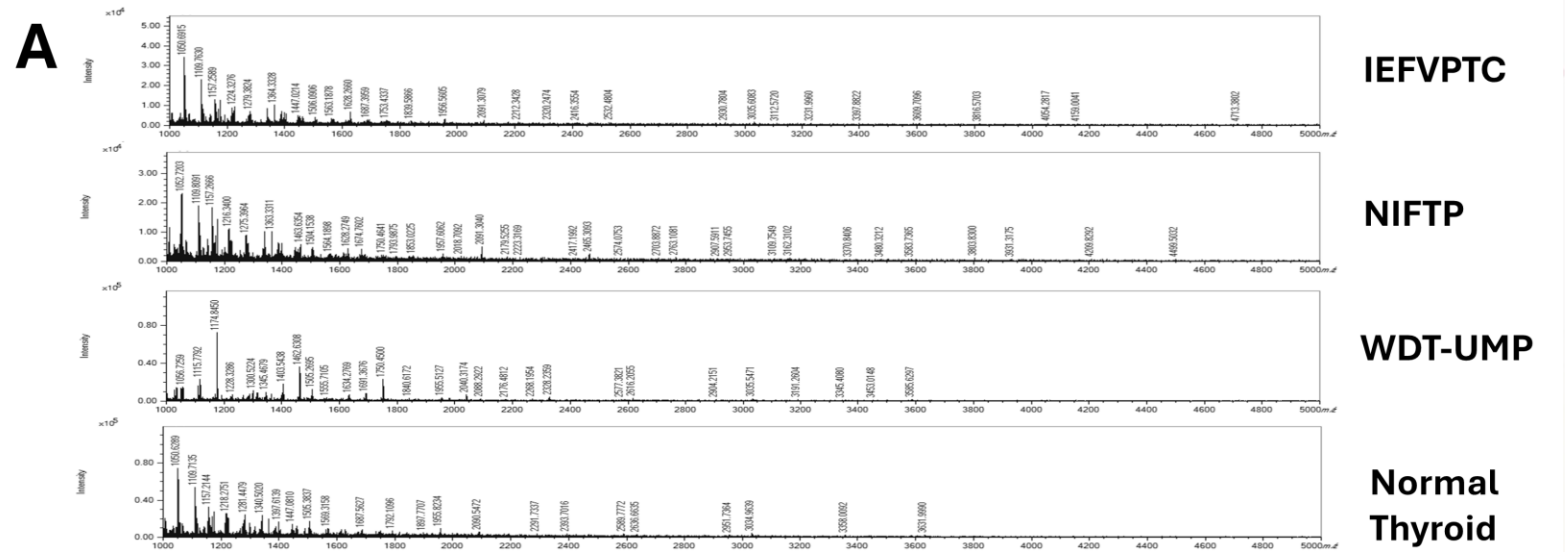
STUDY DESIGN



*The research was approved by the IRB of Faculty of Medicine, Chulalongkorn University (COA.No. 1369/2023-IRB 0628/66)

RESULTS

Detected 1398 proteins
Distinct protein expression profiles across normal thyroid tissue, IEFVPTC and low-risk tumors (NIFTP and WDT-UMP)

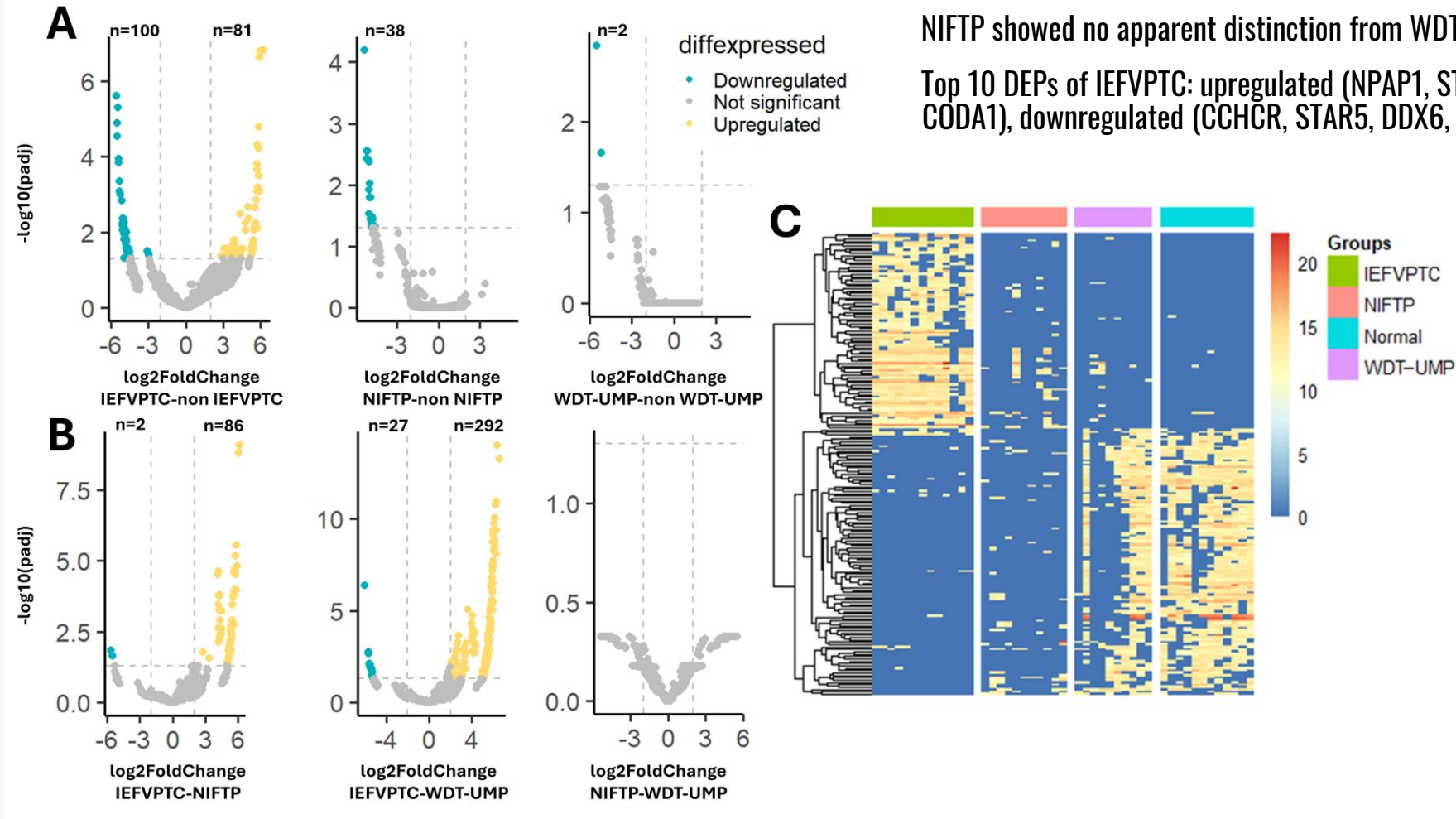


RESULTS

IEFVPTC had the most DEPs when compared to NIFTP and WDT-UMP

NIFTP showed no apparent distinction from WDT-UMP

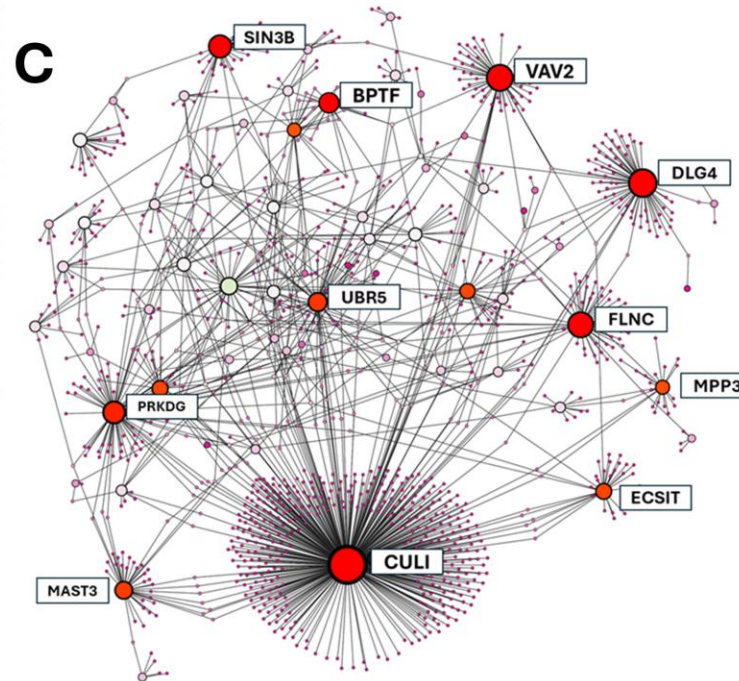
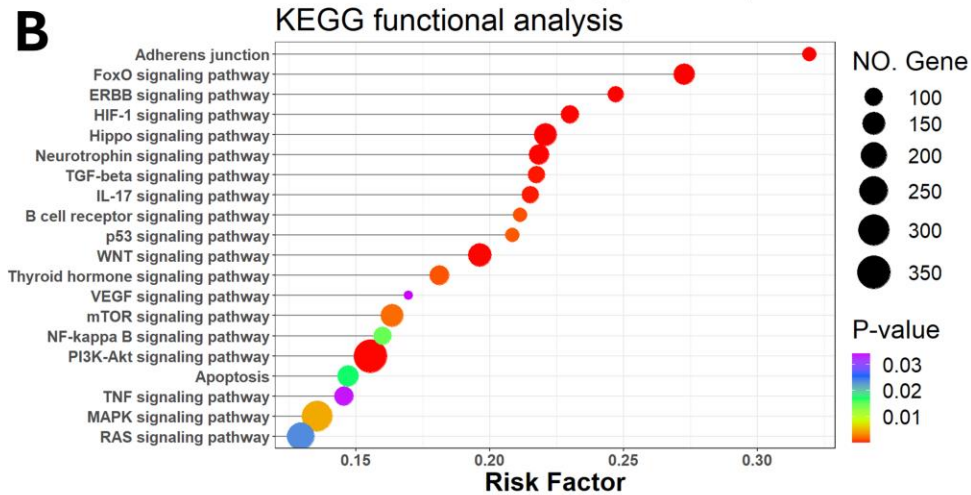
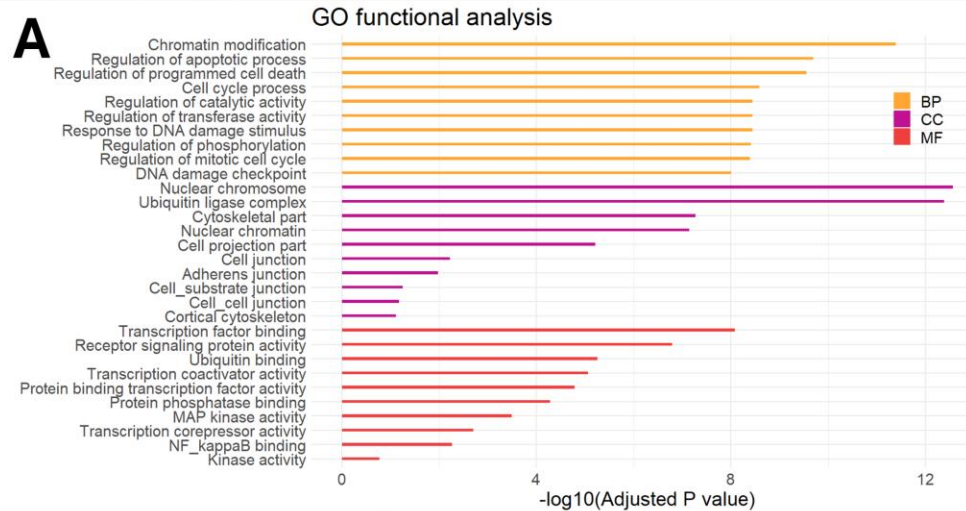
Top 10 DEPs of IEFVPTC: upregulated (NPAP1, STK33, O51I2, DLG4, THUM2, CODA1), downregulated (CCHCR, STAR5, DDX6, LIGO2)



RESULTS

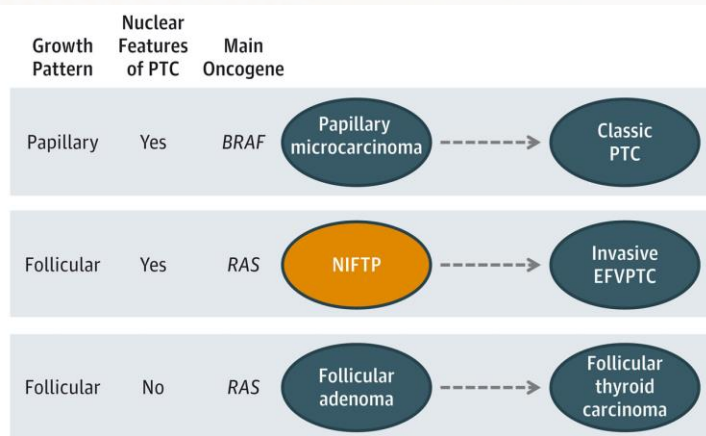
Pathways are known to play roles in the multistep tumorigenic process of thyroid cancer

Hub genes have implications for the response to immune checkpoint inhibitors therapy (*PRKDC*) and offer potential prognostic markers (*CUL1*, *VAV2*), presenting a novel avenue for thyroid cancer therapeutics



<https://www.networkanalyst.ca/>

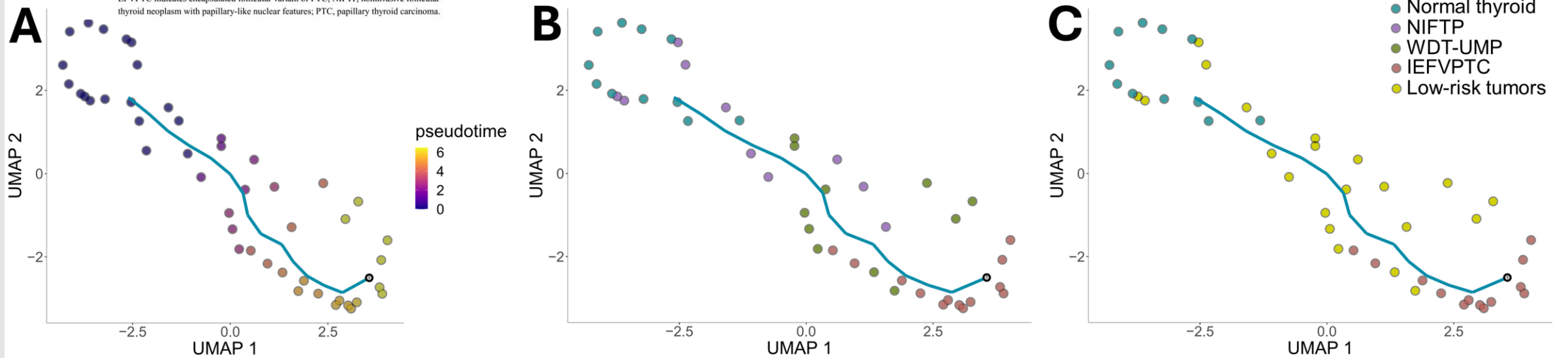
RESULTS



Utilizing proteomics profile, we proposed a trajectory to recapitulate the progression sequence from NIFTP/WDT-UMP to IEFVPTC

→ NIFTP/WDT-UMP or low-risk tumors may indeed serve as the precursors to IEFVPTC

Figure 2. Putative Scheme of Thyroid Carcinogenesis
EFVPTC indicates encapsulated follicular variant of PTC; NIFTP, noninvasive follicular thyroid neoplasm with papillary-like nuclear features; PTC, papillary thyroid carcinoma.



CONCLUSION

The first proteomic analysis of follicular-pattern thyroid tumors aimed at identifying specific protein signatures capable of distinguishing IEFVPTC from low-risk tumors (NIFTP and WDT-UMP).

These discoveries have the potential to offer valuable insights into tumor biology and serve as a basis for the development of novel therapeutic approaches for follicular-patterned thyroid neoplasms.

CONCLUSION

Plan to validate potential biomarker candidates as IHC markers to distinguish IEFVPTC in a larger sample cohort, including fine-needle aspiration (FNA) samples and formalin-fixed paraffin-embedded (FFPE) samples.

THANK YOU FOR YOUR ATTENTION

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