

## *Supplementary Material*

**Supplementary Table S1. Enriched KEGG pathways in malignant thyroid follicular cells**

<b>ID</b>	<b>Description</b>	<b>GeneRatio</b>	<b>BgRatio</b>	<b>pvalue</b>	<b>p.adjust</b>	<b>qvalue</b>
hsa04060	Cytokine-cytokine receptor interaction	44/458	295/8115	0.000	0.000	0.000
hsa04151	PI3K-Akt signaling pathway	33/458	354/8115	0.003	0.028	0.023
hsa04514	Cell adhesion molecules	29/458	149/8115	0.000	0.000	0.000
hsa04510	Focal adhesion	29/458	201/8115	0.000	0.000	0.000
hsa04010	MAPK signaling pathway	28/458	294/8115	0.004	0.035	0.029
hsa05202	Transcriptional misregulation in cancer	27/458	193/8115	0.000	0.000	0.000
hsa05205	Proteoglycans in cancer	27/458	205/8115	0.000	0.001	0.001
hsa04062	Chemokine signaling pathway	23/458	192/8115	0.000	0.007	0.006
hsa04061	Viral protein interaction with cytokine and cytokine receptor	22/458	100/8115	0.000	0.000	0.000
hsa04015	Rap1 signaling pathway	22/458	210/8115	0.004	0.032	0.026
hsa05417	Lipid and atherosclerosis	22/458	215/8115	0.005	0.036	0.029
hsa04640	Hematopoietic cell lineage	20/458	99/8115	0.000	0.000	0.000
hsa04668	TNF signaling pathway	20/458	112/8115	0.000	0.000	0.000
hsa04512	ECM-receptor interaction	19/458	88/8115	0.000	0.000	0.000
hsa05323	Rheumatoid arthritis	19/458	93/8115	0.000	0.000	0.000
hsa04145	Phagosome	19/458	152/8115	0.001	0.010	0.008
hsa04610	Complement and coagulation cascades	18/458	85/8115	0.000	0.000	0.000
hsa05418	Fluid shear stress and atherosclerosis	18/458	139/8115	0.001	0.010	0.008
hsa04933	AGE-RAGE signaling pathway in diabetic complications	17/458	100/8115	0.000	0.001	0.001
hsa04064	NF-kappa B signaling pathway	17/458	104/8115	0.000	0.001	0.001
hsa05410	Hypertrophic cardiomyopathy	16/458	90/8115	0.000	0.001	0.001

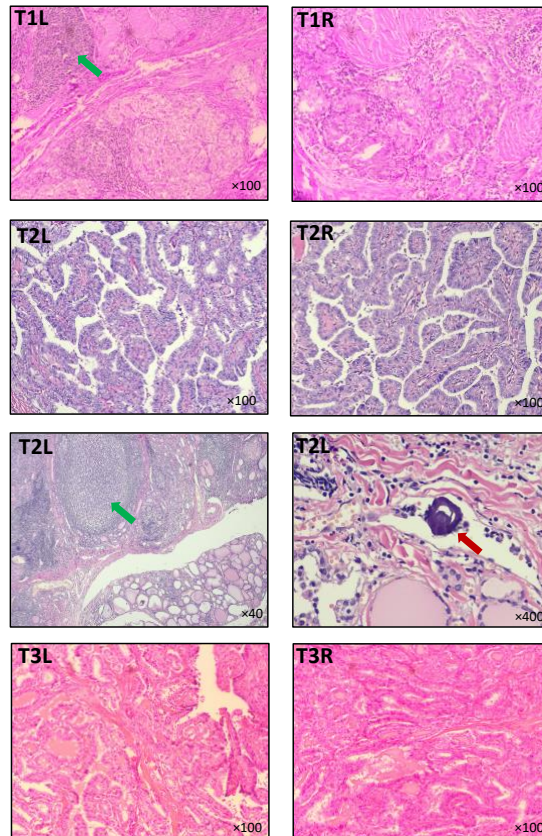
hsa04670	Leukocyte transendothelial migration	16/458	114/8115	0.001	0.008	0.007
hsa04270	Vascular smooth muscle contraction	16/458	134/8115	0.003	0.032	0.025
hsa05144	Malaria	15/458	50/8115	0.000	0.000	0.000
hsa05414	Dilated cardiomyopathy	15/458	96/8115	0.000	0.005	0.004
hsa05142	Chagas disease	15/458	102/8115	0.001	0.008	0.006
hsa05146	Amoebiasis	15/458	102/8115	0.001	0.008	0.006
hsa05150	Staphylococcus aureus infection	14/458	96/8115	0.001	0.010	0.008
hsa04350	TGF-beta signaling pathway	13/458	94/8115	0.002	0.022	0.018
hsa04928	Parathyroid hormone synthesis, secretion and action	13/458	106/8115	0.006	0.046	0.037
hsa04918	Thyroid hormone synthesis	12/458	75/8115	0.001	0.010	0.008
hsa05133	Pertussis	12/458	76/8115	0.001	0.011	0.009
hsa05140	Leishmaniasis	12/458	77/8115	0.001	0.012	0.010
hsa05032	Morphine addiction	12/458	91/8115	0.005	0.036	0.029
hsa04657	IL-17 signaling pathway	12/458	94/8115	0.006	0.046	0.037
hsa05143	African trypanosomiasis	11/458	37/8115	0.000	0.000	0.000
hsa04978	Mineral absorption	11/458	60/8115	0.000	0.007	0.006
hsa05412	Arrhythmogenic right ventricular cardiomyopathy	11/458	77/8115	0.004	0.032	0.026
hsa05219	Bladder cancer	10/458	41/8115	0.000	0.001	0.001
hsa05321	Inflammatory bowel disease	10/458	65/8115	0.003	0.030	0.024
hsa05134	Legionellosis	9/458	57/8115	0.004	0.035	0.029
hsa05340	Primary immunodeficiency	7/458	38/8115	0.005	0.036	0.029

**Supplementary Table S2. 44 of differentially expressed genes in cytokine-cytokine receptor interaction between malignant thyroid follicular cells and non-tumor follicular cells**

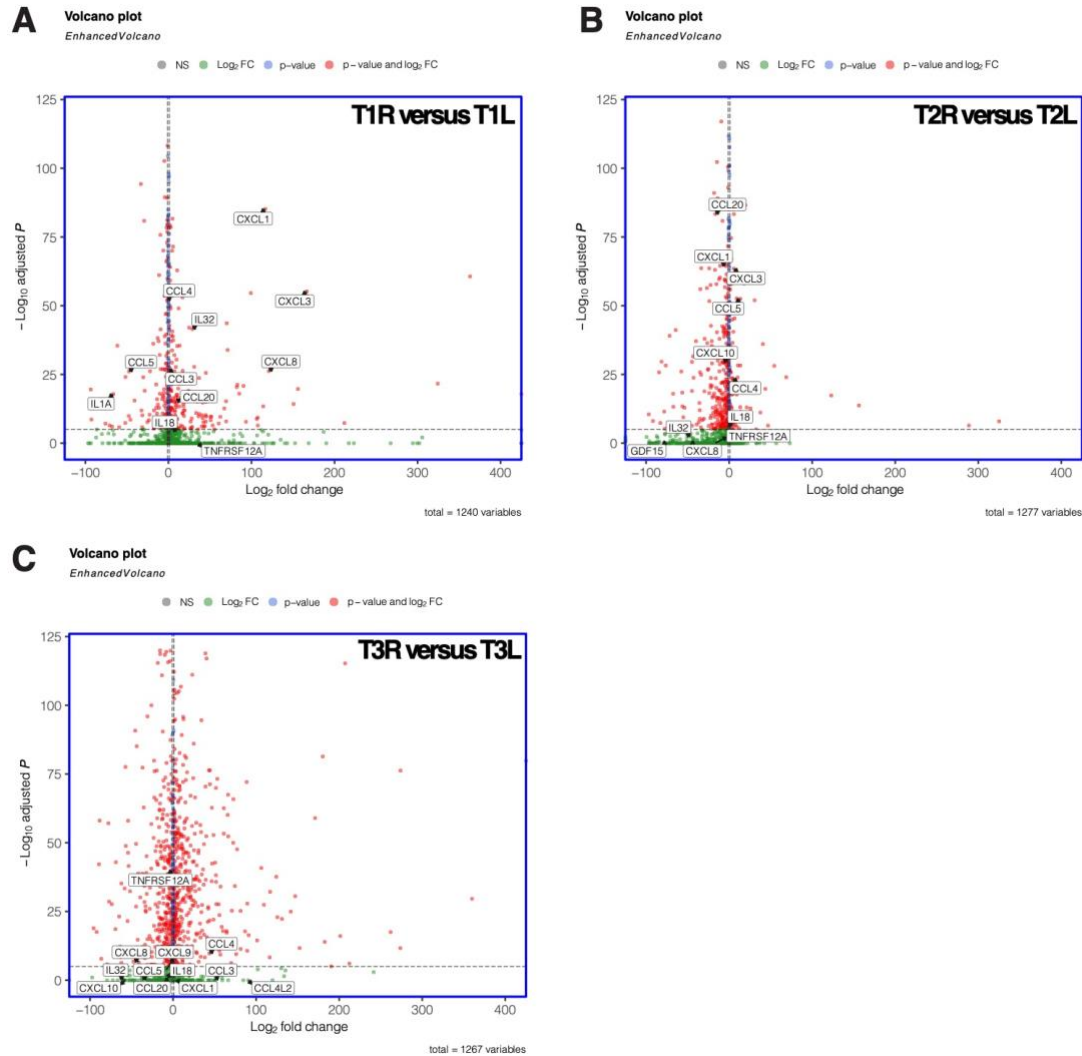
Entrez ID	Gene symbol	p_val	avg_log2FC	pct.1	pct.2	p_val_adj
3627	CXCL10	0.000	384.504	0.628	0.944	0.000
9518	GDF15	0.000	338.986	0.583	0.821	0.000
3576	CXCL8	0.000	264.674	0.313	0.436	0.000
4283	CXCL9	0.000	221.787	0.513	0.726	0.000
2921	<b>CXCL3</b>	0.000	159.369	0.626	0.811	0.000
9235	IL32	0.000	96.989	0.851	0.963	0.000
6351	CCL4	0.000	86.455	0.925	0.997	0.000
9560	CCL4L2	0.000	86.455	0.925	0.997	0.000
6364	CCL20	0.000	77.821	0.794	0.922	0.000
6348	CCL3	0.000	74.304	0.854	0.964	0.000
6349	CCL3L1	0.000	74.304	0.854	0.964	0.000
4050	LTB	0.000	67.271	0.822	0.988	0.000
3552	<b>IL1A</b>	0.000	62.628	0.552	0.766	0.000
8793	TNFRSF10D	0.000	53.046	0.551	0.862	0.000
9966	TNFSF15	0.000	49.338	0.514	0.790	0.000
6352	<b>CCL5</b>	0.000	38.396	0.916	1.000	0.000
6376	CX3CL1	0.000	29.855	0.578	0.720	0.000
8743	TNFSF10	0.000	29.559	0.741	0.737	0.000
3625	INHBB	0.000	29.300	0.886	0.994	0.001
970	CD70	0.000	22.921	0.537	0.903	0.000
3575	IL7R	0.000	21.357	0.810	0.983	0.000
7852	CXCR4	0.000	20.233	0.931	0.995	0.000
7124	TNF	0.000	13.554	0.867	0.882	0.000
51330	<b>TNFRSF12A</b>	0.000	13.554	0.867	0.882	0.000

3557	IL1RN	0.000	13.202	0.616	0.803	0.000
650	BMP2	0.000	12.471	0.663	0.550	0.000
7042	TGFB2	0.000	12.408	0.421	0.493	0.000
3595	IL12RB2	0.000	12.268	0.564	0.942	0.000
7133	TNFRSF1B	0.000	10.789	0.778	0.997	0.000
284340	CXCL17	0.000	9.886	0.528	0.670	0.000
2919	<b>CXCL1</b>	0.000	9.886	0.528	0.670	0.000
3606	<b>IL18</b>	0.000	9.032	0.477	0.617	0.000
7293	TNFRSF4	0.000	7.023	0.859	0.986	0.000
3559	IL2RA	0.000	6.200	0.824	0.993	0.000
58191	CXCL16	0.000	5.850	0.697	0.887	0.000
3976	LIF	0.000	4.528	0.504	0.642	0.000
654	BMP6	0.000	4.288	0.539	0.886	0.000
6846	XCL2	0.000	2.980	0.858	0.986	0.000
6367	CCL22	0.000	2.545	0.445	0.658	0.000
655	BMP7	0.000	1.656	0.702	0.628	0.000
8784	TNFRSF18	0.000	1.606	0.805	0.999	0.000
7048	TGFBR2	0.000	-1.014	0.917	0.987	0.000
6358	CCL14	0.000	-2.887	0.699	0.195	0.000
3977	LIFR	0.000	-5.561	0.696	0.427	0.000

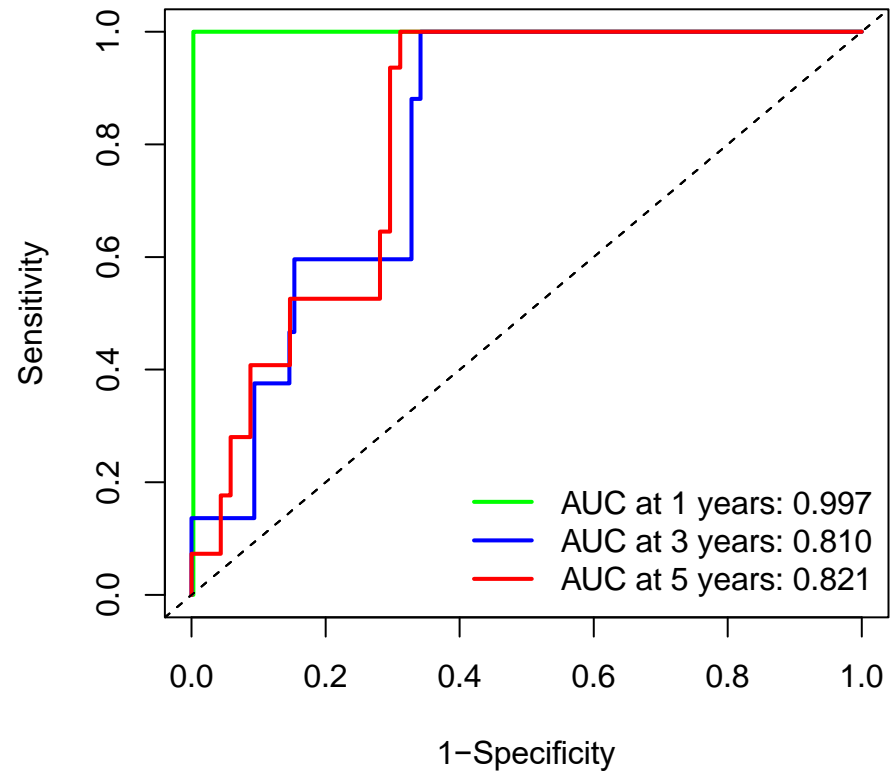
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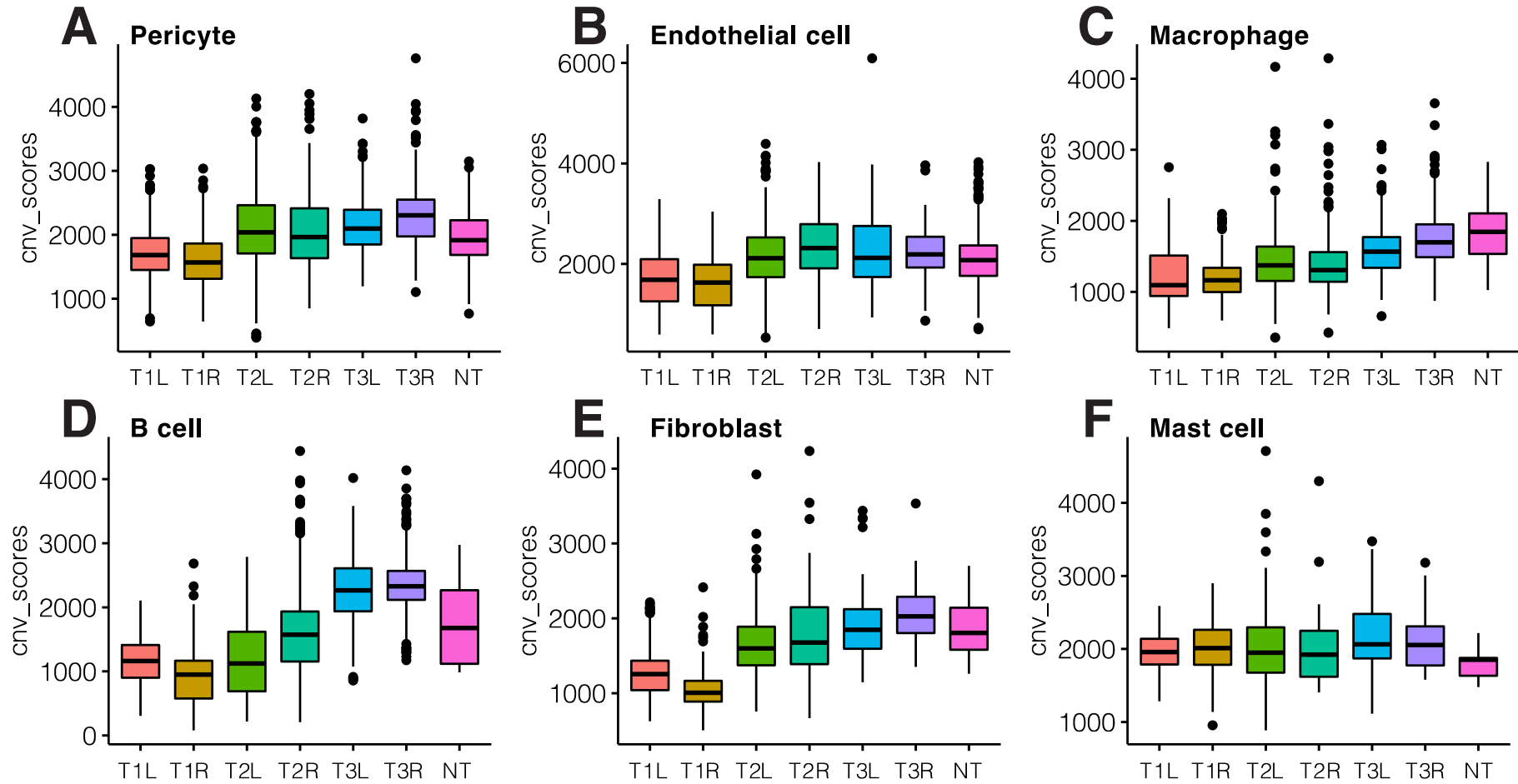
Supplementary Figure S1. Histological assessment of papillary thyroid carcinoma (PTC) in each patient. T1L and T1R: PTC from the left lobe and right lobe of the patient P1, respectively. T2L and T2R: PTC from the left lobe and right lobe of the patient P2, respectively. T3L and T3R: PTC from the left lobe and right lobe of the patient P3, respectively. Green arrow shows lymphocyte infiltration in thyroid tissue, indicative of chronic lymphocytic thyroiditis (CLT). Red arrow shows psammoma body, indicative of intrathyroidal spreading.



Supplementary Figure S2. Differentially expressed genes between the right and left tumor in patient by patient. T1L and T1R: PTC from the left lobe and right lobe of the patient P1, respectively. T2L and T2R: PTC from the left lobe and right lobe of the patient P2, respectively. T3L and T3R: PTC from the left lobe and right lobe of the patient P3, respectively.

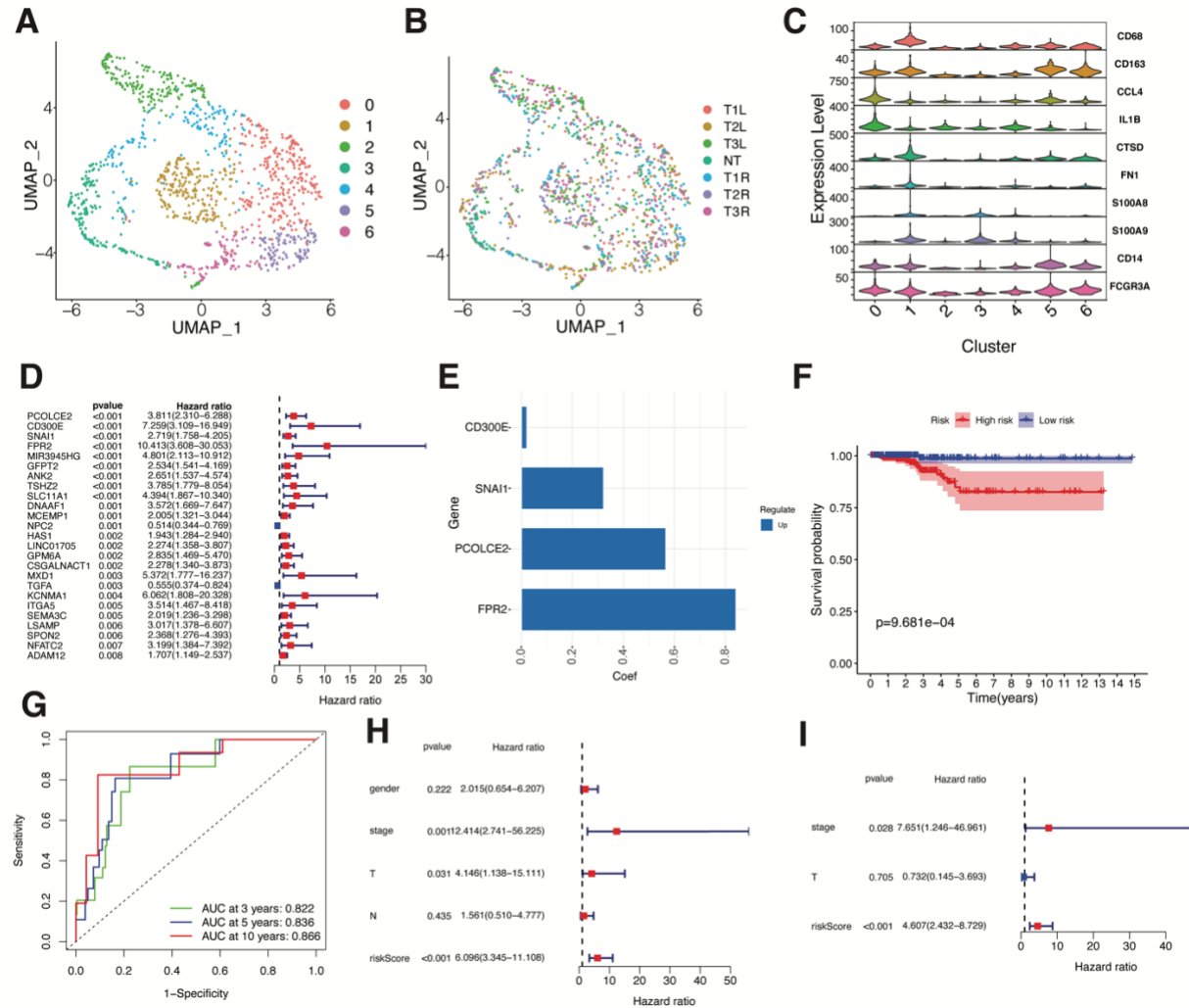


Supplementary Figure S3. Predicting capability of the 6-gene signature for overall survival in patients with PTC. AUC: area under the curve.



Supplementary Figure S4. Comparison of copy number variation (CNV) scores of each cell lineage in different thyroid samples.





Supplementary Figure S5. Prognostic significance of a gene signature of myeloid cells in papillary thyroid cancer. (A) UMAP plot of the classification of myeloid cells (n=1,179) from malignant and non-malignant thyroid tissue in an unsupervised clustering approach. (B) UMAP plot of myeloid cells in different thyroid samples. (C) Violin plot showing the expression distribution of canonical marker genes in each cell cluster. (D) Prognostic value of differentially expressed genes identified in myeloid cells in malignant thyroid tissue as compared to normal

tissue. (E) Coefficient of 4 genes for constructing a multi-gene signature. (F) Kaplan-Meier curve of overall survival in patients from the TCGA PTC cohort group by low and high risk score of 4-gene signature identified in tumor-associated macrophages. (G) Predicting capability of the 4-gene signature for overall survival in patients with PTC. AUC: area under the curve. (H) and (I) Unadjusted and adjusted prognostic significance of 4-gene signature and other clinicopathological factors for overall survival in patients with PTC.