GENE EXPRESSION PROFILING IN DIFFERENTIATED THYROID CARCINOMA

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BACKGROUND

Gene expression microarray technology can be used in the attempt to identify clinically relevant biomarkers of thyroid malignancy.

OBJECTIVES

To find new molecular markers that could improve the diagnostics, follow-up protocols, treatment outcome, prognosis and the quality of life of differentiated thyroid cancer patients.

SUBJECTS AND METHODS

- Tumor and surrounding normal thyroid tissue samples obtained from patients with differentiated thyroid carcinoma referred for surgery in "C.I.Parhon" National Institute of Endocrinology. All patients signed the informed consent. We analysed 6 cases of classical papillary thyroid carcinoma (cPTC) and 6 cases of folicullar variant of papillary thyroid carcinoma (fvPTC).
- RNA extraction - ***RNeasy Mini Kit*** (Qiagen)
- RNA quantification and integrity analysis - ***Infinite® 200 NanoQuant (Tecan), 2100 Bioanalyzer (Agilent).*** Samples with RNA integrity number (RIN) >7 were chosen for microarray gene expression analysis
- Microarray analysis - ***Agilent One-Color Microarray-Based Gene Expression*** protocol, v. 6.6, using **SurePrint G3 Human Gene Expression arrays 8x60K v2**.
- Scanning, data extraction and data analysis **– *Agilent High Resolution C Scanner*** (3 microns resolution), ***Feature Extraction v. 11.5.1.1 and*** **GeneSpring v.12**, respectively

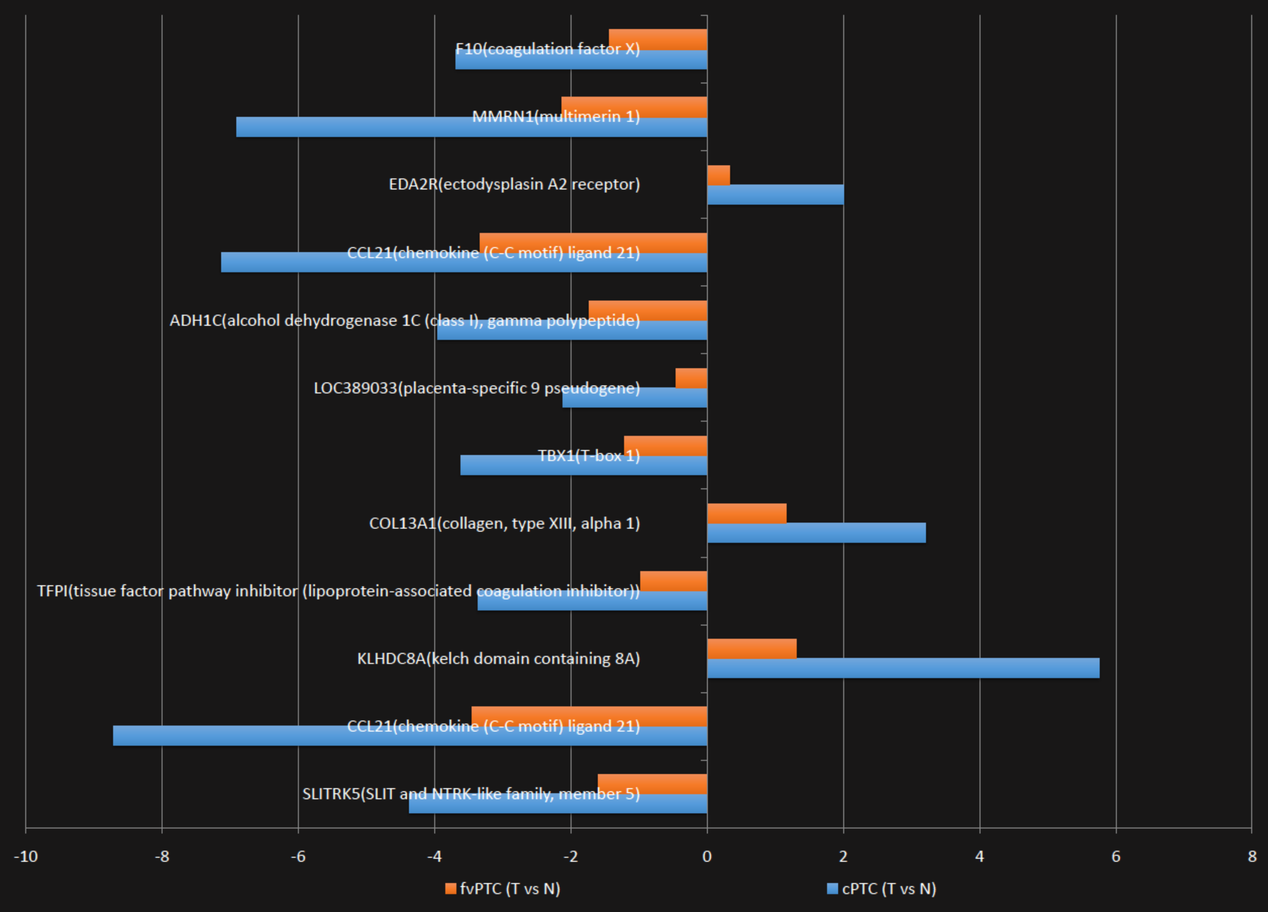
RESULTS

Comparative analysis of **tumoral vs normal tissue** samples revealed **down-regulation** of **25 genes and 2 lincRNA** (long intergenic non-protein coding RNA 1140 and BROAD Institute lincRNA (XLOC_005062)/ lincRNA [TCONS_00010536] (p value<0.05 and fold change ≥ 2 by ***t-test*** and ***Benjamini-Hochberg correction***) (Table 1)

Table 1. Gene expression analysis in tumoral vs normal tissues

Gene symbol	*Gene name*	*Log FC (T vs N)*
EPHA3	EPH receptor A3	-2,64202
RNF112	ring finger protein 112	-1,98909
TNNT3	troponin T type 3 (skeletal, fast)	-3,32808
HHIP	hedgehog interacting protein	-3,18701
NTN1	netrin 1	-3,04401
SLITRK5	SLIT and NTRK-like family, member 5	-2,98442
ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	-2,74412
CCL21	chemokine (C-C motif) ligand 21	-6,08054
RELN	Reelin	-3,21951
BMP5	bone morphogenetic protein 5	-2,12669
SYCP2	synaptonemal complex protein 2	-1,72320
DPT	dermatopontin	-2,66421
GLI1	GLI family zinc finger 1	-3,84289
TBX1	T-box 1	-3,84257
ADH1A	alcohol dehydrogenase 1A (class I), alpha polypeptide	-2,40841
GSTM5	glutathione S-transferase mu 5	-1,45572
ADH1C	alcohol dehydrogenase 1C (class I), gamma polypeptide	-3,36084
C11orf88	chromosome 11 open reading frame 88	-2,48056
MMRN1	multimerin 1	-2,84109
FXYD1	FXYD domain containing ion transport regulator 1	-2,06945
FMO1	flavin containing monooxygenase 1	-4,51870
F10	coagulation factor X	-1,72246
FAM180B	family with sequence similarity 180, member B	-1,24426
NPY5R	neuropeptide Y receptor Y5	-2,56094
PODN	Podocan	-3,10499
LINC01140	long intergenic non-protein coding RNA 1140	-1,45276
XLOC_005062	BROAD Institute lincRNA	-2,44586

Fig.1- Gene expression in tumoral tissues from 12 patients with differentiated thyroid cancer



Gene expression analysis in tumoral vs normal tissues from histological subtypes **cPTC and fvPTC** revealed **3 up-regulated genes** (*COL13A1, EDA2R, KLHDC8A*) and **8 down-regulated genes** (*SLITRK5, CCL21, TFPI, TBX1, LOC389033, ADH1C, MMRN1, F10*) in both cancer sub-types. The level of dis-regulation of gene expression is much higher in classic papillary thyroid carcinoma (Figure 1).

CONCLUSIONS

Gene expression is alterated in papillary thyroid carcinoma.
Our study identified 3 hyper-expressed genes and 8 genes with low expression in tumoral tissues compared to normal ones.
We found a higher dis-regulation of gene expression levels in classic papillary thyroid carcinoma then in follicular variant.
Further studies are undergoing for gene expression data validation by qPCR.

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