Differential gene expression between primary and secondary hyperparathyroidism

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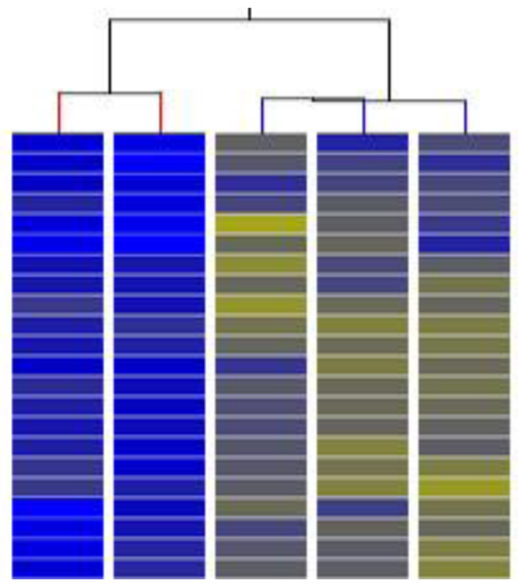
OBJECTIVES

The pathophysiology differs significantly between primary hyperparathyroidism (pHPT) and secondary hyperparathyroidism (sHPT). The underling mechanisms of the occurrence of sporadic pHPT remain largely unknown. In this study, we analyzed the differences in gene expression between pHPT and sHPT to explore potential functional alterations.

METHODS

Total RNA was extracted from tissues obtained during parathyroidectomy. Gene expression microarray were performed. Pathways involving differential gene expressions were analyzed using the Kyoto Encyclopedia of Genes and Genomes (KEGG) database for functional enrichment.



RESULTS

Parathyroid tissues were classified in an unsupervised manner into primary and secondary clusters. A total of 311 genes were upregulated in pHPT, whereas 1358 genes were upregulated in sHPT. The expression of VEGF-A was significantly upregulated in pHPT. The expression of transcription factor Twist was higher in sHPT.

UPREGULATION in pHPT

Pathway	Count	%	P value	Genes
Cell adhesion molecules (CAMs)	10	2.8	0.00091	NRCAM, ALCAM, SELL, PVRL3, HLA-A, NFASC, CLDN10, HLA-C, HLA-B, CD40, CD28
Allograft rejection	4	1.1	0.031	HLA-A, HLA-C, HLA-B, CD40, CD28
Chronic myeloid leukemia	5	1.4	0.056	E2F1, CDKN2A, NFKBIA, MECOM, SHC2
Nitrogen metabolism	3	0.8	0.072	CA4, CA2, CPS1
Autoimmune thyroid disease	4	1.1	0.074	HLA-A, HLA-C, HLA-B, CD40, CD28

UPREGULATION in sHPT

Pathway	Count	%	P value	Genes
Ribosome	30	2.7	2.1E-15	RPL17, RPL15, RPL35, RPS15A, RPS27L, RPL39, RPS2, RPS3, RPS29, RPL6, RPLP0, RPLP1, RPL10, RPL5, RPL11, RPL4, RSL24D1, RPL7A, RPL10A, RPL12, RPS24, RPL26, RPL28, RPS8, RPL29, RPS18, RPL22, RPS17, RPL21, RPS13
Intestinal immune network for IgA production	8	0.7	0.022	HLA-DQB1, CCL25, CD40LG, TNFRSF13B, IL15RA, HLA-DRB5, HLA-DPB1, ITGA4
Complement and coagulation cascades	9	0.8	0.046	C8B, MBL2, F12, C4B, TFPI, C1R, CFI, PROS1, PLG
Hematopoietic cell lineage	10	0.9	0.062	IL3, IL9R, IL2RA, DNTT, FLT3, CD2, HLA-DRB5, ITGB3, ITGA4, IL11RA
mTOR signaling pathway	7	0.6	0.081	EIF4B, RPS6KA1, ULK2, RPS6KB2, IGF1, IGF2, FIGF

CONCLUSION

Previous studies on hyperparathyroidism have focused on mutations in CASR, MEN1, RET, and HRPT2. Our study for the first time demonstrates that different pathophysiology led to differential gene profiling in hyperparathyroidism. It is particularly worth noting that parathyroid adenomas showed higher expression of cell adhesion molecules. On the contrary, secondary hyperparathyroidism exhibited upregulation of complement/coagulation cascades and mTOR signaling pathway.

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