Differential Regulation of Immune Related Genes between Right and Left Side Colorectal Cancer.

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Background

Biobank is an entity that collects, processes, stores and distributes biological samples and related data for basic, translational and clinical research. The aim of this study was to define differences immune related genes in tumor microenvironment between right and left side colorectal cancer (CRC) and explore their therapeutic implications. Paraffin tissues and related information of CRC in biobank were mainly used.

Methods

Gene expression profiling and clinical characteristics of patients with CRC were retrieved from The Cancer Genome Atlas data portal (n=525). The right-side CRC (RCC) and left-side CRC (LCC) have significantly different clinical and pathological features by clinical data analysis. Nine genes were selected by gene differential expression analysis. To further validate the findings, we applied immunohistochemical (IHC) staining of a CRC tissue microarray (TMA).
Furthermore, to reveal the prognostic value of differential genes on RCC and LCC patients, the survival analysis were performed. To study the function of the genes, GO and KEGG databases were used for analysis.

Results

PART-1: Table 1

We first analyzed the clinical and pathological information of 525 samples downloaded from the TCGA database that include 207 LCC and 318 RCC tissue samples.

Results

PART-1: Table 1

✧ We found that RCC and LCC were different in age, pathologic stage, mucus secretion and microsatellite stability. In RCC, the proportion of patients over 70 years old was higher than that of LCC. N-0 cases were significantly more frequent than in LCC. The proportion of mucus secretion and MSI in RCC were higher. All the differences were statistically significant, p<0.01. (Table 1)

Class		RCC(n=318)	LCC(n=207)	p
Age				
	≥70y	177	80	
	<70y	141	127	0.0001
Gender				
	male	164	109	
	female	154	98	0.8079
Pathologic stage				
	I	52	31	
	II	140	71	
	III	85	65	
	IV	34	37	0.1753
Pathology T stage				
	T1	5	4	
	T2	52	38	
	T3	215	147	
	T4	46	18	0.1517
Pathology N stage				
	N-0	202	110	
	Non N-0	116	97	0.0179
Pathology M stage				
	M-0	237	149	
	Non M-0	75	57	0.3533
Mucus secretion				
	yes	53	13	
	no	265	193	0.0005
Microsatellite stability				
	MSI	142	47	
	MSS	176	154	0.0001

Table 1 Comparison of pathological features between RCC and LCC

PART-2: Figure 1

✧ Gene differential expression analysis showed that the expression of 7 genes in RCC was higher than that in LCC, which were CCR5, CD209, CD8A, HCK, HLA-DPB1, HLA-DQA1, HLA-DRA, respectively. Meanwhile, the expression of 2 genes in LCC was higher than that in LCC, which were IL-34 and PROCR. The genes were verified by IHC staining. (Part of results are shown in Figure 2.)

Results

PART-3: Figure 2

✧ Furthermore, survival analysis shows that patients with LCC have a better prognosis than RCC. Among all the differentially expressed genes, we found that HLA-DQA1 was highly expressed in RCC, and HLA-DQA1high patients had a better survival in RCC. IL-34 was highly expressed in LCC, and IL-34 high patients had a better survival in LCC. Enrichment analysis of GO and KEGG indicated that these genes are mainly involved in immune response and MHC-Ⅱ-mediated antigen presentation.

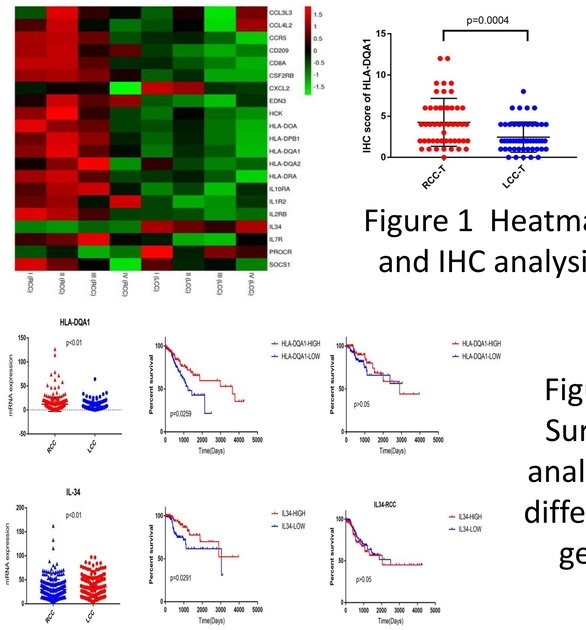

Figure 2 Survival analysis of differential genes

Figure 1 Heatmap and IHC analysis

Conclusions

In this study, we comprehensively compared differences in the immune related genes between right- and left-side CRC. And explored the differences in gene expression and function and their impact on survival. Overall, we hope that our depiction of the differential genes of RCC and LCC could lay a foundation for further research.

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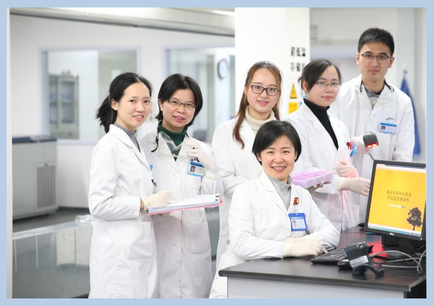

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