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Comprehensive analysis of distal-less homeobox family gene expression in colon cancer

Chen YC *et al*. Role of DLX in colon cancer

Abstract

BACKGROUND

The distal-less homeobox (DLX) gene family plays an important role in several tumors. However, the expression pattern, prognostic and diagnostic value, possible regulatory mechanisms, and the relationship between DLX gene family and immune infiltration in colon cancer have not been systematically reported.

AIM

To analyze the biological role of the DLX gene family in colon cancer in a comprehensive way.

METHODS

The colon cancer tissues and normal colon tissues were collected from the Cancer Genome Atlas and Gene Expression Omnibus databases. Wilcoxon rank sum test and *t*-test were used to assess DLX gene family expression between colon cancer tissues and unpaired normal colon tissues. cBioPortal was used to analyze DLX gene family variants. R software was used to analyze DLX gene expression in colon cancer and the relationship between DLX gene family expression and clinical features and correlation heat map. The survival package and Cox regression module were used to assess the prognostic value of the DLX gene family. The pROC package was used to analyze the diagnostic value of the DLX gene family. The R software was used to analyze the possible regulatory mechanisms of DLX gene family members and related genes. The GSVA package was used to analyze the relationship between the DLX gene family and immune infiltration. The ggplot2, and survminer package, and clusterProfiler package were used for visualization.

RESULTS

DLX 1/2/3/4/5 were significantly aberrantly expressed in colon cancer patients. The expression of DLX genes were associated with M stage, pathologic stage, primary

therapy outcome, residual tumor, lymphatic invasion, T stage, N stage, age, perineural invasion, and history of colon polyps. DLX5 were independently correlated with the prognosis of colon cancer in multivariate analysis. DLX1/2/3/4/5/6 were involved in the development and progression of colon cancer by participating in immune infiltration and pathways, including Hippo signaling pathway, Wnt signaling pathway, signaling pathways regulating pluripotency of stem cells, and staphylococcus aureus infection.

CONCLUSION

The results of this study suggest a possible role for the DLX gene family as potential diagnostic or prognostic biomarkers and therapeutic targets in colon cancer.

Key Words: Colon cancer; The Cancer Genome Atlas; Distal-less homeobox genes; Prognosis; Immune infiltration

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Core Tip: The Distal-less homeobox (DLX) gene family plays an important role in several tumors. However, the expression pattern, prognostic and diagnostic value, possible regulatory mechanisms, and the relationship between DLX gene family and immune infiltration in colon cancer have not been systematically reported. In this study, we aimed to investigate the expression level, clinical significance, and relationship between DLX genes and immune infiltration in colon cancer to establish an adequate scientific basis for clinical decision making and risk management. The DLX gene family holds promise as a potential diagnostic or prognostic biomarker and therapeutic target for colon cancer.

INTRODUCTION

Colon cancer is a widely known tumor whose incidence is on the rise. Approximately 10% of all cancer deaths are caused by colon cancer and related complications[1]. Colon adenocarcinoma (COAD) is the most common, accounting for 98% of colon cancer cases[2]. Colon cancer has a high recurrence rate after treatment, with 42% of patients recurring within 5 years and a median time from recurrence to death of 12 mo[3]. Unfortunately, about 20% of colon cancer patients are diagnosed with stage IV each year[4]. Therefore, exploring novel molecular markers is of great clinical significance to improve the diagnosis and treatment of colon cancer.

The distal-less homeobox (DLX) gene is a homolog of Drosophila Distal-less and consists of six members, including DLX1, DLX2, DLX3, DLX4, DLX5, and DLX6[5]. DLX1 can be used to identify prostate cancer for early diagnosis[6]. Overexpression of DLX2 was associated with poor prognosis in hepatocellular carcinoma (HCC)[7]. High expression of DLX2 was a poor prognostic marker for patients with glioblastoma multiforme[8]. DLX3 was a key regulator of the STAT3 signaling network that maintains skin homeostasis[9]. DLX4 can be used as a prognostic marker for HCC[10]. DLX5 was a potential diagnostic biomarker and therapeutic target for oral squamous cell carcinoma (OSCC)[11]. DLX6 promoted cell proliferation and survival in OSCC[12]. To our knowledge, no studies have systematically assessed the role of the DLX gene family in colon cancer using bioinformatics methods. In this study, we aimed to investigate the expression level, clinical significance, and relationship between DLX family and immune infiltration in colon cancer to establish an adequate scientific basis for clinical decision making and risk management.

MATERIALS AND METHODS

CBioPortal analysis

The cBio Cancer Genomics Portal (cBioPortal) (http://cbioportal.org) was applied to study mutations in DLX genes in colon cancer[13]. Queries for visualization and analysis were performed by entering: (1) Cancer type: COAD; (2) 2 selected studies: COAD (CaseCCC, PNAS 2015), colon cancer (CPTAC-2 Prospective, Cell 2019); (3) Molecular

profile: Mutations and copy number alterations (CNAs); (4) Selection of patients/case sets: All samples (139); and (5) Input genes: DLX1(ENSG00000144355), DLX2(ENSG00000115844), DLX3(ENSG00000064195), DLX4(ENSG00000108813), DLX5(ENSG00000105880), and DLX6(ENSG00000006377). After submission of queries, accessions were made including origin studies, mutation profiles, mutation number, overall survival (OS) status, OS (months), disease-free status, and disease-free period (months) tracks.

Dysregulation of DLX genes in colon cancer

Software was R (version 3.6.3) (statistical analysis and visualization)[14,15]. R package was mainly ggplot2 (version 3.3.3) (for visualization). UCSC XENA (https://xenabrowser.net/datapages/) RNAseq data were uniformly processed by the Toil process into TPM (transcripts per million reads) format for the Cancer Genome Atlas (TCGA) and GTEx[16]. Data for colon cancer were extracted from TCGA and corresponding normal tissue data were extracted from GTEx. RNAseq data were in TPM format and log2 transformed for expression comparisons between samples. The data filtering condition is to retain paired samples.

Correlation heat map

Correlation between every two genes of DLX was assessed using a Pearson's correlation coefficient. R package was mainly ggplot2 (version 3.3.3). The filter condition was to remove data from the normal/control groups (not every item has a normal/control group).

Association of DLX gene expression with clinical features of TCGA-colon cancer

R package was the basic R package[17]. Grouping was based on the median.

Survival analysis

The survminer package (version 0.4.9) was used for visualizing survival data, and the survival package (version 3.2-10) allowed statistical analysis of survival data. Subgroups included 0-50 and 50-100. The prognosis types were OS, progress free interval (PFS), and disease specific survival (DSS). Supplementary data was prognostic data from the reference[18]. The filter condition was to remove data from the normal/control groups (not every item has a normal/control group) and keep the data for clinical information.

Univariate and multivariate Cox regression analysis

R package was the survivor package (version 3.2-10). Statistical analysis was performed using the Cox regression module. Prognosis types were OS, PFS, and DSS, and included variables were DLX1, DLX2, DLX3, DLX4, DLX5, and DLX6. Supplementary data was prognostic data from the reference[18]. The filter condition was to remove data from the normal/control groups (not every item has a normal/control group) and keep the data for clinical information.

ROC curve analysis

There were two R packages used: The pROC package (for analysis) and ggplot2 package (version 3.3.3). Clinical Variables were tumor and normal. UCSC XENA (https://xenabrowser.net/datapages/) RNAseq data are uniformly processed by the Toil process into TPM format for TCGA and GTEx[16]. Data for colon cancer were extracted from TCGA and corresponding normal tissue data were extracted from GTEx. The RNAseq data were in TPM format and log2 transformed for expression comparison between samples. Data were not filtered. The horizontal coordinates were the false positive rate and the vertical coordinates were the true positive rate.

Correlation analysis for genes associated with DLX genes

The R package used was the stat package (version 3.6.3) (base package). The TCGA colon cancer project provided the RNAseq data in level 3 HTSeq-FPKM format. The

TPM format was converted to FPKM, and the log2 transformation was applied to the transformed data. The control/normal groups were removed from the results (not all projects had control/normal groups).

Functional enrichment analysis of genes associated with DLX genes

R packages were mainly ggplot2 package (version 3.3.3) and clusterProfiler package (version 3.14.3).

Correlation between the expression of DLX genes in colon cancer and immune cells

R package was GSVA package (version 1.34.0)[19]. For immuno-infiltration, the GSVA package has a built-in algorithm ssGSEA. Immune cells were activated dendritic cell (aDC), B cells, CD8 T cells, cytotoxic cells, DC, eosinophils, immature DC (iDC), macrophages, mast cells, neutrophils, natural killer (NK) CD56bright cells, NK CD56dim cells, NK cells, plasmacytoid DC (pDC), T cells, T helper (Th) cells, T central memory, T effector memory (Tem), T follicular helper (TFH), T gamma delta (Tgd), Th1 cells, Th17 cells, Th2 cells, and Treg[20]. The data filtering condition was to remove the control/normal group (not all projects had control/normal groups). Markers for 24 immune cells were obtained from the reference[21].

Validation of DLX gene expression

To further verify the accuracy of the TCGA database, we downloaded colon cancer samples from the Gene Expression Omnibus database for analysis. The 30 colon cancer tissues and 30 normal colon tissues contained in GSE74062 were used for DLX gene expression analysis.

Statistical analysis

All statistical analyses were performed using R (v.3.6.3). The Wilcoxon rank sum test, chi-square test, and Fisher exact test were used to analyze the relationship between

clinical characteristics and DLX genes. *P* values less than 0.05 were considered statistically significant.

RESULTS

DLX gene alterations and mRNA expression in colon cancer

The cBioPortal online tool was used to analyze the gene expression of DLX genes in colon cancer patients. Alterations in the DLX genes in colon cancer ranged from 0.7% to 3% (Figure 1). The mutation data, CNA data, and deep deletion from the 2 studies are depicted in Figure 2. The analysis of DLX gene expression was performed based on 41 colon cancer tumor tissue samples and 41 paired samples of normal colon tissues (Figure 3). The results showed that the expression level of DLX1 in colon cancer tumor samples was significantly lower than that of DLX1 in normal colon tissues (0.199 ± 0.026 *vs* 0.867 ± 0.031, $P < 0.001$), the expression level of DLX2 in colon cancer tumor samples was significantly lower than that of DLX2 in normal colon tissues (0.129 ± 0.020 *vs* 0.211 ± 0.011, $P = 0.0074$), the expression level of DLX3 in colon cancer tumor samples was significantly higher than that of DLX3 in normal colon tissues (0.593 ± 0.052 *vs* 0.171 ± 0.008, $P < 0.001$), the expression level of DLX4 in colon cancer tumor samples was significantly higher than that of DLX4 in normal colon tissues (0.635 ± 0.027 *vs* 0.229 ± 0.009, $P < 0.001$), the expression level of DLX5 in colon cancer tumor samples was significantly lower than that of DLX5 in normal colon tissues (0.416 ± 0.036 *vs* 0.463 ± 0.022, $P < 0.001$). However, there was no significant difference in DLX6 expression in colon cancer tumor samples compared to normal colon tissue (0.229 ± 0.014 *vs* 0.449 ± 0.037, $P = 0.554$). We examined the correlation between DLX genes using Pearson correlation analysis. As shown in Figure 4, there was no significant correlation between DLX1 and DLX3, DLX1 and DLX6, and there was a significant positive correlation between other DLX genes.

Relationship between DLX gene expression and clinical characteristics and prognosis of colon cancer patients

Clinical characteristics data and gene expression data for 478 colon cancer tumor samples were downloaded from the TCGA database (Supplementary Table 1). DLX2 expression was associated with M stage (P = 0.005), pathologic stage (P = 0.014), primary therapy outcome (P = 0.036), residual tumor (P = 0.002), and lymphatic invasion (P = 0.013) in colon cancer patients. DLX3 expression was associated with N stage (P < 0.001), M stage (P < 0.001), pathologic stage (P < 0.001), height (P = 0.045), and residual tumor (P < 0.001) in colon cancer patients. DLX5 expression was associated with T stage (P < 0.001), N stage (P < 0.001), M stage (P = 0.005), pathologic stage (P < 0.001), primary therapy outcome (P = 0.005), age (P < 0.001), perineural invasion (P = 0.023), lymphatic invasion (P < 0.001), and history of colon polyps (P = 0.009). However, the expression of DLX1, DLX4, and DLX6 did not significantly correlate with the clinical characteristics of colon cancer patients.

As shown in Figure 5, a low expression of DLX1 was associated with the PFS (P = 0.013) of colon cancer; a low expression of DLX2 was associated with the OS (P = 0.006), PFS (P = 0.003), and DSS (P = 0.007) of colon cancer; a high expression of DLX3 was associated with the OS (P = 0.010), PFS (P = 0.004), and DSS (P = 0.007) of colon cancer; a high expression of DLX4 was associated with the OS (P = 0.030), and PFS (P = 0.023) of colon cancer; a low expression of DLX5 was associated with the poor OS (P = 0.048), PFS (P = 0.002), and DSS (P = 0.007) of colon cancer. However, a high expression of DLX6 was not significantly associated with the prognosis of colon cancer.

As shown in Table 1, univariate cox regression analysis for OS showed that DLX2 (P = 0.007), DLX3 (P = 0.011), DLX4 (P = 0.031), and DLX5 (P = 0.049) were associated with OS in patients with colon cancer, and DLX1 (P = 0.014), DLX2 (P = 0.003), DLX3 (P = 0.004), DLX4 (P = 0.024), and DLX5 (P = 0.002) were associated with PFS in patients with colon cancer. DLX2 (P = 0.008), DLX3 (P = 0.008), and DLX5 (P = 0.009) were associated with DSS in patients with colon cancer. DLX5 was independently correlated with PFS (P = 0.012) and DSS (P = 0.035) of colon cancer in multivariate analysis.

As shown in Figure 6, it can be obtained that the variable DLX1 had some accuracy in diagnosing normal and tumor outcomes [area under curve (AUC) = 0.893, 95%

confidence interval (CI): 0.867-0.920], variable DLX2 had some accuracy in diagnosing normal and tumor outcomes (AUC = 0.731, 95%CI: 0.691-0.771), variable DLX3 had a lower accuracy in diagnosing normal and tumor outcomes (AUC = 0.561, 95%CI: 0.512-0.611), variable DLX4 had some accuracy in diagnosing normal and tumor outcomes (AUC = 0.834, 95%CI: 0.802-0.867), variable DLX5 had low accuracy in diagnosing normal and tumor outcomes (AUC = 0.590, 95%CI: 0.546-0.635), and variable DLX6 had poor accuracy in diagnosing normal and tumor outcomes (AUC = 0.486, 95%CI: 0.439-0.534).

The function of genes associated with DLX genes

The top 10 significantly associated genes for each DLX gene are shown in the single gene co-expression heat map (Figure 7). Genes significantly associated with DLX1 include DLX2, KLF14, CHRND, KCNN1, IGDCC3, ARHGAP36, NCAN, TFAP2B, CNPY1, and CACNG7. Genes significantly associated with DLX2 include DLX1, CNPY1, CHRND, NEUROD1, IGDCC3, TNFRSF19, KLF14, NELL2, HS3ST4, and SLC38A8. Genes significantly associated with DLX3 include NOTUM, NKD1, APCDD1, ADAMTSL2, MYH7B, PRR9, LRRC43, CAB39L, ABCC2, and DLX4. Genes significantly associated with DLX4 include DLX3, TTLL4, DNMT3B, CDK5R1, IGF2BP1, STK36, UNK, AMER3, PHF12, and WNT3. Genes significantly associated with DLX5 include DYNC1I1, DLX6, RASL11B, ID4, SP7, AMBN, KRT31, MYL3, VENTX, and ISM1. Genes significantly associated with DLX6 include DLX5, TRIM71, SH3GL2, SLC46A1, DYNC1I1, PGBD5, GAL, COCH, AXIN2, and CKB. The top 30 genes significantly associated with each DLX gene (147 in total) were analyzed for Gene Ontology and Kyoto Encyclopedia of Genes and Genomes enrichment (Supplementary Table 2). The top ten biological processes, including pattern specification process, regionalization, ossification, connective tissue development, cell fate commitment, hippocampus development, biomineral tissue development, biomineralization, skeletal system morphogenesis, and odontogenesis; the significantly related molecular functions including DNA-binding transcription activator activity, RNA polymerase II-specific,

fibroblast growth factor receptor binding, DNA-binding transcription activator activity, are shown in Figure 8 and Supplementary Table 3. The significantly related pathways, including Hippo signaling pathway, Wnt signaling pathway, signaling pathways regulating pluripotency of stem cells, and staphylococcus aureus infection, were shown in Figure 9 and Supplementary Table 3.

Correlation of DLX gene expression and immune cells in colon cancer

As shown in Figure 10, there was a correlation between DLX gene expression and immune cells in colon cancer. DLX1 gene expression was positively correlated with some tumor-infiltrating immune cells (TIICs), including aDC, cytotoxic cells, DC, eosinophils, iDC, macrophages, mast cells, neutrophils, NK CD56dim cells, NK cells, Tem, TFH, Tgd, Th1 cells, and TReg, and negatively correlated with Th17 cells. DLX2 gene expression was positively correlated with mast cells and TFH, and negatively correlated with pDC and Th17 cells. DLX3 gene expression was negatively correlated with some TIICs, including aDC, CD8 T cells, cytotoxic cells, DC, macrophages, neutrophils, T cells, Th cells, Th1 cells, Th2 cells, and TReg. DLX4 gene expression was positively correlated with NK cells, and negatively correlated with some TIICs, including cytotoxic cells, DC, macrophages, pDC, Th1 cells, and Th2 cells. DLX5 gene expression was positively correlated with some TIICs, including B cells, CD8 T cells, DC, iDC, macrophages, mast cells, neutrophils, NK cells, pDC, Tem, TFH, Tgd, and TReg, and negatively correlated with Th17 cells and Th2 cells. DLX6 gene expression was negatively correlated with some TIICs, including aDC, cytotoxic cells, DC, macrophages, neutrophils, NK CD56dim cells, T cells, Tem, and Th1 cells.

DLX genes were aberrantly expressed in colon cancer tissues

As shown in Figure 11, compared to normal colonic tissues, DLX1 was aberrantly expressed in colon cancer tissues (P = 7.6e-08), DLX2 was aberrantly expressed in colon cancer tissues (P = 5.7e-08), DLX4 was aberrantly expressed in colon cancer tissues (P = 0.00013), and DLX5 was aberrantly expressed in colon cancer tissues (P = 0.0084).

However, DLX3/6 was not significantly aberrantly expressed in colon cancer tissues. In conclusion, DLX1/2/4/5 were aberrantly expressed in colon cancer.

DISCUSSION

DLX1 was significantly upregulated in prostate cancer tissues and cells[22]. DLX2 was significantly upregulated in HCC tissues and cell lines[7,23]. DLX2 expression in gastric cancer was significantly correlated with tumor size, depth of infiltration, lymph node metastasis, and tumor-lymph node metastasis stage[24]. DLX4 was significantly upregulated in nasopharyngeal carcinoma (NPC) cell lines[25]. DLX4 expression was significantly elevated in HCC tissues and correlated significantly with tumor size, histopathological classification, and serum alpha-fetoprotein[10]. DLX5 was upregulated in OSCC tissues and cell lines and was significantly associated with advanced TNM staging, lymph node metastasis, poor cell differentiation, and tumor location[11]. DLX6 was significantly upregulated in oral cancer tissues and was associated with advanced tumor stage and poor prognosis[12]. In this study, DLX 1/2/3/4/5 were significantly aberrantly expressed in colon cancer patients. The expression of DLX gene family was associated with M stage, pathologic stage, primary therapy outcome, residual tumor, lymphatic invasion, T stage, N stage, age, perineural invasion, and history of colon polyps. In the multivariate analysis, DLX5 was independently related to PFS and OS of colon cancer. In diagnosing the outcome of normal and tumor tissues, DXL1/2/4 had some accuracy in diagnosing normal and tumor.

MiR-129-5p impeded the biological function of cancer cells by inhibiting DLX1 expression[26]. DLX1, a key target of FOXM1, promoted ovarian cancer aggressiveness by enhancing transforming growth factor (TGF)-β/SMAD4 signaling[27]. Circ_HIPK3 promoted HCC progression by mediating the miR-582-3p/DLX2 pathway[23]. In tumor cells, DLX2/3/4 can be involved in the control of fenretinide (4HPR)-mediated apoptosis[28]. DLX3 was down-regulated by miR-133[29]. The homology domain protein DLX4 promoted NPC progression through upregulation of YB-1[25]. DLX5 regulation of CCND1 affected the progression of OSCC[11]. DLX5 promoted osteosarcoma

progression through activation of NOTCH signaling pathway[30]. DLX6 regulated OSCC cell proliferation through the EGFR-CCND1 axis[12]. In this study, the DLX gene family was involved in the development and progression of colon cancer by participating in pathways, including breast cancer, gastric cancer, Hippo signaling pathway, Wnt signaling pathway, signaling pathways regulating pluripotency of stem cells, basal cell carcinoma, melanoma, and staphylococcus aureus infection. Dlx-2 is involved in TGF-β- and Wnt-induced inhibition of mitochondria by epithelial-mesenchymal transition, glycolytic conversion, and Snail activation[31]. The specific mechanisms by which the DLX gene family mediates the pathways involved in the development of colon cancer need to be further investigated.

Immune-related mechanisms play an important role in colon cancer, and immunotherapeutic strategies are considered a promising direction for the treatment of colon cancer[32]. Another important aspect of this study was that the expression of the DLX gene family correlated with different levels of immune infiltration. In this study, the expression DLX genes were negatively correlated with some TIICs, and positively correlated with some TIICs. The DLX gene family plays an important role in the recruitment and regulation of immune infiltrating cells in colon cancer.

The present study has several limitations. Firstly, colon cancer shows strong heterogeneity, and the mRNA expression levels in the TCGA database are the average mRNA expression levels for all cell types within the tumor. Single-cell sequencing is needed to further elucidate the role of DLX genes in colon cancer. Secondly, the study lacks validation by biological or molecular experiments.

CONCLUSION

DLX 1/2/3/4/5 were significantly aberrantly expressed in colon cancer patients. DLX 2/3/5 were associated with M stage, pathologic stage, primary therapy outcome, residual tumor, lymphatic invasion, T stage, N stage, age, perineural invasion, and history of colon polyps. DLX5 were independently correlated with the prognosis of colon cancer in multivariate analysis. DXL 1/2/4 had some accuracy in diagnosing

normal and tumor. The DLX gene family is involved in the development and progression of colon cancer by participating in immune infiltration and pathways, including Hippo signaling pathway, Wnt signaling pathway, signaling pathways regulating pluripotency of stem cells, and staphylococcus aureus infection. The results of this study suggested a role for DLX gene family as a potential diagnostic or prognostic biomarker and therapeutic target in colon cancer.

ARTICLE HIGHLIGHTS

Research background

The distal-less homeobox (DLX) gene family plays an important role in several tumors. However, the role of DLX gene family in colon cancer is not clear.

Research motivation

The aim of this study is to investigate the role of the DLX gene family in colon cancer and to establish a sound scientific basis for clinical decision making and risk management.

Research objectives

In this study, we aimed to analyze the biological role of the DLX gene family in colon cancer in a comprehensive way.

Research methods

The colon cancer tissues and normal colon tissues were collected from the Cancer Genome Atlas (TCGA) and Gene Expression Omnibus databases. We used Wilcoxon rank sum test and t-test to assess DLX gene family expression between colon cancer tissues and unpaired normal colon tissues, cBioPortal to analyze DLX gene family variants, R (version 3.6.3) to analyze DLX gene expression in colon cancer and the relationship between DLX gene family expression and clinical features and correlation heat map, the survival package [version 3.2-10] and the Cox regression module to assess

the prognostic value of the DLX gene family, the pROC package [version 1.17.0.1] to analyze the diagnostic value of the DLX gene family, the R (version 3.6.3) to analyze the possible regulatory mechanisms of DLX gene family members and related genes, the GSVA package [version 1.34.0] to analyze the relationship between the DLX gene family and immune infiltration, and the ggplot2 [version 3.3.3], and survminer package [version 0.4.9] and clusterProfiler package [version 3.14.3] for visualization.

Research results

DLX 1/2/3/4/5 expression was significantly abnormal in patients with colon cancer. DLX gene family expression in patients with colon cancer was significantly associated with clinical characteristics, including M stage, pathological stage, primary treatment outcome, residual tumor, lymphatic invasion, T stage, N stage, age, peripheral invasion, and history of colonic polyps. Results of the multivariate Cox analysis showed DLX5 to be an independent prognostic factor in patients with colon cancer. DLX1/2/3/4/5/6 mediated the development and progression of colon cancer through multiple pathways, including the Hippo signaling pathway, Wnt signaling pathway, and signaling pathways regulating pluripotency of stem cells. DLX1/2/3/4/5/6 are associated with immune infiltration.

Research conclusions

The DLX gene family may function as potential diagnostic or prognostic biomarkers and therapeutic targets for colon cancer.

Research perspectives

It is possible to use the DLX gene family as a diagnostic or prognostic biomarker and therapeutic target for colon cancer.

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