Characterization of immunogenic cell death-related genes predicting prognosis in colon adenocarcinoma

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Abstract

**Background:** Colon adenocarcinoma (COAD) is a gastrointestinal malignancy with a high mortality rate. Studies have confirmed the role of immunogenic cell death (ICD) in different cancer types. However, there is a lack of research on ICD-related genes (ICD-RGs) in COAD. This study aimed to examine the impact of ICD-RGs on COAD and their interaction with the immune microenvironment. **Methods:** Using data from The Cancer Genome Atlas and Gene Expression Omnibus databases, we identified 107 ICD-RGs in COAD. Using a one-way Cox regression analysis, we examined the relationship between these ICD-RGs and overall survival in COAD. **Results:** Following the regression analyses, we identified 14 overall survival-related genes. Furthermore, we examined the predictive impact of the ICD-RGs using the least absolute shrinkage and selection operator regression analysis and developed a nine-genes prognostic model. The Cancer Genome Atlas and Gene Expression Omnibus datasets were used for training and validation. Kaplan-Meier analysis was used to confirm that the high-risk group had a lower survival rate than the low-risk group. Finally, following a multifactorial analysis, we created a prognostic nomogram that integrated clinical data and risk scores. **Conclusions:** The nine-genes model exhibits robust stability and can provide valuable insights for guiding the development of tumor immunotherapy strategies and personalized drug selection for patients with COAD.

**Keywords:** colon adenocarcinoma; least absolute shrinkage and selection operator; prognosis; immunogenic cell death-related genes
Background

Colon adenocarcinoma (COAD) is a cancerous growth that starts in the glandular cells lining the colon, making it the most common type of colon tumor. COAD ranks third in prevalence among malignant tumors and has the second-highest cancer fatality rate worldwide [1, 2]. Globally, COAD-related deaths account for approximately 10% of all cancer deaths each year [3]. Although the diagnosis and treatment of COAD have evolved significantly in recent years, its incidence is still on the rise [4]. Currently, radical surgery is the predominant treatment for early-stage COAD; however, most patients are diagnosed at the late stage. The advances in medical technology, surgery, and targeted therapies have led to a significant improvement in the five-year postoperative survival rate of patients with COAD, but treatment failure due to recurrence or metastasis remains a clinical problem [5].

The poor treatment outcomes suggest the need for more in-depth research into the mechanisms of tumor progression to identify promising new therapeutic targets and reliable prognostic biological indicators to provide precise individualized treatment for each patient and improve overall outcomes.

Immunogenic cell death (ICD) is a type of controlled cell death in response to stress and triggers of the immune system’s response to antigens from dying cells. Research has indicated that cellular antigens such as those found in infected cancer cells can trigger a strong immune response from cytotoxic T lymphocytes, resulting in the development of immune memory, highlighting the significance of ICD for boosting the immune system [6].

Understanding the mechanisms underlying ICD induction by tumor cells can reveal new strategies for stimulating ICD in cancer cells, disrupting the inhibitory tumor microenvironment, and restoring antitumor effects. However, only a few studies have investigated the role of ICD in COAD. This study aimed to clarify the involvement of ICD in COAD and discover novel prognostic biomarkers and therapeutic targets.

Methods

Data download and ICD-related gene acquisition

The RNA-seq transcriptomics and clinical information for 453 patients with COAD and 41 patients without tumors were acquired from the Cancer Genome Atlas (TCGA) database. Furthermore, we also obtained two separate datasets, GSE39582 (n = 585) and GSE87211 (n = 243), from the Gene Expression Omnibus (GEO) database (http://www.ncbi.nlm.nih.gov/geo/), which included gene expression data and clinical information pertaining specifically to COAD.

TCGA-COAD was used as the training set, and GSE39582 and GSE87211 were used as external validation sets. To identify relevant genes associated with ICD, we manually curated a list of 107 ICD-related genes (ICD-RGs) based on existing literature [7]. The clinical information is detailed in Table 1.

Discovery of ICD-RGs linked to overall survival (OS)

Genes linked to OS in the TCGA-COAD cohort (n = 453, P < 0.1) were identified using one-way COX regression.

Model construction and validation for COAD patients

Least absolute shrinkage and selection operator (LASSO) regression was performed on the training dataset using the ‘glmnet’ R package to determine the most significant ICD-RGs and their corresponding correlation coefficients. Consequently, nine ICD-RGs were obtained. Based on the expression of these ICD-RGs, we assessed each patient’s risk using the following equation:

Table 1 Clinicopathological parameters of COAD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall (n = 453)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>67.03 (13.05)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>69.00 (58, 77)</td>
</tr>
<tr>
<td>CEA (SD)</td>
<td>37.77 (199.22)</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>3.00 (1.70, 7.51)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>212 (46.8)</td>
</tr>
<tr>
<td>Male</td>
<td>239 (52.8)</td>
</tr>
<tr>
<td>NA</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>American indian or alaska native</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Asian</td>
<td>11 (2.4)</td>
</tr>
<tr>
<td>Black or african american</td>
<td>59 (13)</td>
</tr>
<tr>
<td>Not reported</td>
<td>171 (37.7)</td>
</tr>
<tr>
<td>White</td>
<td>209 (46.1)</td>
</tr>
<tr>
<td>NA</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>LVI</td>
<td>247 (54.5)</td>
</tr>
<tr>
<td>NO</td>
<td>163 (36)</td>
</tr>
<tr>
<td>YES</td>
<td>43 (9.5)</td>
</tr>
<tr>
<td>Tumor stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>75 (16.6)</td>
</tr>
<tr>
<td>II</td>
<td>176 (38.9)</td>
</tr>
<tr>
<td>III</td>
<td>126 (27.8)</td>
</tr>
<tr>
<td>IV</td>
<td>63 (13.9)</td>
</tr>
<tr>
<td>Not reported</td>
<td>13 (2.9)</td>
</tr>
<tr>
<td>OS status</td>
<td></td>
</tr>
<tr>
<td>Alive</td>
<td>336 (74.2)</td>
</tr>
<tr>
<td>Dead</td>
<td>94 (20.8)</td>
</tr>
<tr>
<td>Missing</td>
<td>23 (5.1)</td>
</tr>
</tbody>
</table>

COAD, colon adenocarcinoma; SD, standard deviation; IQR, interquartile range; OS, overall survival; CEA, carcinoembryonic antigen; LVI, lymphovascular invasion.
Risk score = (0.2549 × IFNE expression) + (0.1897 × HSPA1A expression) + (0.3180 × VAMP1 expression) + (0.1308 × LTB4R expression) + (−0.0595 × IL17RB expression) + (−0.0335 × CXCL1 expression) + (−0.0656 × ERAPI expression) + (−0.1051 × CTLA4 expression) + (−0.0053 × IFNGR1 expression).

Based on the training cohort’s median risk score, Kaplan-Meier survival curves were plotted for high-risk and low-risk patients. To confirm the accuracy of the model’s predictions, we used GSE39582 (n = 585) and GSE87211 (n = 243) as separate validation groups. The validation sets helped calculate individual risk scores using a consistent formula, and the performance of the risk score model was assessed by examining the OS using Kaplan-Meier survival curves.

**Prognostic line chart construction**

To assess the predictive accuracy of the ICD-RGs in patients with COAD, we performed univariate and multivariate Cox regression analyses. Using the ‘rms’ R package, we created line plots for columns to forecast the survival rate for patients at 3, 5, and 10 years. The predictor variables incorporated in the analysis were sex, age, tumor stage, lymphovascular infiltration, and risk score.

**Detection of differentially expressed genes (DEGs)**

DESeq2 was used to detect DEGs in the high- and low-risk groups. DEGs were defined as \( \log_{2}\text{FC} \geq 1, P < 0.05 \).

**Functional enrichment analysis**

The functional consequences of the identified genes were analyzed using Gene Ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. These analyses were performed using the “ClusterProfiler” R package. Furthermore, we used Gene Set Enrichment Analysis (GSEA) to investigate the enrichment of KEGG pathways in the high- and low-risk groups.

**Linkage of risk modeling to tumor microenvironment**

Using the R package ‘IOBR’, we analyzed the immune microenvironment disparities between low-risk and high-risk groups.

**Immune checkpoints and cancer-infiltrating cells**

To examine the relationship between immune status and the risk model, we analyzed variations in immune-infiltrating cells among the high- and low-risk groups. To this end, two techniques were used: single-sample GSEA and CIBERSORT.

In addition, 79 immune checkpoint genes were analyzed in high-risk and low-risk cohorts. The regulation of immune responses is significantly influenced by immune checkpoints, and changes in their levels have been linked to the advancement of tumors and the effectiveness of immunotherapy.

**Drug forecasting analysis**

To explore the effectiveness of our risk model, we used two openly accessible cell line databases, Cancer Cell Line Encyclopedia (CCLE) and Genomics of Drug Sensitivity in Cancer (GDSC). Based on gene expression profiles, we categorized the cells into high- and low-risk groups using our risk model. Subsequently, we compared drug sensitivity between the two groups.

**Statistical analysis**

R (4.3.1) software was used for all analyses, and \( P \) values < 0.05 were considered significant (\( P < 0.05, ^{**} P < 0.01, ^{***} P < 0.001 \)).

**Results**

ICD-RGs that have important predictive significance in COAD

Figure 1 illustrates the study workflow for the analysis of the gene profiles associated with ICD. Clinical data and survival information from 453 patients were collected from the TCGA dataset (Table 1). Through a comprehensive literature review, 107 ICD-RGs were identified.

Next, we performed a one-way Cox regression analysis to assess the effects of these ICD-RGs on the outcomes in patients with COAD. We identified 14 ICD-RGs that had a notable impact (\( P < 0.1 \)) on patient outcomes (Figure 2B, 2C). Subsequently, using LASSO Cox analysis, we further narrowed down the selection to nine genes with significant prognostic values. These genes include IFNE, HSPA1A, VAMP1, CTLA4, LTB4R, ERAPI, CXCL1, IL17RB, and IFNGR1. While CTLA4, ERAPI, CXCL1, IL17RB, and IFNGR1 were associated with favorable prognosis, IFNE, HSPA1A, VAMP1, and LTB4R were associated with unfavorable prognosis (Figure 2A).

**Modeling and validation of ICD-RGs**

We tested the reliability and applicability of our model using TCGA-COAD as the internal training dataset and GSE39582 and GSE87211 as external validation datasets.

In the training set, higher risk scores were associated with lower OS and increased mortality rates. To explore prognostic variations, we categorized the patients into high- and low-risk groups using the median risk score.

Kaplan-Meier survival curves were plotted to illustrate the differences in OS between the high- and low-risk categories after three, five, and ten years. The high-risk group had notably lower OS rates than the low-risk group, suggesting a poorer prognosis (Figure 3).

![Figure 1 Study flow chart. COAD, colon adenocarcinoma; TCGA, The Cancer Genome Atlas; ICD-RGs, immunogenic cell death-related genes; LASSO, least absolute shrinkage and selection operator.](https://doi.org/10.53388/MDM202407023)
Figure 2 One-way Cox and Lasso analysis were used in the training set to identify ICD-related genes in COAD patients. (A) Forest plots were generated to illustrate the results of one-way Cox and Lasso regression analyses for nine genes. (B & C) Lasso regression results for 14 genes from one-way Cox regression analysis. COAD, colon adenocarcinoma; ICD, immunogenic cell death; LASSO, least absolute shrinkage and selection operator; HR, hazard ratio.

Figure 3 KM curves and heatmaps are used to show the prognostic values of the nine ICD-RG models in the training and validation sets. (A–C) KM curves at 3, 5, and 10 years for patients in the TCGA-COAD training set. (D–F) KM curves at 3, 5, and 10 years for patients in the GSE39582 validation set. (G–I) KM curves at 3, 5, and 10 years for patients in the GSE87211 validation set. (J) Heatmap representing the expression levels of the nine identified ICD-RGs in the training set based on the risk scores. ICD-RGs, immunogenic cell death-related genes; KM, Kaplan-Meier; COAD, colon adenocarcinoma; TCGA, The Cancer Genome Atlas; HR, hazard ratio.
Developing a predictive nomogram based on clinical features

To validate the clinical applicability and reliability of the prognostic aspects of ICD-RGs, we analyzed the risk scores of patients with COAD in relation to clinical indicators. Multifactorial Cox analysis was used to investigate the relationship between risk scores and clinical variables. Notably, multifactorial Cox analysis clearly demonstrated that both the risk score and tumor stage were significant factors affecting patient prognosis (Figure 4).

After analyzing the data, we combined the risk assessments with medical markers to create a detailed bar graph that enabled quantitative prognostic prediction and clinical decision-making. Using this method, a nomogram was created to forecast the likelihood of survival of patients with COAD at 3, 5, and 10 years. The receiver operating characteristic values of the nomograms were determined to be 0.81, 0.747, and 0.726 at 3, 5, and 10 (Figure 4). Collectively, these findings highlight the effectiveness of the nomograms in predicting patient prognosis.

Figure 4 Predictive risk models for the 9 ICD-RGs in the COAD training set were assessed using multifactorial Cox analyses, time-dependent receiver operating characteristic, and clinical prognostic column line graphs. (A) Multifactorial Cox analyses illustrating the association between model risk scores and clinical characteristics. (B) Time-dependent receiver operating characteristic plots at 3, 5, and 10 years for the column line graphs. (C) Clinical prognostic column line graphs depicting patient outcomes at 3, 5, and 10 years. ICD-RGs, immunogenic cell death-related genes; COAD, colon adenocarcinoma; AUC, area under curve; LVI, lymphovascular invasion; AIC, Akaike information criterion.
Functional enrichment analysis
Using Gene Ontology and KEGG analyses, we evaluated the functional consequences of the identified genes, such as biological processes, cellular components, and molecular functions.

Biological processes showed an enrichment of DEGs involved in the regulation of chemical synaptic transmission, trans-synaptic signaling, postsynaptic membrane potential, quadruple SLU4/5/6 snRNP formation, and mRNA reverse splicing through the spliceosome.

Under cellular components, DEGs associated with structures, such as synaptic membranes, presynaptic membranes, postsynaptic membranes, neuronal projection endpoints, and neuronal cell bodies, were enriched.

DEGs associated with molecular functions, including hormone activity, passive transmembrane transporter activity, channel activity, receptor-ligand activity, and G protein-coupled peptide receptor activity, were enriched.

Additionally, KEGG pathway analysis revealed DEGs associated with interactions between neuroactive ligands and receptors, calcium signaling pathways, adrenergic signaling in heart muscle cells, and PPAR signaling pathways.

Furthermore, using GSEA, we pinpointed distinct KEGG pathways that were significantly enriched in the high-risk cohort compared to the low-risk cohort. These included pathways associated with neuroactive ligand-receptor interactions, calcium signaling, peroxisomal signaling, oxidative phosphorylation, MAPK signaling, STAT3 signaling, and PI3K/AKT signaling (Figure 5).

Immune infiltration analysis for risk modeling
We used CIBERSORT analysis to compare the tumor microenvironment in high-risk vs. low-risk groups. While the low-risk group had higher infiltration of activated memory CD4+ T cells, the high-risk group had higher infiltration of regulatory T cells (Tregs) (Figure 6). Nevertheless, no notable statistical variances were found in B cells, neutrophils, monocytes, or macrophages.

CD4+ T cells are essential for an anti-tumor immune response, as they trigger the activation of CD8+ T cells, which then transform into cytotoxic T lymphocytes through various pathways. Even in the absence of CD8+ T cells, CD4+ T lymphocytes can mediate anti-tumor effects via IFN-γ-associated pathways, indicating their crucial and significant role in protecting against tumors. Memory CD4+ T cells, which persist long after pathogen clearance, contribute to rapid and efficient immune responses upon reinfection.

Tregs have been implicated in impairing immune surveillance against cancer and suppressing the host antitumor immune response, thereby promoting tumor progression across various cancer types. Consistent with their functions, we saw an increased infiltration of Tregs in the high-risk group and of activated CD4+ memory T cells in the low-risk group.

Owing to the importance of immune checkpoint molecules in tumor immunotherapy, we further investigated the relationship between immune checkpoint genes and risk scores, as illustrated in Figure 6. The examination showed a direct relationship between risk assessment and specific genes such as ADORA2A and BTN2A1.

Predictive drug analysis for risk modeling
To investigate the potential treatment options for high-risk patients with COAD, we utilized the CCLE and GDSC databases. The cells were categorized into high- and low-risk categories based on their risk scores, and drug sensitivities were predicted for each category. Dasatinib and bendamustine had lower IC50 values in high-risk patients than in low-risk patients (Figure 7). These findings imply that high-risk individuals may exhibit a more robust reaction to these medications, suggesting their potential as viable therapeutic choices for a better prognosis.

Figure 5 Functional enrichment analysis of nine ICD-RGs models in high and low risk groups based on the COAD training set. (A) DEGs associated with the biological characteristics of patients in the high-risk and low-risk groups. (B) GSEA results. (C) Gene Ontology analysis. (D) KEGG pathway analysis. ICD-RGs, immunogenic cell death-related genes; COAD, colon adenocarcinoma; DEGs, Differentially Expressed Genes; GSEA, Gene Set Enrichment Analysis; KEGG, Kyoto Encyclopedia of Genes and Genomes; BP, biological process; CC, cell composition; MF, molecular function.
Figure 6 Immune cell infiltration in different risk groups in the training set. (A) The CIBERSORT algorithm was used to assess the differences in immune cell infiltration between the high-risk and low-risk groups. Statistical significance is represented by P-values with * indicating $P < 0.05$, ** indicating $P < 0.01$, *** indicating $P < 0.001$, and "ns" indicating not significant. (B & C) Pearson correlation analysis depicting the relationship between risk scores and immune checkpoint genes.

Figure 7 Training focus sensitivity prediction of dasatinib and bendamustine in high and low risk populations. (A) Dasatinib; (B) Bendamustine.
COAD, the most common cancer of the digestive system, is associated with high rates of illness and death. The 5-year survival rate in patients with distant metastases is only 11% [8].

In recent years, the treatment approaches for COAD have extended beyond conventional radiotherapy. Immunotherapy, particularly with immune checkpoint inhibitors, has emerged as a breakthrough therapy for improving the prognosis of patients with advanced COAD, highlighting the effectiveness of harnessing the patient’s immune system to suppress tumor progression. Consequently, there is a need for further research on strategies aimed at modulating the immune microenvironment of tumors and developing innovative approaches for antitumor immunotherapy.

The primary objective of this study was to develop a predictive model for COAD. Through an extensive literature review, we identified 107 ICD-RGs. Subsequently, using univariate Cox and LASSO analyses of the training set, we derived a subset of nine prognostically relevant ICD-RGs. Following the analysis of these genes, risk scores were derived. Based on the risk scores, we grouped patients into high- and low-risk categories.

The low-risk group exhibited better prognoses and presented an activated immune microenvironment. To further validate the prognostic significance of these ICD-RGs, we included two GEO datasets and performed Kaplan-Meier survival analyses. Consistently, the low-risk group showed significantly better survival outcomes compared to the high-risk group at 3, 5, and 10 years in both the training and validation sets.

Among the identified ICD-RGs, IFNE modulated the expression of genes involved in cell cycle regulation, such as p21, which inhibits cell proliferation [9]. LTBR, which includes BLT1 and BLT2, is involved in a range of functions, including leukocyte movement, wound healing, and skin barrier maintenance [10]. The presence of BLT1 in CD8+ T cells has been shown to affect the spread of tumors and control the movement of cytotoxic T lymphocytes and the body’s ability to fight tumors [11, 12]. Elevated CTLA4 levels in monocytes have been linked to negative outcomes and immunosuppression in liver cancer [13]. Reduced ERAP1 levels could potentially be linked to the advancement of colorectal cancer and negative outcomes by affecting the infiltration of immune cells and the ability of CD8+ T cells to kill tumors [14]. IL17RB, CXCL1, and IFNGR1 have also been implicated in tumor progression based on previous literature [15-17].

These findings demonstrated the potential clinical relevance of the identified ICD-RGs and their role in tumor progression and immune responses in COAD.

Tumor progression is intricately linked to the immune microenvironment, particularly the immune cell component, which has significant implications for the development of therapeutic strategies and preventive measures. In this study, we found higher infiltration of Tregs in the high-risk group, a specific type of CD4+ T cells, compared to the low-risk group. The involvement of Tregs in cancer development is debatable, as they are often linked to an unfavorable outlook [18]. However, in another study on endometrial cancer, a higher level of Treg infiltration was seen in the low-risk group, which is inconsistent with our findings [19]. Interestingly, in certain types of tumors, such as head and neck melanoma, higher Treg counts are associated with a better prognosis [20, 21]. This discrepancy may be due to a variety of functional phenotypes of immunosuppressed Tregs that can exert antitumor resistance under certain conditions [22]. On the other hand, we saw higher levels of activated memory CD4+ T cell infiltration in the low-risk group than in the high-risk group, consistent with the findings reported by Liu et al. [23, 24].

Beyond adjuvant strategies, chemotherapy is an effective treatment option for COAD; however, cases of relapse after treatment are still seen. Recent studies have demonstrated the safety and efficacy of immune checkpoint inhibitors in COAD patients, suggesting their potential as effective adjuvants in this context [25].

Given the positive association between risk scores and ADORA2A and BNT2A1, targeting these genes may hold promise for patients with COAD. We performed a correlation analysis between these two immune checkpoints and ICD-RGs and found that ADORA2A was most strongly correlated with IL10RA and that BNT2A1 was most strongly correlated with NOD1. ADORA2A acts as an adenosine receptor and immune checkpoint protein that prevents T cells from inappropriate activation and is an immunooxology target. Anti-BNT2A1 monoclonal antibody regulates Vγ9Vδ2 T cell (the predominant γδ T cells in peripheral blood)-mediated killing of cancer cells by inhibiting the binding of BNT2A1 to Vγ9Vδ2TCR [26]. This demonstrates the potential of BNT2A1 as a therapeutic target and adds to the emerging pathway of dystrophin family cooperation in T-cell activation [26].

We also utilized the GDSC and CCLE databases to identify potentially effective drugs for the high-risk groups identified using our model. Dasatinib and bendamustine have demonstrated benefits in high-risk patients. Dasatinib is a tyrosine kinase inhibitor taken by mouth that blocks multiple kinases such as BCR-ABL, SRC family kinases, c-KIT, EPH receptor kinase, and PDGFRB receptor. It has shown synergistic effects with curcumin and oxiplatin in preclinical studies [27, 28]. Additionally, when combined with oxaliplatin, dasatinib was found to reduce microvesSEL density, indicating clinically relevant anti-angiogenic effects [28]. These results indicate that dasatinib could be beneficial for high-risk patients with COAD, especially when paired with other treatments.

Our study has some limitations. First, the TCGA database, although a valuable resource, has limitations, such as providing limited information on clinical characteristics and lacking certain important clinical parameters that could impact patient outcomes. Therefore, our analysis may not fully capture the complexity of the disease. Second, retrospective studies, including those based on TCGA data, are inherently susceptible to selection bias, which may affect the generalizability of our findings to broader patient populations. Prospective studies with larger cohorts and more diverse patient demographics would be beneficial for further validation.

Third, the TCGA data as a training set and the GEO data as a validation set are part of the cross-platform analysis. However, as observed from the high- and low-risk scores, although the platforms are different, they can still suggest prognostic risk stably, which indicates that the genes and models selected for this methodology have the potential to be used across platforms. At present, this study also lacks the exploration to find a uniform threshold between different platforms, which is also a limitation of this study and one of our follow-up efforts. Finally, although we discovered predictive genes in our COAD risk model, it is essential to confirm their accuracy through the use of experimental methods such as quantitative RT-PCR and protein blotting, which would strengthen the reliability and accuracy of our findings. Recognizing these constraints is crucial when analyzing the outcomes of our research, underscoring the necessity for additional investigation and confirmation to strengthen the reliability of our conclusions.

Conclusion

In summary, our study focused on identifying prognostically relevant ICD-RGs and developing a nine-gene risk model for COAD. We thoroughly evaluated the predictive performance of this risk model and found it to be stable in predicting patient prognosis. Additionally, we screened potential therapeutic agents and immunosuppressive targets based on our findings. We believe our findings will help enhance our understanding of the molecular processes involved in the advancement of COAD and offer valuable perspectives on possible treatment approaches and immune system adjustments. The identification of prognostically relevant ICD-RGs and the development of risk models have the potential to enhance personalized treatment approaches and improve patient outcomes in COAD.

References