COMPUTATIONAL INTELLIGENCE METHODS FOR PREDICTING TREATMENT OUTCOMES IN ULCERATIVE COLITIS

[1]MEHMET KUTALMIS TOPKARAOGLU, [2]ISMAIL CANTURK

[1]Research Assistant, Yildiz Technical University, Istanbul/Türkiye
[2]Associated Professor,Yildiz Technical University, Istanbul/Türkiye
E-mail: [1]kutalmis.topkaraoglu@yildiz.edu.tr, [2]icanturk@yildiz.edu.tr

Abstract - Ulcerative colitis (UC) is a chronic inflammatory bowel disease with variable responses to infliximab therapy. This study aimed to predict treatment outcomes using transcriptomic data and machine learning. Two microarray datasets (GSE12251, GSE14580) and one RNA-seq dataset (E-MTAB-7604) were analyzed after preprocessing, normalization, and feature selection. ReliefF and SelectFromModel methods were applied, followed by classification with algorithms including LightGBM, Extra Trees, and KNN. On the combined microarray data, ReliefF + LightGBM and SFM + Extra Trees achieved the best performance (F1-Score = 0.74). In contrast, the RNA-seq dataset yielded lower F1-Score, with SFM + KNN reaching F1-Score = 0.55. These results suggest that gene expression-based signatures have potential for guiding infliximab therapy decisions in UC, though performance varies across data types and validation cohorts.

Keywords - Computational Intelligence, Ulcerative colitis, Machine learning, Bioinformatics, Feature selection.

I. INTRODUCTION

Ulcerative colitis (UC) is a chronic IBD characterized by continuous inflammation of the colon (often starting at the rectum) leading to symptoms like bloody diarrhea and abdominal pain[1]. There is no cure for UC; treatment aims to induce and maintain remission (e.g. with 5-aminosalicylates, steroids, immunosuppressants), and biologics (anti-TNF agents like infliximab) are used for moderate-to-severe disease when other therapies fail[2]. However, response to infliximab/anti-TNF therapy is highly variable. Estimates show that roughly 18–50% of treated UC patients have no clinical improvement and 50–90% fail to reach remission[3, 4]. Indeed, about one-third of IBD patients do not respond to anti-TNF drugs [5]. Many factors influence this variability, including patient demographics and disease characteristics such as age, sex, weight, smoking status, disease location/severity [6]. These challenges underscore the need for precision-medicine tools to predict which UC patients will benefit from infliximab. Several recent studies have analyzed mucosal gene expression to predict response to biologics. For example, Feng et al. (2021) used pre-treatment colon biopsy microarrays from UC patients (GEO datasets) to identify a signature of 28 downregulated and 2 upregulated genes that distinguish infliximab non-responders. Their ML model (random forest + neural network) achieved an AUC of 0.93 in training and 0.81 on an independent validation cohort[7]. Penrose et al. (2021) used network analysis on an UC expression data and found ~20 resistant genes enriched in patients who failed infliximab or vedolizumab; four of these had strong predictive power for non-response[8]. More broadly, meta-analyses of multiple datasets have identified overlapping biomarkers: for instance, five genes (SELE, AQP9, FPR2, TREM1, HCAR3) were consistently differentially expressed in UC biopsies of future infliximab non-responders [9]. These transcriptomic profiling studies demonstrate that baseline mucosal RNA patterns can form predictive signatures of drug response in UC. Machine-learning (ML) methods are increasingly applied to IBD data for predictive modelling. ML have been used to integrate complex clinical and molecular data. For example, random forests trained on clinical/trial data have successfully predicted response to biologics UC[10].

II. MATERIAL AND METHODS

The microarray datasets GSE12251 and GSE14580 were merged and used as a combined dataset for model training and evaluation using leave-one-out cross-validation (LOOCV), allowing maximum utilization of limited samples. Additionally, the RNA-seq dataset E-MTAB-7604 was included in model developments. In all datasets, response labels were assigned based on clinical assessment of infliximab treatment efficacy (response vs. no response). The distribution of response classes is provided in Table 1.

Dataset	Responders (Yes)	Non-responders (No)
GSE12251+14580	20	27
E-MTAB-7604	4	7

Table 1

Differential expression analysis (|log2FC| > 1, adj. $FDR <$ 0.05) was performed on merged GSE12251 and GSE14580 dataset and yielding 94 genes. Expression values were already log-transformed and standardized using z-score normalization. To minimize technical batch effects across datasets, the pyCombat algorithm was applied.

To optimize model performance, hyper parameter tuning was performed using **Grid Search CV** with least respond class-fold cross-validation on the datasets. This approach systematically evaluated combinations of key hyper parameters for each algorithm (e.g., number of estimators, learning rate, max depth) to identify configurations that maximized validation accuracy. The best parameters obtained from Grid Search CV were then used in the final evaluations. The following classifiers were evaluated: Decision Tree, Random Forest, XG Boost, K-Nearest Neighbors (KNN), Extra Trees, Light GBM, Cat Boost, Gradient Boosting from sk-learn python library. Select K Best was used to select the top 30 features with the highest statistical relevance. Additional feature selection methods including Lasso, Elastic Net CV, and wrapper-based approaches were tested, but these showed suboptimal results in external validation.

III. RESULTS AND DISCUSSION

Dataset	Method	Model	F1-Score
GSE12251 + GSE14580	Relief F (Top30)	LGBM	0.74
	SFM	Extra Tree	0.74
EMTAB	Relief F (Top30)	KNN	0.36
	SFM	KNN	0.55

Table 2

Model performance across datasets varies depending on the feature selection method and classification algorithm. On the combined GSE12251 & GSE14580 dataset, both ReliefF (Top 30 genes) with LightGBM and SelectFromModel (SFM) with Extra Trees achieved the highest F1 score of 0.74.

In contrast, performance on the RNA-seq-based EMTAB dataset was more limited. Using ReliefF (Top 30 genes) with KNN yielded a relatively low F1 score of 0.36, while SFM with KNN improved the performance to 0.55.

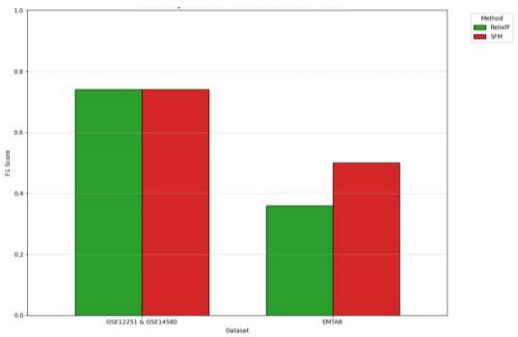


Figure 1: F1 Scores by Dataset and Feature Selection Method

IV. CONCLUSION

s study demonstrates that transcriptomic profiles combined with machine learning can help predict infliximab treatment outcomes in ulcerative colitis patients. Feature selection methods such as ReliefF and SelectFromModel, when coupled with classifiers like LightGBM and Extra Trees, achieved good predictive performance on microarray datasets, while RNA-seq data yielded more modest results. These findings highlight both the promise and challenges of developing robust predictive models across heterogeneous data sources. Future work should focus on integrating larger multi-omics cohorts and clinical variables to improve generalizability and support precision medicine strategies in inflammatory bowel disease.

ACKNOWLEDGMENTS

This work has been supported by Yildiz Technical University Scientific Research Projects Coordination Unit under project number FYL-2025-6738.

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