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USING MACHINE LEARNING FOR DRUG DISCOVERY IN IBD

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1. Introduction

Inflammatory Bowel Disease (IBD) refers to two conditions: ulcerative colitis (UC) and Crohn disease (CD) [1]. IBD has a range of clinical symptoms including abdominal pain, diarrhoea, weight loss, constipation, and fatigue [2]. The main cause of IBD is unknown, but it is the result of a weakened immune system. The possible causes of IBD involve genetic and environmental factors. Unfortunately, with conventional diagnostic methods it is hard to predict therapeutic responsiveness of patients beforehand [3]. Genetic expression may be a valuable prediction tool to determine patient's responsiveness to treatment.

2. Materials and Methods

mRNA data from *Arijs et al* [4] was analysed with Recursive Ensemble Feature Selection (REFS). The data has 120 colonic biopsies of patients and 12 healthy controls. The REFS algorithm uses 8 classifiers from the sci-kit toolbox [5] in a nested 10-fold cross-validation and then we validate our results with 5 new classifiers to avoid overfitting. Finally, as a measure for diagnostic accuracy we used the ROC curve[6].

3. Results

5 resulting features were selected from the original 33252: 7922994 (*FAM5C*), 7905881 (*ADAM15*), 7894470 (N/A), 7995803 (*MTIJP*) and 7927288 (*SHLD2P3*).

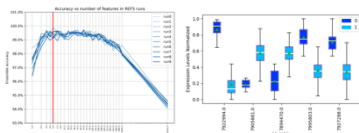


Figure 1: 10 runs of REFS algorithm, with best answer at 5 genes (left). Boxplot of the 5 selected features comparison between healthy controls and IBD (right).

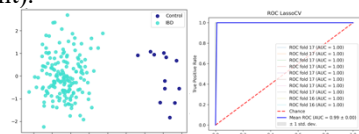


Figure 2: PCA plot of IBD and control groups (left), ROC Curve with an AUC of 0.99 using the 5 selected features(right).

4. Discussion and Conclusions

FAM5C is the most important gene found by REFS to differentiate IBD patients compared to healthy controls. In colonic tissue, gene expression sites are mainly located in the cytoskeleton region of the brush border membrane. Smith et al. suggested that *FAM5C* under expression may cause membrane damage in patients, therefore serving as a susceptibility factor for IBD [7]. *FAM5C* expression is upregulated by inflammatory stimuli such as TNF- α [8]. By inhibiting proinflammatory pathways such as NF- κ B, increased *FAM5C* expression could be reversed. These results correlate with new IBD therapy, Cyclosporine's effects. Cyclosporine decreases the expression of *FAM5C*, and it is also a NF- κ B and JNK inhibitor [9].

5. References

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