#59 - GENETIC VARIANTS IN IBD CHILEAN PATIENTS ARE RELATED TO CLINICAL OUTCOMES.

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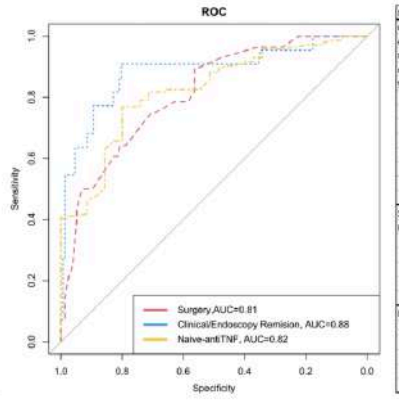
Background: IBD genetics research has primarily focused on Causasian populations, resulting in underrepresentation of Latin populations in these studies. **Method:** 192 Chilean individuals with IBD (145 UC and 47 CD) were genotyped using Illumina GSA Arrays. From IBD GWAS (Jostin et al. and Liu et al.), we selected gene variants related to IBD. Then, we built a Chilean dataset (clinical-genotype information). Using this dataset, we performed a Spearman correlation matrix to correlate clinical outcomes with IBD variants. Further, we built regression models to predict the clinical outcomes using the variants obtained from the correlation matrix ($p < 0.05$). The best models were selected using significance testing or likelihood-based information criterion, such as the Akaike Information Criterion (AIC), and plotted using a Receiver Operating Characteristic Curve (ROC). Finally, to evaluate the association among variants in each model, we perform a Gene Ontology biological process enrichment analysis using PANTHER (Fisher, FDR). **Results.** As shown in Figure 1, the best predictive regression models (more than 80%) for the clinical outcomes were surgery, clinical/endoscopy remission for more than five years, and naïve anti-TNF. Association with genetic variants was observed significantly ($p<0.05$) in the enrichment analysis for the model Clinical/endoscopy remission of more than five years. Finally, for each variant in this model, a Chi-square test was conducted to determine whether there was a significant difference among patients genotypes in terms of clinical/endoscopic prolonged remission outcome (yes/no). The analysis revealed significant differences for the following variants: rs6837335, rs11742570, rs7134599, and rs6142618. **Conclusion.** Candidates' genes related to clinical outcomes in our Chilean IBD cohort were related to epithelial, innate, and adaptative immune responses and host-microbial interactions. Future research is needed to validate these findings.

Figure 1. Best Predictive Models for Surgery, Clinical/Endoscopy Remission and Naïve-anti TNF.



Model	AIC	True/False	Variant	Pvalue*	Gene candidate
Clinical and/ endoscopy remission more than 5 years	104.5	91.96/8.04	rs6837335	0.00452	TXK, TEC, SLC10A4
			rs11742576	0.02633	PTGER4
			rs6871626	0.04555	IL12B
			rs38904	0.01510	WNT2, CFTR
			rs7133914	0.02012	LRRK2
			rs7134599	0.00908	IFNγ, IL26, IL22
			rs17085007	0.01812	GPR12-USP12
			rs6142618	0.01394	TMBSF4/HCK
Surgery Resective	134.28	85.87/14.13	rs12568930	0.000359	WNT4, CDC42
			rs7608910	0.017982	REL, C2orf74, KIAA1841, AHSA2
			rs12663356	0.011451	(-)
			rs6651252	0.027148	Desert region on chr 8
			rs2836878	0.032515	PSMG1
Naive Anti-TNF	150	82.58/17.41	rs12654812	0.01008	DOK3
			rs212388	0.01919	TAGAP
			rs4246215	0.00712	C11orf9,FADS3,FADS2
			rs7954567	0.00512	CD27, TNFRSF1A, LTBR
			rs12458916	0.01873	MEX3C
			rs6142618	0.00249	TMBSF4/HCK

Surgery: IBD related surgery. **Clinical/endoscopy remission for more than five years** (UC: Total Mayo score less than 3, Endoscopy Mayo score 0; CD: Harvey Bradshaw less than 5, Simple Endoscopy Activity Score less than 3).
Naïve-anti TNFa. Not previous use antiTNFa.