



RACP Foundation Research Awards

FINAL REPORT

Project / Program Title	Investigation of New Indicators of Disease Activity in Inflammatory Bowel Disease (NIDA-IBD)	
Name	Dr Akhilesh Swaminathan	
Award Received	2019 New Zealand Fellows Research Entry Scholarship	
Report Date	28 April 2020	
Chief Investigator / Supervisor	Professor Richard Geary	
Administering Institution	University of Otago, Christchurch	
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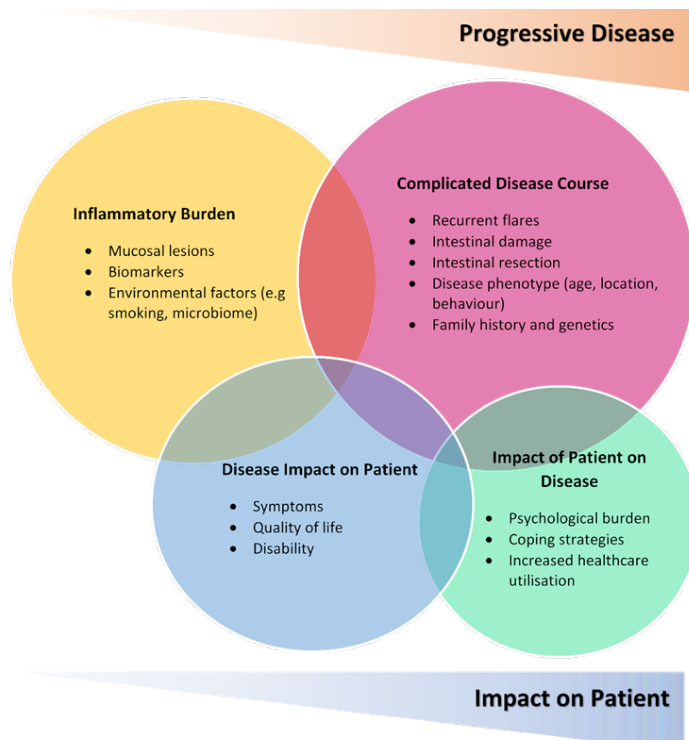
PROJECT SUMMARY

The “New Indicators of Disease Activity in Inflammatory Bowel Disease (NIDA-IBD)” study aimed to develop novel non-invasive markers of inflammation in IBD, a chronic relapsing-remitting illness characterised by gastrointestinal inflammation, comprising of Crohn’s disease (CD) and ulcerative colitis (UC). The overall impact of IBD on an individuals’ life is determined by multiple factors but a significant proportion of this is driven by the inflammatory burden of this illness, as shown below in Figure 1. Currently, assessment of disease activity is best achieved through endoscopic assessment, which is invasive and expensive. Thus, the development of a sensitive and specific biomarker of disease activity in IBD, which has ease of use for both patient and clinician is likely to improve IBD related morbidity and reduce the need for invasive investigations such as colonoscopy, a limited resource within the Public Health Sector.

The principle biomarkers investigated in this study were urinary methionine sulfoxide (Met(O)), a product of inflammation in the body that is excreted in the urine, and faecal myeloperoxidase (fMPO), an enzyme that is linked with and is a potential driver of inflammation in diseases such as IBD. These markers were compared with a patients’ symptoms, currently used biomarkers, and endoscopic disease activity.

The results from this study showed that clinical symptoms are a poor guide to the inflammatory burden of illness in CD. Currently used biomarkers in IBD are better predictors of endoscopic disease activity in UC than in CD. Urine Met(O) does not correlate with endoscopic disease activity in IBD and is unlikely to be a useful biomarker in this disease. Faecal myeloperoxidase is a useful biomarker of disease activity in both CD and UC and further work should be conducted to improve upon the assays that have been developed to measure this.

Figure 1. The multiple facets influencing long term outcomes in IBD



PROJECT AIMS / OBJECTIVES

Project Objectives (to date):

1. To recruit a cohort of 200 IBD patients undergoing endoscopic disease assessment into the NIDA-IBD study. To date, 179 study participants have been recruited.
2. To characterise the clinical phenotype of study participants using medical notes and validated questionnaires (Harvey-bradshaw index, simple clinical colitis index).
3. To measure currently used biomarkers (full blood count, C-reactive protein, faecal calprotectin) and correlate these with the gold standard measurement of disease activity in IBD (endoscopy).
4. To optimise an assay to measure Met(O) in the urine and to measure this novel biomarker in the urine of IBD patients undergoing colonoscopy.
5. To optimise an assay to measure fMPO protein and activity of fMPO, and to measure this in the stool of IBD patients undergoing colonoscopy.
6. To correlate levels of Met(O) and fMPO with currently used biomarkers, endoscopic disease activity, and IBD symptom scores using Spearman rank correlations.
7. To compare the utility of fMPO with faecal calprotectin (FC) in predicting endoscopic disease activity in IBD using receiver operating characteristic (ROC) analysis

SIGNIFICANCE AND OUTCOMES

1. The results from this study demonstrate the lack of accuracy of a patients' symptoms in assessing for the inflammatory burden of Crohn's disease. As current treatments target

mucosal inflammation in IBD, this reiterates the need for biomarkers of intestinal inflammation to help guide a patients' therapy.

2. Urinary Met(O) does not correlate with endoscopic activity in IBD and is unlikely to be a useful biomarker in this disease. This could be due to the instability of reactive oxygen species and their by-products, such as Met(O), even though they play a significant role in driving inflammatory illnesses such as IBD.
3. Faecal myeloperoxidase is an alternative biomarker to non-invasively investigate intestinal inflammation in a more cost-effective manner to conventional modalities such as calprotectin.
4. Further analyses are required to improve upon the cost effectiveness and efficiency of current fMPO techniques, including assays assessing MPO activity.

PUBLICATIONS / PRESENTATIONS

Publications and Presentations:

1. Swaminathan A, Borichevsky G, Hoskin T, Mules T, Day A, Hampton M, Kettle A, Geary R. Faecal myeloperoxidase is a potential biomarker of disease activity in Inflammatory Bowel Disease (IBD): results from the New Indicators of Disease Activity in Inflammatory Bowel Disease (NIDA-IBD) cohort. Poster presentation at Digestive Diseases Week (2020).
2. Swaminathan A, Borichevsky G, Hoskin T, Mules T, Day A, Hampton M, Kettle A, Geary R. Clinical and biochemical markers are more closely associated with endoscopic disease activity in Ulcerative colitis than Crohn's disease: results from the New Indicators of Disease Activity in Inflammatory Bowel Disease (NIDA-IBD) cohort. Poster presentation at New Zealand Society of Gastroenterology Annual Scientific Meeting (2019).
3. Swaminathan A, Borichevsky G, Hoskin T, Bathish B, Mules T, Day A, Hampton M, Kettle A, Geary R. Evaluation of Methionine sulfoxide as a potential biomarker of disease activity in Inflammatory Bowel Disease (IBD): results from the New Indicators of Disease Activity in Inflammatory Bowel Disease (NIDA-IBD) cohort. Poster presentation at New Zealand Society of Gastroenterology Annual Scientific Meeting (2019).
4. Mules T, Swaminathan A, Borichevsky G, Frampton C, Geary R. The impact of disease activity on psychosocial factors in Inflammatory Bowel Disease. Poster presentation at New Zealand Society of Gastroenterology Annual Scientific Meeting (2019).
5. Wall CL, Swaminathan A, Borichevsky G, Geary R. Patients can accurately use an inflammatory bowel disease-specific nutrition self- screening tool (IBD-NST). Poster presentation at New Zealand Society of Gastroenterology Annual Scientific Meeting (2019).

This project has allowed for the establishment of future research students investigating further novel biomarkers in IBD from the biobank created as part of the NIDA-IBD study.

Further analyses of the quality of life indices collected as part of this project will allow future researches to investigate the impact of the IBD on a patient in a more holistic manner than a purely laboratory-based approach.

The establishment of the NIDA-IBD study cohort allows for future collaboration between researchers and patients involved in this study. Such engagement with patients may contribute to more meaningful research for key stakeholders.

ACKNOWLEDGEMENTS

As per all academic outputs listed above