Scottish Government Health Directorates Chief Scientist Office

CHIEF SCIENTIST OFFICE

FOCUS ON RESEARCH

Comparing the immunological signatures of common inflammatory diseases, to identify potential therapeutic targets.

Researchers
Simon Milling (PI), Carl Goodyear, Stefan Siebert, and Iain McInnes

Aim
To compare blood samples from patients with inflammatory bowel disease (IBD), ankylosing spondylitis (AS), psoriasis (Ps), and psoriatic arthritis (PsA), to understand immunological factors associated with each disease.

Project Outline/Methodology
The four inflammatory conditions we are studying all occur in people who share common genetic predisposing factors, yet they affect different organs. We therefore reasoned that patients might have specific disease-associated characteristics, but that they might all also share some immunological differences not found in age-matched healthy individuals. We have therefore collected fresh blood samples from each of the four groups (IBD – 25; AS – 32; Ps – 38; PsA – 30, healthy – 31) and measured the frequencies of 74 discrete, defined populations of immune cells, using fluorescently-labelled antibodies and a technique called flow cytometry. This study has generated a large volume of data that we are currently analysing in detail. The analysis and sample collection were interrupted towards the end of the project when the postdoctoral researcher accepted an excellent position with a pharmaceutical company. Although we have completed recruitment, the data analysis is still ongoing. While our preliminary findings, described below, are already proving to be very interesting, our ongoing analyses will yield additional conclusions in the coming months.

Key Results
We have completed in-depth analysis of our HC, AS and Ps samples – these were the first groups in which the recruitment was completed. Because of the large number of parameters measured per sample, and the large numbers of samples in the study, we have generated a bespoke bioinfirmatic workflow to interrogate the dataset. This workflow will be applied to the remaining samples once the initial flow cytometric data analysis has been completed.
From our AS and Ps samples, a principal component analysis reveals that for 71 of our 74 parameters the two groups cluster very closely together. This indicates that the majority of parameters we can measure in blood do not differ between individuals with these conditions.
For three specific parameters, however, there are statistically significant differences between the healthy controls and the samples from people with AS and Ps. These three parameters all reflect the frequencies of two specific types of T cell. The function of T cells, in general, is to co-ordinate the immune response, and to drive inflammation. Thus, our preliminary conclusion is that this specfic type of T cell may be responsible for generating the specific inflammatory symptoms observed in people with AS and Ps. Further analysis of the remaining datasets will, we hope, reveal additional differences between the groups of samples.

Conclusions
Our preliminary results indicate that we may have identified immunological differences between controls and samples from people with AS and Ps. We have not yet placed these differences in the context of the other related conditions. Although we have finished the recruitment phase of the project, we have not yet completed the analysis of the resulting datasets. This analysis is continuing and firm conclusions will become available in the coming months.

What does this study add to the field?
Preliminary analysis has revealed that specific T cell may drive pathology in Ps and AS. Once the analyses have been completed, we hope this study will reveal additional immunological differences between healthy blood, and blood samples from our four patient groups. These differences may be used for diagnostic purposes, or may provide targets for novel therapeutic strategies.

Implications for Practice or Policy
None, yet.

Where to next?
Once the analysis is complete, we will engage with our extensive existing network of clinical and industrial partners to identify the optimum pathways for generating impact.

Further details from
Simon Milling
120 University Place, Glasgow, G12 8TA
simon.milling@glasgow.ac.uk
Tel: 0141 330 6419