



## TRAM (Train and Retain Academic Musculoskeletal clinicians) MB-PhD Project Summary

### PhD project Title

Exposing the anti-inflammatory effect of physical activity in patients with inflammatory rheumatic disease

### PhD supervisors (please provide name, affiliation and email) [At least two supervisors]

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### Background

Physical activity (PA) is commonly recommended for patients with inflammatory rheumatic disease (IRD), although, research examining its effects in these patient populations has been limited and its benefits have yet to be fully realised.

It is often said that physical activity (PA) has an anti-inflammatory effect and indeed there is a host of data to support this assertion in the general population (Gleeson et al. 2011). There is, however, a dearth of data to support such a claim in people with IRDs, the populations where the benefits of such an effect are likely to be most important.

Whilst there have been major advances in the treatment and management of inflammatory rheumatic diseases (IRDs), the burden on the patient remains high. In particular, patients continue to report chronic levels of fatigue which in turn drives poor quality of life and work disability in these populations. It is assumed, but yet to be proven, that this symptom is caused by persisting systemic inflammation.

We have recently completed the LIFT trial (Martin et al. 2019) where we investigated the effect of a PA intervention in patients with IRDs. This intervention delivered statistically and clinically significant improvements in our primary outcome of fatigue. We now hypothesise that this treatment effect was mediated by reductions in systemic inflammation. Moreover, we predict that this anti-inflammatory effect will be associated with other patient gains, including improved disease control.

The current studentship will leverage clinical data and samples banked in the LIFT trial from >300 IRD patients. These include granular accelerometry derived PA metrics and plasma samples which will enable proteomic profiling of inflammation.

The overall aim of the thesis, therefore, would be to investigate the effect of PA on inflammation in people with IRDs. The student would join a vibrant multidisciplinary team with a supervisory team with expertise physical activity (SG) and clinical rheumatology (NB).

**Aims**

- 1) Quantify PA patterns in a cohort of people with IRDs and investigate the association of these with baseline levels of inflammation
- 2) Determine the effects of PA on established and novel markers of inflammation
- 3) Investigate whether changes in inflammation, with PA, contribute to its beneficial clinical effects

**Training and experience provided** *[Include types of methodologies that will be employed]*

The student will join a research team which spans the disciplines of physical activity and academic rheumatology and will benefit from this broad expertise. The student will benefit from the general academic training provided within the research themes including journal clubs, seminar series, departmental presentation and the generic PGR training provide from the graduate school.

For the current project the first task will be to quantify standard and novel physical activity parameters from the accelerometer data. Training will be provided for this analysis and will primarily utilise excel and R.

Stata and/or R will also be used to determine with association between PA and markers of inflammation with training provided for the statistical techniques needed.

For the measurement of novel markers of inflammation the student will be trained in the laboratory techniques to perform multiplex and proteomic techniques to quantify a panel of cytokines/chemokines, with subsequent statistical analysis perform in Stata and/or R accounting for subsequent statistical analysis.

**Expected outcomes**

The outputs from this PhD will result in high impact publications and importantly will generate data that dramatically improve our understanding of the effects of increasing physical activity on inflammation in people with IRDs. Furthermore, this information will be important in optimising PEP for patient benefit.

**References**

- Gleeson M, Bishop NC, Stensel DJ, et al (2011) The anti-inflammatory effects of exercise: mechanisms and implications for the prevention and treatment of disease. *Nat Rev Immunol* 11:607–615. <https://doi.org/10.1038/nri3041>
- Martin KR, Bachmair E-M, Aucott L, et al (2019) Protocol for a multicentre randomised controlled parallel-group trial to compare the effectiveness of remotely delivered cognitive-behavioural and graded exercise interventions with usual care alone to lessen the impact of fatigue in inflammatory rheumati. *BMJ Open* 9:e026793. <https://doi.org/10.1136/bmjopen-2018-026793>