**University of Leicester**

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| **Project Reference** | BRC Studentships |

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| **First Supervisor** | Dr Luke Baker |
| **School/Department** | Respiratory Sciences |
| **Email** | Lab69@leicester.ac.uk |

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| **Second Supervisor** | Dr Neil Greening |
| **School/Department** | Respiratory Sciences |
| **Email** | neil.greening@leicester.ac.uk |

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| **Additional Supervisor** | Dr Thomas Wilkinson |

**Section 2 – *Project Information***

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| **Project Title** | ​Understanding how resolution physiology influences skeletal muscle endotype in those with multiple long-term conditions (MLTCs)​ | |
| **Project Highlights:** | 1. | Sarcopenia prevalence in those with MLTCs |
| 2. | Understanding the role of inflammation in sarcopenic endotype |
| 3. | Cluster specific mechanisms in those with MLTCs |
| **Project Summary** | | |
| **Background**: ​People with multiple long-term conditions (MLTCs) suffer from muscle loss and dysfunction, leading to reduced quality of life and poorer outcomes. Unresolved inflammation is a common characteristic in those with MLTCs, and as such presents an opportunity to intervene. The resolution of inflammation is an active process, directed by a set of compounds termed specialised pro-resolving mediators (SPMs). To date, work has focused on understanding how systemic levels of SPM clusters are associated with disease severity in various conditions, but work investigating tissue-specific responses to different SPMs and their mechanisms is in its infancy. Our group have shown that an SPM termed Resolvin E1 is able to attenuate endotoxin-induced muscle loss *in* vitro, whilst others have shown the potential for Resolvin D1 to play a role in skeletal muscle in the context of ageing.  This project will seek to identify the role of SPMs in skeletal muscle loss and dysfunction in those with MLTCs, as a disease-agnostic mechanism which could have potential applications independent of MLTC combination.​  **Research Plan**: ​The first stage of this project will be to conduct a systematic review to understand the prevalence of sarcopenia in those with MLTCs. This will help inform whether there are specific disease clusters which have a greater prevalence of sarcopenia. The applicant will also use published in-vitro methodologies to investigate the mechanistic role of inflammatory-induced muscle loss and how SPMs influence skeletal muscle phenotype. To pull findings together, patient investigations in those with MLTCs will confirm the translation of mechanism in patient biopsies, coupled with lipidomic analysis to investigate SPM circulatory profiles in different disease clusters.​  **Expected outcomes and impact:** ​This project is expected to have a significant impact in the fields of sarcopenia in MLTCs and resolution physiology. It will shed light on potential disease clusters which present with sarcopenia and make significant strides into understanding how dysfunctional SPM-related processes may contribute to changes in skeletal muscle endotype in these populations. | | |
| **References**  Baker, L. A., Martin, N. R. W., Kimber, M. C., Pritchard, G. J., Lindley, M. R., & Lewis, M. P. (2018). Resolvin E1 (Rv E1 ) attenuates LPS induced inflammation and subsequent atrophy in C2C12 myotubes. *Journal of cellular biochemistry*, *119*(7), 6094–6103. https://doi.org/10.1002/jcb.26807  Baker, L. A.,  O'Sullivan, T. F.,  Robinson, K. A.,  Graham-Brown, M. P. M.,  Major, R. W.,  Ashford, R. U.,  Smith, A. C.,  Philp, A., and  Watson, E. L. (2022)  Primary skeletal muscle cells from chronic kidney disease patients retain hallmarks of cachexia *in vitro*, *Journal of Cachexia, Sarcopenia and Muscle*,  13,  1238– 1249, <https://doi.org/10.1002/jcsm.12802>. | | |