

Page 1 – General Information

Project Code	NTAB04
Partner University	Nottingham Trent University
Faculty/School/Department/Research Centres	School of Science and Technology Department of Biosciences & Department of Sports Sciences; CHAUD and SHAPE Research Centres.
First supervisor Please provide name and weblink	Dr Neil Williams https://www.ntu.ac.uk/staff-profiles/science-technology/neil-williams
Second supervisor Please provide name and weblink	Dr Carl Nelson https://www.ntu.ac.uk/staff-profiles/science-technology/carl-nelson
Third supervisor Please provide name and weblink	Professor Philip McTernan https://www.ntu.ac.uk/staff-profiles/science-technology/philip-mcternan
Fourth supervisor Please provide name and weblink	Dr Graham Sharpe https://www.ntu.ac.uk/staff-profiles/science-technology/graham-sharpe
Fourth (external) supervisor	Professor Helen Maddock https://pureportal.coventry.ac.uk/en/persons/helen-maddock
External/industrial supervisor	Professor Glen Gibson and Dr Gemma Walton (University of Reading)
Which of the supervisors listed above is an early-career-researcher	Dr Neil Williams
Contact details for project for informal applicant queries	Dr Neil Williams and Dr Carl Nelson Neil.williams@ntu.ac.uk ; carl.nelson@ntu.ac.uk
DTA Programme	DTA Applied Biosciences for Health
Project title	Gut microbiota as a novel nutritional target to influence systemic inflammation in overweight participants with asthma



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Page 2 – Project Description

<p>Scientific Excellence (500 words)</p>	<p>Drs Sharpe and Williams have a proven track record of respiratory research and will have access to unique expertise and asthma patients with <i>in vitro</i> respiratory expertise offered by Dr Carl Nelson. With over 100+ original publications, Professor McTernan provides in depth expertise into chronic inflammatory conditions supported by international leading work of Prof Helen Maddock, coupled with industrial support. This interdisciplinary approach will innovate research outputs and strengthen alliance-training opportunities between institutes.</p>
<p>Aim (400 words)</p>	<p>Asthma and obesity are globally important chronic inflammatory disorders that require urgent action, therefore the research aims of this proposed PhD are to:</p> <p>(1) Define the difference in gut permeability and gut microbe derived endotoxin (bacterial fragments) between subjects with and without asthma; before and after a prebiotic galactooligosaccharide feeding;</p> <p>(2) investigate the effect of prebiotic intervention on the quality of life, physical activity, asthma symptoms, and disease control in obese asthmatics;</p> <p>(3) Delineate the mechanisms of endotoxin and prebiotic galactooligosaccharide action using <i>in vitro</i> lung and adipose cells and <i>ex vivo</i> peripheral mononuclear blood cells derived from obese asthmatics.</p> <p>Methodology: We will use a variety of <i>in vivo</i> and <i>in vitro</i> analysis using molecular biology and physiology state of the art equipment within NTU and in conjunction with external collaborators.</p> <p>Research Design: Double blinded cross-over prebiotic dietary intervention ((n=40; single daily dose; 4 weeks with placebo or treatment, 2 weeks wash out, 4 weeks with placebo or treatment) using participants with and without asthma (over</p>



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	<p>varying BMIs)). Samples taken will include breath, blood (PBMCs), urine and faecal samples.</p> <p>Study 1 –Define gut microbiota composition and systemic inflammation; gut microbiota analysis support from Professor Glenn Gibson and Dr Gemma Walton Reading University.</p> <p>Study 2 –Analyse biochemical markers, asthma severity, gut permeability, VOCs and physiology.</p> <p>Study 3 – <i>in vitro</i> molecular work on lung and adipose tissue will assess inflammatory pathways and mitochondrial function. Prof Philip McTernan has accessible tissue banks; mitochondrial expertise support provided by Prof Helen Maddock Coventry University.</p> <p>Ambition & Innovation: This novel intervention could be a key adjunct therapy to improve disease management, enhance quality of life and reduce the health related costs of managing asthma in weight gain.</p>
<p>Strategic Relevance (300 words)</p>	<p>This research is strategically aligned to the DTA Applied Bioscience and Health as the PhD proposal examines health outcomes in participants with weight gain and Asthma. Obesity is a serious health concern for the increased risk of other detrimental diseases including Asthma. The team working with participants will be able to explore both the underlying mechanisms of disease as well as how a dietary intervention may deliver public health benefits. This work aligns to the strategic remits of the individual departments in the Alliance Universities and has public impact relevance, a key strategic importance.</p>
<p>Interdisciplinarity and fit with DTA3</p>	<p>Together the research team will investigate mediators and mechanisms in obesity that contribute to Asthma and its development. The successful applicant will gain an interdisciplinary perspective with molecular, biochemical and clinical participant based training from support from both the Department of Biosciences, and the Department of Sport Science respectively, within the School of Science and Technology. Drs Williams and Sharpe have established a reproducible model for assessing airway hyper-responsiveness</p>



	<p>in adults with asthma (Williams et al., 2015) and have a proven track record of dietary intervention research in asthma patients (Williams et al., 2016; Williams et al., 2017). Furthermore, the team have established collaborations that allow for the assessment of gut microbial composition and metabolomics at Reading University and Imperial College London. Our Industrial support is via Reading University's prebiotic spin out company (Clasado Biosciences) who would be happy to support the candidate with a placement at Reading University Department of Food and Nutritional Sciences to gain insight into ongoing prebiotic research trials, and an understanding into the commercial side of the company producing prebiotics. The research team are also developing links with Friesland Campina who manufacture a prebiotic ingredient (Vivinal-Galactooligosaccharide) and there may be opportunities for further industry collaboration here.</p> <p>Professor Philip McTernan, as head of Biosciences has also delineated the role of gut bacteria in metabolic disease over several years and within NTU secured capital equipment to support delivery of this project. Prof Glenn Gibson (industrial and academic partner) will also provide support for gut microbiota analysis and the prebiotic requirements, mitochondrial expertise will be provided as part of a joint training programme with Coventry University and Prof Helen Maddock.</p> <p>The ambition for the research in the DTA framework is to continue to foster international world leading research as part of this programme, which will contribute to the success of the research theme that sits across Biosciences and Sport Sciences around Diabetes, Chronic diseases and Ageing. This DTA student will also work in the new ISTEK facility within NTU and work within a dedicated and focussed team of aligned researchers able to support and contribute to the research endeavours across the Alliance partnership.</p>
<p>Industrial Relevance (300 words) Detail external placement</p>	<p>The student would have the exciting opportunity of an industrial placement within the Food and Nutritional Sciences Department at The University of Reading, (Prebiotic manufacturer) under the supervision of Professor Glenn Gibson,</p>



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<p>opportunities or collaborations available as part of the project</p>	<p>and Dr Gemma Walton. Professor Glenn Gibson developed the prebiotic product and associated spin out company (Clasado Biosciences), which is a commercial venture with the product used in a range of research studies (IBD, asthma, depression, metabolic disease), it is commercially available and was used by Team GB in the build up to the Rio 2016 Olympics. Insight into a spin out company will provide a great opportunity to view how academic research can develop into commercial endeavour. The student would also be able to secure training into conducting metagenomic and/or metabolomic analysis of faecal and urine samples collected as part of study 1.</p>
<p>Economic and Societal Impact (300 words)</p>	<p>Whilst the role of the gut microbiota in health and disease has received much attention in recent years, <i>in vivo</i> human prebiotic intervention studies in common seemingly westernised diseases such as asthma and obesity are still limited. Despite reports indicating some promising observations, studies have heavily relied on murine models to investigate the effects of nutritional interventions on gut bacteria and autoimmune disease. Our recent work (Williams et al., 2016) is the only study to date in human asthma patients and this has been externally rated as 4*. The strong collaborative nature of the proposed project underpins both the applied and detailed mechanistic focus of the research to further elucidate the role of the gut microbiota and mucosal barrier in obesity and asthma to target 3* / 4* publications. The measurements and primary outcome variables are critical to underpinning both the mechanistic understanding and applied impact upon physical activity and quality of life. The research is of a highly novel nature with originality, significance, and rigour that is consistent with 3*/4* activity. Furthermore as our collaborators have mainly explored other diseases the understanding of how asthma is impacted by obesity and potential interventions has clear impact case potential for NTU as a future case.</p>



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Page 3 – Admission Requirements

<p>Specific Admission Requirements Detail any subject specific degree qualifications or disciplines, relevant skills, experience</p>	<p>Entrants must have a Bachelors Honours degree, with an Upper Second Class or a First Class grade, in [Biological Sciences, Biochemistry, Sport Sciences]. Entrants with a Lower Second Class grade in their Bachelors Honours degree must also have a postgraduate Masters Degree at Merit.</p>
<p>Minimum IELTS score</p>	<p>You will need an overall IELTS (International English Language Testing System) score of 6.5 with minimum sub-scores of 6.0 in all component sections (writing, reading, listening and speaking).</p>



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