

| Project Details |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
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| Project Code    | IIAR27Ex Borah Slater                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Title           | Cracking the Host-Pathogen Metabolic Code in Tuberculosis: Discovering New Therapeutic Strategies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Research Theme  | Infection, Immunity & Antimicrobial Resistance                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Project Type    | Wet lab                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Summary         | Tuberculosis (TB) remains one of the world's leading infectious killers, with the urgent need for new treatments. This exciting PhD project will explore how the body's own cells can be harnessed to fight TB by targeting lipid metabolism. You will investigate oxysterols and oxylipins, specialised molecules that regulate immune responses and may also be exploited by Mycobacterium tuberculosis as nutrients. Building on our discovery of a novel immunomodulatory compound, you will determine how it reprograms host lipid pathways to boost immunity and eliminate infection. Using lipidomics, zebrafish models and clinical samples, this research will identify innovative therapeutic strategies.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Description     | <p>Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains one of the world's leading infectious killers, responsible for over one million deaths annually. The emergence and spread of drug-resistant TB has created an urgent need for new therapeutic strategies that can complement conventional antibiotics. One promising approach is host-directed therapy, which aims to enhance the body's natural ability to control infection rather than directly targeting the bacterium.</p> <p>Mtb survives and persists within immune cells by manipulating host metabolism, particularly lipid pathways. Our research has shown that oxysterol metabolism is reprogrammed during TB infection and may play important roles in regulating immune responses. These specialised lipid molecules can influence inflammation, antimicrobial activity and cellular metabolism. However, it remains unclear whether these lipids primarily benefit the host by promoting immunity, benefit the pathogen as nutrient sources, or perform both functions simultaneously.</p> <p>This studentship will investigate a fundamental question at the interface of infection biology and metabolism:</p> <p>Research Question: How does host-cell lipid remodelling shape bacterial phenotype and virulence during tuberculosis infection, and can these pathways be targeted to develop effective host-directed therapies?</p> <p>The project will build on exciting preliminary findings from our laboratory, including the discovery of a novel immunomodulatory molecule that promotes clearance of Mtb. The student will investigate how this compound reprograms host lipid metabolism and establish whether these changes can enhance antimicrobial immunity and reduce bacterial survival.</p> <p>Research Objectives:</p> <p>The project will establish the metabolic crosstalk between host and pathogen by combining infection models, lipidomics, metabolomics and molecular biology approaches.</p> <p>Objective 1: Define host lipid remodelling during TB infection</p> <p>The student will characterise changes in oxysterols, oxylipins and related lipid pathways during infection using:</p> <ul style="list-style-type: none"> <li>• In vitro macrophage infection models</li> <li>• Zebrafish-Mycobacterium marinum infection models</li> </ul> |

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|  | <ul style="list-style-type: none"> <li>• Clinical samples from TB patients</li> </ul> <p>Using state-of-the-art lipidomics, metabolomics and isotope tracing approaches, the student will determine how infection alters host lipid profiles and metabolic fluxes and identify pathways associated with protective immune responses.</p> <p>Objective 2: Determine how host lipid metabolism influences bacterial physiology</p> <p>The student will investigate how host metabolic changes affect the pathogen itself by measuring:</p> <ul style="list-style-type: none"> <li>• Bacterial lipid composition</li> <li>• Metabolic fluxes within the bacterium</li> <li>• Changes in bacterial phenotype associated with virulence and survival</li> </ul> <p>This work will provide new insights into whether Mycobacterium species exploit specific host-derived lipids as nutrient sources and how host metabolic remodelling influences bacterial adaptation during infection.</p> <p>Objective 3: Identify host and bacterial pathways involved in metabolic crosstalk</p> <p>To understand the molecular mechanisms underpinning host-pathogen interactions, the student will perform:</p> <ul style="list-style-type: none"> <li>• Gene expression analysis</li> <li>• Molecular pathway analysis</li> <li>• Bioinformatic integration of lipidomic and metabolomic datasets</li> </ul> <p>These studies will identify key genes and pathways in both the host and pathogen that regulate lipid metabolism and contribute to infection outcomes.</p> <p>Objective 4: Evaluate a novel host-directed therapeutic strategy</p> <p>Building on our discovery of a novel immunomodulatory molecule, the student will:</p> <ul style="list-style-type: none"> <li>• Determine how the compound reprograms host lipid metabolism</li> <li>• Investigate its effects on immune activity and bacterial clearance</li> <li>• Validate its efficacy in macrophage infection models and zebrafish infection models</li> </ul> <p>These studies will assess the potential of this molecule as a new host-directed therapy for TB.</p> <p>Training Opportunities</p> <p>The student will receive comprehensive interdisciplinary training in:</p> <ul style="list-style-type: none"> <li>• Infection biology</li> <li>• Immunology</li> <li>• Lipidomics and sterolomics</li> <li>• Metabolomics</li> <li>• Stable isotope tracing and metabolic flux analysis</li> <li>• Cell culture and infection models</li> <li>• Zebrafish disease models</li> <li>• Molecular biology and gene expression analysis</li> <li>• Multiomics data integration</li> </ul> <p>This combination of skills is highly relevant to careers in academia, biotechnology, pharmaceutical research and translational medicine.</p> <p>Student Ownership and Project Development</p> |
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|                             | <p>While the project has clearly defined objectives, there will be exciting opportunities for the student to develop their own scientific interests and shape the direction of the research. Following initial training, the student will be encouraged to:</p> <ul style="list-style-type: none"> <li>• Prioritise the most promising oxysterol and lipid pathways identified during discovery studies</li> <li>• Develop and test new hypotheses regarding host-pathogen lipid metabolic interactions</li> <li>• Explore additional mechanisms of action of the immunomodulatory compound</li> <li>• Design follow-up experiments arising from omics datasets</li> <li>• Contribute to collaborative studies involving clinical samples and translational research</li> </ul> <p>The student will play a central role in advancing our understanding of how lipid metabolism shapes TB infection while helping to develop innovative therapeutic strategies against a major global health threat.</p> |
| Can be completed part time? | Yes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Supervisory Team            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Lead Supervisor             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Name                        | Dr Khushboo Borah Slater                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Affiliation                 | Exeter                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| College/Faculty             | Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Department/School           | Biosciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Email Address               | k.borah-slater@exeter.ac.uk                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Co-Supervisor 1             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Name                        | Professor Valerie O'Donnell                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Affiliation                 | Cardiff                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| College/Faculty             | School of Medicine                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Department/School           | Infection and Immunity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Co-Supervisor 2             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Name                        | Professor Tetsu Kudoh                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Affiliation                 | Exeter                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| College/Faculty             | Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Department/School           | Biosciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Co-Supervisor 3             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Name                        | Professor Charles Tyler                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Affiliation                 | Exeter                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| College/Faculty             | Health and Life Sciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Department/School           | Biosciences                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |