**University of Leicester**

**Future 50 PhD Scholarship**

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| **Project Reference** | RI LISCB Ash |

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| **First Supervisor** | Dr Philip Ash | | |
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| **Second Supervisor** | Dr Patricia Rodriguez Macia | | |
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| **Additional Supervisor** |  |

**Section 2 – *Project Information***

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| **Project Title** | Photocatalysis with [FeFe] Hydrogenases: Time-resolved Spectroscopic Methods for Mechanistic Studies | |
| **Project Highlights:** | 1. | Molecular biology combined with synthetic chemistry |
| 2. | Photocatalysis/photochemistry |
| 3. | Advanced spectroscopy and time-resolved methods |
| **Project Summary** | | |
| Hydrogenases are key metalloenzymes for hydrogen metabolism, operating at very high rates under ambient conditions using only sustainable metals. Among all hydrogenases, [FeFe] hydrogenases are the fastest, most efficient catalysts. The catalytic performance of [FeFe] hydrogenases is enabled by a unique combination of organometallic chemistry and protein biology. Chemistry of the bimetallic Fe-Fe active-site cofactor is optimised by the protein scaffold, which provides exquisitely timed transport of gas, protons (H+), and electrons.  Due to the extremely high catalytic rates of [FeFe] hydrogenase, with turnover frequencies of several thousand *per second*, mechanistic information is very hard to obtain. Therefore, there is a need to develop more advanced time-resolved spectroscopic methods in order to reveal hidden mechanistic details. An increased understanding of how these enzymes work is important to answer fundamental questions in chemistry and biology as well as to develop better synthetic catalysts and to learn how to couple these enzymes with other systems for their application in biotechnology.  In this project, semi-synthetic [FeFe] hydrogenases will be prepared by combining apo-hydrogenase scaffolds (the protein containing the electron transfer cofactors, but lacking the active site) recombinantly expressed in *E. coli* with synthetic active-site cofactors. Importantly, this method provides a dual approach to tune the semi-synthetic catalyst: either via modification of the synthetic cofactor through synthetic chemistry or via engineering the protein scaffold through molecular biology. This project aims to engineer the hydrogenase scaffold to allow covalent attachment of photosensitizers to the protein. This will allow investigation of visible-light-driven hydrogen production, and open up possibilities for greater mechanistic understanding using time-resolved spectroscopic methods.  Overall this interdisciplinary project involves bioinorganic chemistry, biochemistry, biophysics, electrochemistry, and catalysis. The project will be suited to a candidate with a background in any of these areas, and who is keen to gain experience of a highly multidisciplinary research environment to learn and develop crucial lab-based and interpersonal skills.  This project is a collaboration between the Ash and Rodriguez-Macia groups, enabling the student to gain experience of a broad range of skills. There will also be opportunities to undertake research at national and international facilities throughout. | | |