**University of Leicester**

**MRC AIM Studentship Project 2025-6 entry.**

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| **First Supervisor** | Dr James Hodgkinson |
| **School/Department** | School of Chemistry and Leicester Institute of Structural and Chemical Biology |
| **Email**  | jthodgkinson@leicester.ac.uk  |

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| **Second Supervisor** | Dr Emma Hesketh |
| **School/Department** | Leicester Institute of Structural and Chemical Biology |
| **Email**  | emma.hesketh@leicester.ac.uk |

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| **Additional Supervisor** | Prof John Schwabe |

**iCASE partners, Sygnature Discovery (Peak Proteins):**

Alex Brown

Duncan Smith

Valerie Pye

**Section 2 – *Project Information***

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| **Project Title** | iCase: Using CryoEM to trap and visualise PROTAC drugs in action against cancer targets |
| **Project Summary**  |
| This PhD project is an exciting opportunity to explore the innovative drug strategy PROTACs by Cryo-Electron microscopy, a cutting-edge structural biology technique. This project involves a close partnership and collaboration with a world-leading drug discovery CRO where the student will learn protein expression/purification amongst industry experts, producing the therapeutic target proteins SOS1 and LSD1. At Leicester you will learn the chemistry of making PROTACS – novel bi-functional drugs that promise to ‘drug the undruggable’ by marking target proteins for degradation rather than inhibition. To determine the structure-activity relationship of these PROTACS, you will use state of the art cryo-electron microscopy at the regional facility based at Leicester. SOS1 and LSD1 are both important cancer therapeutic targets with substantial prospect for future drug development: SOS1 is cytoplasmic guanine nucleotide exchange factor that plays a critical and essential role in the KRAS signalling pathway. Inhibitors of SOS1 have shown considerable potential for targeting RAS-driven tumours. LSD1 is a histone demethylase enzyme that plays a critical role in the endothelial to mesenchymal transition that is a key step in allowing tumours to metastasize. Inhibition of LSD1 has been shown to be a promising treatment for melanoma in mouse models. |
| **References** |
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