**University of Leicester**

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

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| **Additional Supervisor** | Prof Dean Fennel / Dr Yolanda Markaki |

**Section 2 – *Project Information***

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| **Project Title** | Targeted protein injections to combat tumour suppressor loss and restore the epigenetic landscape in mesothelioma |
| **Project Summary**  |
| This PhD project focuses on developing a novel protein-based therapeutic approach to tackle mesothelioma, a highly lethal cancer with limited treatment options. Mesotheliomas often exhibit mutations in the epigenetic regulator and tumour suppressor gene BAP1, making the restoration of its function a key therapeutic strategy. Using a bacterial injection system in combination with various BAP1-deficient cell lines, we aim to deliver functional BAP1 protein directly into tumour cells and restore the epigenetic landscape. We will compare this cutting-edge approach with the traditional lentiviral restoration of BAP1 function. We will investigate how this changes the oncogenic gene expression program and how it can trigger cell death through apoptosis or necroptosis. This groundbreaking approach may open the door to innovative treatments for not only mesothelioma but other cancers with tumour suppressor mutations.This project will be jointly led by PIs at the Universities of Birmingham and Leicester with experiments performed in both locations. As a PhD student, you will be guided by biochemistry, cell biology and mesothelioma research experts. You will gain expertise in advanced techniques like protein engineering, gene expression analysis, microscopy, and flow cytometry, working closely with leaders in epigenetics, cell and cancer biology, molecular biology, and bioinformatics. |
| **References** |
| Bott et al., Nat Genet 43, 668–672 (2011).Carbone et al., Journal of Thoracic Oncology 11, 1246–1262 (2016).Fursova et al., Genes Dev. 35, 749–770 (2021).Kreitz et al., Nature, 1–8 (2023).Scheuermann et al., Nature 465, 243–247 (2010).Sime et al., Cell Death Dis 9, 1–16 (2018).Ventii et al., Cancer Research 68, 6953–6962 (2008). |