University of Leicester
AIM studentship project 2026

First Supervisor	Dr James T. Hodgkinson
School/Department	School of Chemistry and LISCB
Email	Jh669@le.ac.uk https://le.ac.uk/people/james-hodgkinson

Second Supervisor	Dr Harriet S. Walter
School/Department	Genetics and Genome Biology
Email	hw191@le.ac.uk https://le.ac.uk/people/harriet-walter

Additional Supervisor	Prof. Sarah Dimeloe, Department of Immunology and Immunotherapy, University of Birmingham

Section 2 – *Project Information*

Project Title	Synthesis and Evaluation of Novel BCL6 Targeting Degraders for Aggressive B Cell Malignancies

Project Summary

B-cell lymphoma 6 (BCL6) is a transcription factor that drives aggressive B-cell cancers such as diffuse large B-cell lymphoma (DLBCL), enabling cancer cells to survive and resist treatment. While small-molecule inhibitors of BCL6 have been developed, they show limited clinical benefit and none remain in clinical development.

This PhD project takes a cutting-edge approach: targeted protein degradation. Rather than inhibiting BCL6, we aim to eliminate it from cancer cells through targeted degradation. This strategy, using molecular glue degraders and proteolysis targeting chimeras (PROTACs), is pioneering new cancer therapies, with two BCL6 degraders already in clinical trials.

You will design and synthesise novel molecules that induce BCL6 degradation (Dr J.T. Hodgkinson, University of Leicester) and evaluate their effects on cancer cell viability and growth (Dr H. Walter and Prof M.J. Dyer, University of Leicester) and metabolism (Prof S. Dimeloe, University of Birmingham).

This interdisciplinary studentship spans synthetic organic chemistry, chemical biology, and translational cancer research, offering access to world-class facilities and joint training at the University of Leicester and the University of Birmingham. Ideal for candidates with a background in synthetic chemistry, chemical biology, or related disciplines who are motivated to contribute to fundamental research with potential for real clinical impact.

References

1. Wagner, S.D., et al. 2011. The role of BCL6 in lymphomas and routes to therapy. *British journal of haematology*, 152(1), pp.3-12.
2. Phelan, J.D., et al. 2018, A multiprotein supercomplex controlling oncogenic signalling in lymphoma. *Nature*, 560(7718), pp.387-391.
3. Pearce, A.C. et al. 2021. GSK137, a potent small-molecule BCL6 inhibitor with in vivo activity, suppresses antibody responses in mice. *Journal of Biological Chemistry*, 297(2), p.100928.
4. Kerres, N. et al., 2017. Chemically induced degradation of the oncogenic transcription factor BCL6. *Cell reports*, 20(12), pp.2860-2875.
5. Biochempeg. Clinical PROTACs targeting different protein targets. https://www.biochempeg.com/article/434.html. Accessed September 11, 2025.
6. Cheng, B. et al., 2025. Recent advances in developing targeted protein degraders. *European Journal of Medicinal Chemistry*, 284, p.117212.

7. Caimi, P.F. et al., 2024. Phase 1 study of ARV-393, a PROTAC BCL6 degrader, in advanced non-hodgkin lymphoma. *Blood*, 144, p.6505.
8. Groocock, L. et al., 2024. BMS-986458 a potential first-in-class, highly selective, potent and well tolerated BCL6 ligand directed degrader (LDD) demonstrates multi-modal anti-tumor efficacy for the treatment of B-cell non-Hodgkin's lymphoma. *Blood*, 144, p.957.
9. Mi, D. er al. 2024. Discovery of novel BCL6-Targeting PROTACs with effective antitumor activities against DLBCL in vitro and in vivo. *European journal of medicinal chemistry*, 277, p.116789.
10. Loberg, L.I., et al. 2025. Nonclinical teratogenicity safety assessment of CRBN-engaging targeted protein degraders: Points to consider. *Regulatory Toxicology and Pharmacology*, 158, p.105793.
11. Moreau, K., et al., 2020. Proteolysis-targeting chimeras in drug development: a safety perspective. *British journal of pharmacology*, 177(8), pp.1709-1718.
12. Ishida, T. and Ciulli, A., 2021. E3 ligase ligands for PROTACs: how they were found and how to discover new ones. *SLAS DISCOVERY: Advancing the Science of Drug Discovery*, 26(4), pp.484-502.
13. Zhang, X. et al., 2019. Electrophilic PROTACs that degrade nuclear proteins by engaging DCAF16. *Nature chemical biology*, 15(7), pp.737-746.
14. Kiely-Collins, H. et al., 2021. The role of reversible and irreversible covalent chemistry in targeted protein degradation. Cell chemical biology, 28(7), pp.952-968.
15. Lim, M. et al., 2024. DCAF16-based covalent handle for the rational design of monovalent degraders. *ACS Central Science*, 10(7), pp.1318-1331.
16. Campos, M.A. et al., 2025. Discovery of DCAF16 binders for targeted protein degradation. *ACS chemical biology*, 20(2), pp.479-488.
17. Barrio, S. et al., 2020. IKZF1/3 and CRL4CRBN E3 ubiquitin ligase mutations and resistance to immunomodulatory drugs in multiple myeloma. Haematologica, 105(5), p.e237.
18. Hanzl, A., et al., 2023. Functional E3 ligase hotspots and resistance mechanisms to small-molecule degraders. *Nature chemical biology*, 19(3), pp.323-333.