DOCTORAL SCHOOL

PhD Opportunity

The BCAT1 CXXC motif and oncogenesis in acute myeloid leukaemia

Director of Studies: Dr Steven Coles

Supervisors: Dr Amy Cherry, Dr Joanne Whittaker

Research Group: Worcester Biomedical Research Group (WBRG)

The PhD Opportunity

The BCAT1 gene is implicated in the pathogenesis of many cancer types, including acute myeloid leukaemia (AML)1–4. Recently, our group identified a novel antioxidant role for BCAT1 in AML cells5. We demonstrated that BCAT1 was able to protect AML cells from damaging effects mediated by oxidative stress, keeping the AML cells in a tumorigenic state.

Oxidative stress is known to interact with numerous signalling processes that promote tumorigenesis in AML6,7, however the role BCAT1 plays in these wider signalling processes remains unknown. Given that BCAT1 represents a potential target for treating AML, this project aims to understand these processes, and how they may be targeted therapeutically.

This project incorporates numerous methodologies, including, human cell culture, multiparameter flow cytometry, fluorescence microscopy, toxicology screening assays and western blotting. Applications from candidates with knowledge or previous experience in these techniques are encouraged.

References

1. Mayers, J. R. & Vander Heiden, M. G. BCAT1 defines gliomas by IDH status. Nat Med 19, 816–817 (2013).
2. Xu, M. et al. BCAT1 promotes tumor cell migration and invasion in hepatocellular carcinoma. Oncol Lett 12, 2648–2656 (2016).
3. TSENG, Y. H. et al. Curcumin induces apoptosis by inhibiting BCAT1 expression and mTOR signaling in cytarabine-resistant myeloid leukemia cells. Mol Med Rep 24, (2021).
4. Zhu, W., Shao, Y. & Peng, Y. MicroRNA-218 inhibits tumor growth and increases chemosensitivity to CDDP treatment by targeting BCAT1 in prostate cancer. Mol Carcinog 56, 1570–1577 (2017).
5. Hillier, J. et al. The BCAT1 CXXC Motif Provides Protection against ROS in Acute Myeloid Leukaemia Cells. Antioxidants 11, 683 (2022).

6. Hole, P. S. et al. Overproduction of NOX-derived ROS in AML promotes proliferation and is associated with defective oxidative stress signaling. Blood 122, 3322–3330 (2013).
7. Trombetti, S. et al. Oxidative Stress and ROS-Mediated Signaling in Leukemia: Novel Promising Perspectives to Eradicate Chemoresistant Cells in Myeloid Leukemia. Int J Mol Sci 22, 1–19 (2021).

Additional costs
Given that this is a laboratory-based project, bench fees will apply to cover the procurement of reagents essential to delivering the research objectives. This will include cell culture media and antibodies.

Application Process
To begin the application process please go to: https://www.worc.ac.uk/research/research-degrees/applying-for-a-phd/.

The Interview
All successful applicants will be offered an interview with the proposed Supervisory Team. You will be contacted by a member of the Doctoral School Team to find a suitable date. Interviews can be conducted in person or over Microsoft Teams.

Funding your PhD
For information about Doctoral Loans please visit: https://www.worc.ac.uk/study/fees-and-finance/doctoral-loans.aspx

During your PhD you can access the Research Conference Support Scheme to support the costs of presenting your research at an external conference.

Research at the University of Worcester
Research is central to the University's mission to make a difference in everything that we do. We are committed to delivering excellent research which extends the boundaries of human knowledge, but which also improves people's lives by enabling better health outcomes, improving food security, developing environmentally sustainable solutions for crop production and socially sustainable solutions to our ageing population, enhancing public knowledge and understanding of the past and present.

The University hence focuses its research around five high-level challenges facing society, locally, nationally and globally:

- **Human Health and Wellbeing**
- **Sustainable Futures**
- **Digital Innovation**
- **Culture, Identity and Social Exclusion**
- **Professional Education**

The success of our research is reflected in our continuous improvement in external research assessment processes. In the most recent Research Excellence Framework, REF 2021, the University saw a near 50% increase in the scale of its research and 12% increase in quality, building on its performance in REF 2014 when it was the UK's most improved university in terms of Research Power, a combination of scale and quality.

DOCTORAL SCHOOL

Research Degrees at Worcester
Our research students are central to our overall mission for research. They are working at the cutting edge of their disciplines and driving forward the quality of our research whilst enriching our research culture. We are looking to increase our research student numbers as a strategic imperative.

Our commitment to our students is reflected in the results of the Postgraduate Research Experience Survey 2023 in which we ranked 3rd for overall research student satisfaction nationally. Key to our success in his area is the Doctoral School, a focal point for all our research students.

It provides:

- day-to-day support for our students, both administrative and practical, through our dedicated team.
- a Research Student Study Space with both PCs and laptop docking stations.
- a comprehensive Researcher Development Programme for students and their supervisors.
- a programme of student-led conferences and seminars.

Widening Participation
As part of its mission statement the University is committed to widening participation for its higher degrees. Although most candidates will have an undergraduate and/or a Masters degree, the University is happy to accept applications from candidates with relevant professional qualifications and work related experience.

For further information or an informal discussion on this project, please contact Dr Steven Coles (s.coles@worc.ac.uk)