

University of Leicester
AIM studentship project 2026

First Supervisor	Dr. Abhinav Koyamangalath Vadakkepat
School/Department	Division of Molecular & Cell Biology (MCB) and Leicester Institute of Structural and Chemical Biology (LISCB),
Email	akv10@leicester.ac.uk https://le.ac.uk/people/abhinav-koyamangalath-vadakkepat

Second Supervisor	Prof. Julie Morrissey
School/Department	Division of Microbiology and Infection/ Leicester Microbial Sciences and Infectious Disease Research Centre (LeMID)
Email	jam26@leicester.ac.uk https://le.ac.uk/people/julie-morrissey

Additional Supervisor	Prof. Joan Geoghegan Institute of Microbiology and Infection, Department of Microbes, Infection and Microbiomes, University of Birmingham
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Section 2 – Project Information

Project Title	Targeting Copper Efflux ATPases in Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) as a strategy to overcome persistence in macrophages
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Project Summary

We invite applications for a fully-funded PhD project to study how methicillin resistant *Staphylococcus aureus* (MRSA) manages copper toxicity. The human immune-system uses copper toxicity to kill bacteria during infections. However, *S. aureus* has evolved mechanisms to survive this by using copper-transporting proteins called CopA, CopB and CopX. This project will focus on understanding structure and function of these proteins and how they help MRSA survive copper-rich environments. Using molecular biology, membrane-protein biochemistry, and cryo-electron microscopy (cryo-EM), you will investigate how these pumps work to export copper from bacterial cells. This project provides a unique opportunity to be at the cutting edge of antimicrobial-resistance research, working with an interdisciplinary supervisory team involving research groups from University of Leicester (UoL) and University of Birmingham (UoB). The knowledge gained could lead to new ways of targeting these pumps to weaken MRSA and improve infection control. You will be based within UoL which offers a vibrant multicultural interdisciplinary research environment and access to world-class research facilities for structural-biology including the state-of-the art 300 kEV Titan Krios and all sample-vitrification facilities. We welcome candidates with a background in microbiology, biochemistry, or structural biology who are interested in addressing the global challenge of AMR.

References

- Halliwell B, Gutteridge JM. Oxygen toxicity, oxygen radicals, transition metals and disease. *Biochem J.* 1984; 219:1-14.
- Achard ME, Stafford SL, Bokil NJ, Chartres J, Bernhardt PV, Schembri MA, Sweet MJ, McEwan AG. Copper redistribution in murine macrophages in response to *Salmonella* infection. *Biochem J.* 2012; 444:51-7.
- Baker J, Sengupta M, Jayaswal RK, Morrissey JA. The *Staphylococcus aureus* CsoR regulates both chromosomal and plasmid-encoded copper resistance mechanisms. *Environ Microbiol.* 2011; 13:2495-507.

4. Shafeeq S, Yesilkaya H, Kloosterman TG, Narayanan G, Wandel M, Andrew PW, Kuipers OP, Morrissey JA. The cop operon is required for copper homeostasis and contributes to virulence in *Streptococcus pneumoniae*. *Mol Microbiol*. 2011; 81:1255-70.
5. Zapotoczna M, Riboldi GP, Moustafa AM, Dickson E, Narechania A, Morrissey JA, Planet PJ, Holden MTG, Waldron KJ, Geoghegan JA. Mobile-Genetic-Element-Encoded Hypertolerance to Copper Protects *Staphylococcus aureus* from Killing by Host Phagocytes. *mBio*. 2018; 9:e00550-18.
6. White C, Lee J, Kambe T, Fritsche K, Petris MJ. A role for the ATP7A copper-transporting ATPase in macrophage bactericidal activity. *J Biol Chem*. 2009; 284:33949-56.
7. Purves J, Thomas J, Riboldi GP, Zapotoczna M, Tarrant E, Andrew PW, Londoño A, Planet PJ, Geoghegan JA, Waldron KJ, Morrissey JA. A horizontally gene transferred copper resistance locus confers hyper-resistance to antibacterial copper toxicity and enables survival of community acquired methicillin resistant *Staphylococcus aureus* USA300 in macrophages. *Environ Microbiol*. 2018; 20:1576-1589.
8. Kaur I, Purves J, Harwood M, Ketley JM, Andrew PW, Waldron KJ, Morrissey JA. Role of horizontally transferred copper resistance genes in *Staphylococcus aureus* and *Listeria monocytogenes*. *Microbiology (Reading)*. 2022; 168:001162.
9. Macé K[#], Vadakkepat AK[#], Redzej A, Lukyanova N, Oomen C, Braun N, Ukleja M, Lu F, Costa TRD, Orlova EV, Baker D, Cong Q, Waksman G. Cryo-EM structure of a type IV secretion system. *Nature*. 2022, 607:191-196. ([#]: equal contribution)
10. Vadakkepat AK, Xue S, Redzej A, Smith TK, Ho BT, Waksman G. Cryo-EM structure of the R388 plasmid conjugative pilus reveals a helical polymer characterized by an unusual pilin/phospholipid binary complex. *Structure*. 2024; 32:1335-1347.e5.
11. Abhinav KV, Al-Otaibi NS, Xue S, Ho BT, Waksman G. Cryo-EM structure of *E. coli* pKM101 type IV secretion system reveals the activation step of pilus biogenesis. (*unpublished*).