**University of Leicester**

**College of Life Sciences**

**CLS / HPRU Grant studentship**

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| **Second Supervisor** | Dr Emma Marczylo UK Health Security Agency (UKHSA) |

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| **Additional Supervisor** | Kate Jones Health and Safety Executive Emma-Jane Goode  |

**Section 2 – *Project Information***

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| **Project Title** | **How exposure to metals adapts bacteria to increase bacterial persistence, antimicrobial resistance and potentiate infection** |
| **Project Summary**  |
| Metals such as copper are essential micronutrients required by most organisms. But due to toxicity at higher concentrations these metals are used as antimicrobials in healthcare and within a host. To counteract antimicrobial activity bacteria have evolved dedicated resistance mechanisms to regulate metal concentrations. Exposure to environmental metal pollution increases risk of pathogen acquisition of additional genes to combat metal toxicity. This has the potential for significant health implications through the increased infectivity of pathogens and potential changes of the balance of microbial communities.Our data show that community acquired and healthcare associated epidemic methicillin resistant Staphylococcus aureus (CA-MRSA and HA-MRSA respectively) strains have acquired additional resistance mechanisms that confer copper-hyper resistance and increased resistance to killing by macrophages. This provides evidence that exposure to copper and acquisition of genes can increase pathogen infectivity.Furthermore, our recent data show that copper at relevant biological concentrations changes MRSA expression of antibiotic resistance, virulence and immune evasion factors and alters the interaction of MRSA with human epithelial cells. Therefore, metal exposure has the potential to increase AMR and alter colonisation of Staphylococcus aureus. However, the mechanisms of how copper increases antibiotic resistance and alter epithelial interaction are still undefined.The aim of this interdisciplinary project is to test our hypothesis that **metal exposure alters host-pathogen interaction and AMR increasing the risk to human health.** We will test this hypothesis by the following objectives:1. Elucidate the impact of copper-adapted bacteria on the immune response and host-pathogen interactions.
2. Determine the risk of copper on antimicrobial resistance.
3. Establish the importance of copper-regulated pathways in the colonisation of the host.

We will initially continue with ongoing projects using the data sets obtained on copper. However, there we can use the current methodologies and research strategy and build on our data to investigate other metals or chemicals highlighted from Theme 1. The student will be supervised by a multi-disciplinary project supervisory team Morrissey (UoL), Marczylo and Goode (UKHSA) and Kate Jones (HSE) and will be well-provided with all the necessary training and facilities. The student will be registered with the University of Leicester for the PhD but will spend time at HSE and UKHSA becoming familiar with public health and expertise with epithelial models. Expected outcomes and training. The student will benefit from being part of large inter-disciplinary Health Protection Research Unit (HPRU) funded by the National Institute of Health Research (NIHR) at the University of Leicester (UoL). The student will be part of a lively and friendly interdisciplinary research group and will be trained in a wide range of methodologies including molecular microbiology, mammalian tissue culture, omics methodologies, and advanced microscopy. Additionally, the student will benefit from active research project meetings with respiratory and infectious disease clinicians and chemists, and association with the NIHR Biomedical Research Centre and Health Protection Research Unit, Health and Safety Executive and UK Health Science Agency. |