**University of Leicester**

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| **Project Reference** | BRC Studentships |

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**Section 2 – *Project Information***

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| **Project Title** | How does exposure to air pollutants impacts respiratory bacteria and subsequent disease? |
| **Project Highlights:** | 1. | We will establish the mechanisms involved in the impact of air pollutants on bacterial pathogens and how this affects respiratory tract health and infectious disease. |
| 2. | Using state of art technologies, we will determine the effect of inhaled external influences on host-pathogen interaction. |
| 3. | Clinical samples will be used to validate biomarkers for exacerbation of COPD and other chronic respiratory tract infections. |
| **Project Summary**  |
| **Background:** Our interdisciplinary research shows that air-borne particulate pollutants impact directly on bacteria to potentiate infection. We found that interaction of bacteria with particulate pollutants results in an unusual pattern of gene expression, increasing colonisation of abiotic and biotic surfaces including the respiratory tract. However, understanding of how air pollutants alter bacterial interaction with the human respiratory tract is severely lacking. Identifying the impact of pollutant exposure and the biological mechanisms key for COPD exacerbation is crucial for better treatment of patients because exacerbation can lead to significant decline in patient lung function, quality of life, and survival.  COPD exacerbation and longer-term severity is dependent on the complex interplay between environmental factors such as exposure to air pollution, the immune system, and the balance of pathogens and commensal bacteria found in the respiratory tract. Our studies show that with increasing severity of COPD, the airway microbiome shifts to having a decreased abundance of commensals (e.g. Prevotella) and an increased abundance of pathogenic bacteria (e.g Moraxella). There is also an associated decrease in expression of genes promoting epithelial integrity. However, little is known about what drives these fluctuations in the COPD microbiome and the relationship with the environment. Establishing the molecular mechanisms and exploitation of an innovative *in vitro* human airway model will transform understanding of environment-bacteria-host dynamics to advance diagnostics and novel interventions.The aim of this project is to increase understanding of the biological mechanisms involved in the interplay between air pollution exposure, bacteria and respiratory tract health, and validate clinical associations that can lead to novel therapeutic strategies for respiratory disease.**Research Plan: ​**The objectives are to: 1. Understand the biological mechanisms and the impact of inhaled pollutants on host pathogen interaction.
2. Use *in vitro* human airway lung tissue model, multi-omics and advanced imaging to determine the effect of inhaled external influences on microbiome disruption.
3. Use clinical samples, to validate biomarkers identified from the discovery science associated with COPD severity, microbiome dysbiosis and exposure to environmental pollutants.  ​

**Expected outcomes and impact:** This project will help establish the mechanisms involved in the impact of air pollution on host-pathogen interaction, and how this affects respiratory tract health. It will also use state of art technologies to determine the effect of inhaled external influences on host-pathogen interaction to transform biomarker identification, and clinical samples to validate biomarkers for exacerbation of COPD and other chronic respiratory tract infections. ​  |
| **References**1. Purves, J.,Hussey, S. J. K., Corscadden, L., Purser, L., Hall, A., Misra, R., Selley, L., Monks, P. S., Ketley, J. M., Andrew, P. W., Morrissey, J. A. (2022) Air pollution induces *Staphylococcus aureus* USA300 respiratory tract colonisation mediated by specific bacterial genetic responses dependent on the global virulence gene regulators Agr and Sae. *Environmental Microbiology*. 2022 doi:10.1111/1462-2920.16076
2. Ramsheh et al. Lung microbiome composition and bronchial epithelial gene expression in patients with COPD vs healthy individuals: a bacterial 16S rRNA gene sequencing and host transcriptomic analysis. (2021) Lancet Microbe 2: e300–10
3. Hussey S. J. K., Purves J., Allcock N., Fernandes V. E., Monks P. S., Ketley J. M., Andrew P. W., Morrissey J. A. Air pollution alters *Staphylococcus aureus* and *Streptococcus pneumoniae* biofilms, antibiotic tolerance, and colonisation. (2017) Environ. Microbiology 19:1868-1880.
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