

## **PaM Associate Faculty project: Respiratory microbiome analytics**

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All respiratory pathogens must encounter the respiratory microbiome through continuous carriage in healthy individuals and during primary or secondary infection. As such, the respiratory microbiome plays a key role in the survival and evolution of respiratory pathogens and the pathways towards disease. Furthermore, the microbiome acts as a barrier to pathogen infection and plays a key role in modulation of immune responses. As already demonstrated for intestinal infections, understanding the composition and dynamics of healthy and diseased respiratory microbiomes has the potential to bring new understanding of these processes. However, respiratory infectious diseases are behind the curve of microbiome research due to the problem of low biomass samples which presents challenges in both sample processing and data analysis.

Building on our successes in gut microbiome and respiratory pathogen research, our aim is to develop a world-class platform for studying the respiratory microbiome. We will exploit access to rare high-value samples to test and validate the application of current technologies and to inform design of potential new approaches. Larger scale studies will then be conducted in collaboration with partners in LMICs to study cohorts of healthy and diseased individuals to allow for statistically rigorous interpretations.

We propose to hire a postdoc who will be dedicated to development of analytics for these future studies. The work will exploit data from large gut microbiome studies (and pilot respiratory microbiome studies) to inform the development of simulations representing equivalent scenarios in the respiratory microbiome that will be used to test potential analytical approaches. Parallel work will focus on the processing and analysis of real respiratory microbiome data. To understand the complex nature of longitudinal microbiome data and its connections to disease and health of the individuals, it is necessary to amend advanced bioinformatics, which process the raw data into analyzable formats, with a range of statistical and computational techniques that include network analysis, supervised machine learning with high-dimensional predictors and unsupervised machine learning to structure data and to identify outliers.

This project fits very naturally with the experience and ambitions of the PaM programme and will greatly benefit from the engagement to the Associate Faculty. While the initial focus is on human respiratory tract samples/studies, in the long term this work will develop a platform that will be valuable to any microbiome research, particularly studies that are restricted to working with complex and low biomass samples.