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# Rachel Wheatley, DPhil

Biology

University of Oxford

from September to December 2021

Born in 1993 in Devon, United Kingdom

Studied Molecular Biology and Biochemistry at the University of Durham and Biology at the University of Oxford

FELLOWSHIP

College for Life Sciences

## PROJECT

### Determinants of Success in the Ecosystem of the Lungs

The lungs can be considered an ecosystem. From birth, the lungs are continually exposed to microorganisms. They host a diversity of microorganisms, collectively known as the microbiome, both in healthy and in diseased states. It is fascinating to think that the concept of a lung microbiome is a relatively new one; the lungs have historically been considered a sterile environment. We know now that a healthy lung can contain common key microbiome members, and that the lung microbiome and other environmental factors may in fact play a fundamental role in determining an individual's susceptibility to respiratory disease. The focus of my research is to understand how a single pathogen species is able to emerge in a lung microbiome, and to characterise the genetic and metabolic determinants of this success. I am especially interested in the opportunistic pathogen *Pseudomonas aeruginosa*, which is a major cause of healthcare-associated respiratory infection. During my stay at the Wissenschaftskolleg, I would like to explore how understanding bacterial metabolism can help advance pathogen treatment strategies. Successful infection of a human host is dependent on multiple pathogen behaviours, including successful resource competition, virulence factor production, and antibiotic and host immune evasion. Success of these behaviours can be linked to bacterial metabolism, and investigating metabolism can help identify metabolites or pathways with the potential to suppress pathogens. Identifying potential therapeutic targets given the wide range of environmental variables and metabolic targets remains a significant challenge, however, which high-throughput metabolic screening approaches and computational metabolic models have tried to overcome. This explorative work will form an important cornerstone for directing future studies I wish to approach. Outside of these interests, my additional research enthusiasms include antibiotic resistance evolution, transposon-based functional genomics approaches, and phage defence mechanisms.

#### Recommended Reading

Wheatley, Rachel M., Brandon L. Ford, Li Li, Samuel T. N. Aroney, Hayley E. Knights, Raphael Ledermann, Alison K. East, Vinoy K. Ramachandran, and Philip S. Poole (2020). "Lifestyle Adaptations of *Rhizobium* from Rhizosphere to Symbiosis." *Proceedings of the National Academy of Sciences* 117, no. 38: 23823-23834.

<https://doi.org/10.1073/pnas.2009094117>.

Wheatley, Rachel M., and R. Craig MacLean (2020). "CRISPR-Cas Systems Restrict Horizontal Gene Transfer in *Pseudomonas aeruginosa*." *The ISME Journal*. <https://doi.org/10.1038/s41396-020-00860-3>.

Wheatley, Rachel, Julio Diaz Caballero, Natalia Kapel, Fien H. R. de Winter, Pramod Jangir, Angus Quinn, Ester del Barrio-Tofiño, et al. (2021). "Rapid Evolution and Host Immunity Drive the Rise and Fall of Carbapenem Resistance during an *Acute Pseudomonas aeruginosa* Infection." *Nature Communications* 12: 2460.

<https://doi.org/10.1038/s41467-021-22814-9>.

## Party In and Outside the Petri Dish: How Can We Understand Bacteria and their Genomes?

Bacteria are everywhere – in our bodies, the soil, and even thermal vents. We see them involved in a huge range of processes, from disease and health, to food production, oxygenation of the atmosphere, and producing insulin like little cell factories. As a microbiologist I'm interested in understanding bacteria and the key biological processes they drive.

In trying to understand bacteria, a good starting place is the genome, effectively a "code book" of all the possibilities available to a bacterial cell. What determines what this genome looks like? And, out of all these possibilities, how do we work out how it's actually being used? My talk will be broadly centered around these two questions, and I will use examples from my previous work to illustrate how we can address them. I will explore the 'inputs and outputs' of bacterial genome evolution and discuss how we can investigate these processes in clinical settings: the lungs of ICU patients. Then moving to the question of how can we then link genome to function, I will discuss this problem in the light of legumes and investigate the mechanisms underpinning symbiotic nitrogen fixation.

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### PUBLICATIONS FROM THE FELLOWS' LIBRARY

Wheatley, Rachel (Palo Alto, Calif., 2022)

Understanding the impacts of bacteriophage viruses : from laboratory evolution to natural ecosystems

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=183322471X>

Wheatley, Rachel (Reading, 2022)

Fitness costs of CRISPR-Cas systems in bacteria

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=1814900632>

Wheatley, Rachel (Washington, DC [u.a.], 2021)

Metabolic control of nitrogen fixation in rhizobium-legume symbioses

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=177986969X>

Wheatley, Rachel ([London], 2021)

Rapid evolution and host immunity drive the rise and fall of carbapenem resistance during an acute *Pseudomonas aeruginosa* infection

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=1762667568>

Wheatley, Rachel (Basingstoke, 2021)

CRISPR-Cas systems restrict horizontal gene transfer in *Pseudomonas aeruginosa*

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=1762664836>

Wheatley, Rachel (Washington, DC, 2020)

Lifestyle adaptations of *Rhizobium* from rhizosphere to symbiosis

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=1762666057>

Wheatley, Rachel (Oxford, 2018)

Mechanisms of bacterial attachment to roots

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=177987099X>

Wheatley, Rachel (Washington DC, 2017)

Role of O<sub>2</sub> in the growth of *Rhizobium leguminosarum* bv. *viciae* 3841 on glucose and succinate

<https://kxp.kioplus.de/DB=9.663/PPNSET?PPN=1779872089>  
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