# Mechanism of host-pathogen interactions at the ciliated surface

**Project ID:** 3703

## Supervisory team

**Main supervisor:** Prof Kirsty Wan (University of Exeter)
**Second supervisor:** Prof Andrew Preston (University of Bath)
**Other supervisors:** Dr Hannah Laeverenz-Schlogelhofer (University of Exeter)

**Host institution:** University of Exeter



**Project description:** Motile cilia have highly conserved functions, enabling fluid transport in animals and propulsion of microorganisms. Emerging evidence suggests they may also fulfil key sensory functions in mammalian ciliated tissues, in mediating host-pathogen defence, and in detecting the presence of harmful viruses or microbes in the first instance. Indeed, in their ancestral state, cilia in unicellular eukaryotes (protists) not only enable active motility but have well-established functions across a range of sensory modalities, from chemosensing to mechanosensing, mating and kin-recognition. It has also been shown in animal models that infection by a small number of bacteria, such as Bordetella which infects several mammalian species, can trigger large-scale ciliostasis -- cessation of ciliary beating. Meanwhile, in ciliates such as Tetrahymena, motile cilia beating can be inhibited by detected signals from microbes or chemical agents that alter swimming behaviour. This may be accompanied by mucocyst secretion and calcium dependent exocytosis that helps to trap bacteria, making them an excellent single-cell analogue of mucociliary secretion. This unique proposal leverages two complementary perspectives to reveal the uncharacterised sensory role of motile ciliated mucosal surfaces. By comparing across unicellular and mammalian systems, the project will establish core biophysical mechanisms underlying host-pathogen interactions, identifying possible conserved features of this fascinating sensory defence strategy. Specifically, we will: 1. Characterise native beating patterns and flow generation in ciliated epithelia in both unicellular and multicellular (tissue culture) systems2. Characterise how these dynamics (changes in beat patterns or ciliary coordination) are perturbed or disrupted by microbial peptides, coated microspheres, or pharmacological agents to mimic ciliostasis, using the ciliate model3. Investigate how ciliary beating is disrupted by bacterial adhesin-coated microspheres, in mammalian airway liquid cultures/organoids4. Investigate cilia-pathogen interactions upon manipulating external viscosity using inert polymer or synthetic mucus.5. Develop a physical model of these interactions combining acquired data with computational simulations This project bridges understanding from the sub-cellular scale of individual cilia to the tissue level, to provide fundamental insights into the important mechanism of host-pathogen interactions at the ciliated surface. The student will develop skills in microbiology, cell and tissue culturing, live-cell quantitative imaging and manipulation, high-speed brightfield and fluorescence microscopy, PIV, microfluidics, and biophysical modelling. They will receive excellent training across a variety of techniques and disciplines and will be supported across these topics by the combined expertise of the supervisors at Exeter and Bath.

**Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities,**

**disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.**