

# *Investigating the rescue of cystic fibrosis-causing mutations by CFTR modulators with patch-clamp electrophysiology*

*Main supervisor:* Prof. David N. Sheppard University of Bristol ([d.n.sheppard@bristol.ac.uk](mailto:d.n.sheppard@bristol.ac.uk))

*Secondary supervisor:* Dr. Paola Vergani, UCL Division of Biosciences ([p.vergani@ucl.ac.uk](mailto:p.vergani@ucl.ac.uk))

*Funding:* 1 Fully Funded (UK Home fees) PhD project.

As well as funding materials, consumables and use of imaging facilities, the award provides a generous tax-free stipend (£19,919, £ 21,542 and £ 23,298 per annum during the PhD years) and covers tuition fees (at home student rates). Funds are also available for attending specialised training workshops and relevant international scientific conferences to increase awareness of scientific advances, but also to provide opportunities for networking and team building.

## *Project details:*

A 3-year PhD studentship funded by the Cystic Fibrosis Trust is available at the University of Bristol from September 2023. In this project, we aim to understand better the molecular defects at the root of the genetic disease cystic fibrosis (CF) and how they impact the function of different organs affected by the disease, including the lungs, intestine, liver and pancreas. Results from this research might guide the development of better drug therapies that target the root cause of CF.

In this project, you will use patch-clamp electrophysiology to investigate the epithelial anion channel cystic fibrosis transmembrane conductance regulator (CFTR). By applying the patch-clamp technique to heterologous cells transiently expressing CF-causing CFTR mutations, you will identify how different mutations disrupt anion transport by CFTR, paying particular attention to the anions chloride and bicarbonate. Building on these studies, you will investigate how clinically-approved CFTR modulators, such as ivacaftor, restore anion transport to different mutations before examining CFTR function in native epithelia to identify tissue-specific differences in anion transport and the response to CFTR modulators.

The project brings together a multi-disciplinary team of researchers in Bristol (Prof. David Sheppard) and London (Dr Paola Vergani) that are part of a Cystic Fibrosis Trust-funded Strategic Research Centre (SRC), a virtual research centre, with other researchers from London, Paris and Rotterdam, led by Dr Vergani. Through the SRC, you will receive thorough training in cutting-edge biomedical research methods, network with other SRC trainees and visit Dr Vergani's laboratory. Start date permitting, you will be an incorporated student of the GW4 BioMed2 DTP funded by the MRC (<https://gw4biomed.ac.uk/>) and benefit from its exceptional training opportunities.

You will be based with Prof. Sheppard's group in the School of Physiology, Pharmacology and Neuroscience (<https://www.bristol.ac.uk/phys-pharm-neuro/>), where you will be part of a vibrant community of researchers investigating ion channel function in different organ systems at the molecular, cellular and tissue levels. Recent publications from Dr Vergani and Prof. Sheppard, include Prins S *et al. J Biol Chem.* 2020; 295:16529-16544 and Liu J *et al. Br J Pharmacol.* 2022; 179:1319-1337.

The PhD studentship is available to start in September 2023. Informal enquiries are very welcome and can be sent to Prof. Sheppard ([d.n.sheppard@bristol.ac.uk](mailto:d.n.sheppard@bristol.ac.uk)) or Dr Vergani ([p.vergani@ucl.ac.uk](mailto:p.vergani@ucl.ac.uk)).

This PhD studentship is fully funded for home fees and stipend at Cystic Fibrosis Trust-funded rates.

*Application deadline:* 11/12/2022

*Application details:* Please visit <https://www.ucl.ac.uk/biosciences/cystic-fibrosis-bicarbonate-centre>

The application will include:

- your latest CV with contact details for two referees
- a 2-3 paragraph statement explaining your interest in the project and what you feel you will bring to the role
- an official University transcript.

A first or upper second-class honours degree (or international equivalent) in a biomedical science discipline is required for this PhD studentship.