Combining artificial intelligence based drug discovery and automated patch clamping to revolutionise our understanding of lysosomal ion channels

Supervisory team:
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Project description:
Ion channels and transporters control everything an organism does, from initiating life through to cell death. Ion channels are found on all cellular membranes, but the least studied are those found in the lysosome. The lysosome is an organelle that acts as the degradative centre of the cell, containing numerous enzyme that digest proteins, carbohydrates and lipids so that their parts can be recycled. The lysosome is also an important signalling hub. Lysosomal ion channels and transporters are vital in fundamental processes such as fertilisation and cell death, and have been implicated in neurological disease and ageing. However, research into exactly how lysosomal ion channels and transporters function is difficult because there are not many ways that we can measure how they are working.

This PhD aims to determine how currently uncharacterised lysosomal ion channels and transporters work. Firstly, in order to measure how the lysosomal ion channels are working, we need to develop assays to measure their activity. Secondly, we need to discover small molecules that can activate and inhibit these ion channels so that their function can be characterised. We will develop assays that directly measure electrical conductance through channels using a suite of cutting edge automated electrophysiology equipment that we have at Cardiff University, and using fluorescent indicators that detect changes in ion levels. To discover new small molecules that affect these ion channels, we will develop and use artificial intelligence programs that use structural information about the channels to find places where compounds could bind, and any information on known activators to find similar molecules that can affect the channels, and could be developed into tools. Artificial intelligence (AI) is being used much more in small molecule discovery, and an understanding of how to use AI to find drugs will be hugely beneficial to any student thinking of a career in ion channel research or drug discovery. The successful candidate will join a multidisciplinary team of experts, with access to cutting edge ion channel and AI research facilities and expertise.

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.