

EPSRC PhD Studentship

Structure/Function studies of voltage-gated sodium channels

This 3.5 year EPSRC-funded studentship is to work with [Professor B.A. Wallace](#) at Birkbeck College, University of London on studies of bacterial and chimeric voltage-gated sodium channels.

The aim of this project is to enhance our knowledge of sodium channel structure, function and ligand binding with the ultimate goal of understanding the molecular basis of neurological and cardiovascular diseases associated with mutations in sodium channels, and to provide the basis for development of new pharmacological agents for their treatment.

The aim is to train the student in a wide range of techniques and disciplines, giving them a broad interdisciplinary background in the Basic Sciences as well as the opportunity to gain knowledge of a clinically-important system.

The project will encompass molecular biology, biochemical and biophysical characterisation (including circular dichroism, NMR and fluorescence spectroscopy), molecular modelling, structural (crystallography) biology and electrophysiological studies. The electrophysiology studies will be undertaken in collaboration with Professor Hywel Morgan and Dr. Maurits de Planque of Southampton University. The project will entail travel to collaborating labs, as well as to international synchrotrons for data collection.

References

1. Cronin, N., O'Reilly, A., Duclohier, H., and Wallace, B.A. (2003) Binding of the Anticonvulsant Drug Lamotrigine and the Neurotoxin Batrachotoxin to Voltage-gated Sodium Channels Induces Conformational Changes Associated with Block and Steady-State Activation. *J. Biol. Chem.* 278:10675-10682.
2. Nurani, G., Radford, M., Charalambous, K., O'Reilly, A.O., Cronin, N., Haque, S., and Wallace, B.A. (2008) Tetrameric Bacterial Sodium Channels: Characterisation of Structure, Stability, and Drug Binding. *Biochemistry* 31:8114-8121.
3. Wallace, B.A. (2007, 2008) Chimeric Constructs for Membrane Protein Expression. *Patent P522507GB/ International PCT/003573*
4. O'Reilly, A.O., Charalambous, K., Nurani, G., Powl, A.M. and Wallace, B.A. (2008) G219S Mutagenesis as a Means of Stabilising Conformational Flexibility in the Bacterial Sodium Channel NaChBac. *Molecular Membrane Biology* 25:670-676.
5. O'Reilly, A.O., Khambay, B.P.S., Williamson, M.S., Field, L.M., Wallace, B.A*, and Davies, T.G.E. (2006) Modelling insecticide binding sites at the voltage-gated sodium channel. *Biochemical Journal* 396:255-263.
6. Lampert, A., O'Reilly, A.O., Dib-Hajj, S.D., Tyrrell, L., Wallace, B.A.*, and Waxman, S.G. (2008) A pore-blocking hydrophobic motif at the cytoplasmic aperture of the closed-state Nav1.7 channel is disrupted by the erythromelalgia-associated F1449V mutation. *J. Biol. Chem* 283:24118-24127
7. Powl, A.M., O'Reilly, A.O., Miles, A.M. and Wallace, B.A. (2010) Synchrotron radiation circular dichroism spectroscopy-defined structure of the C-terminal domain of NaChBac and its role in channel assembly. *Proc. Natl. Acad. Sci. USA*, 107: 14064-14069.

How to apply

Applications should be submitted using the [Birkbeck online application form](#).