

An Indian-Australian research partnership

<b>Project Title:</b>	<b>Design and Synthesis of Small Organic Molecules as Blockers of Neuronal Calcium Ion Channels Relevant to Neuropathic Pain</b>	
<b>Project Number</b>	IMURA0331	
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## Research Academy Themes:

**Highlight which of the Academy's Theme(s) this project will address?**

*(Feel free to nominate more than one. For more information, see [www.iitbmonash.org](http://www.iitbmonash.org))*

1. Advanced computational engineering, simulation and manufacture
2. Infrastructure Engineering
3. Clean Energy
4. Water
5. Nanotechnology
6. Biotechnology and Stem Cell Research

## The research problem

Neuropathic pain is a pathology of the nervous system that is often highly debilitating and is thought to affect up to one-sixth of the world's population. There are numerous causes for the condition including nerve damage resulting from surgery, trauma, infection and disease. This type of pain can be unresponsive to existing therapies. A combination of opioids, antidepressants and anticonvulsants is often prescribed, but this usually only provides moderate pain relief and only in about 50% of cases, thus effective treatments for neuropathic pain represent a significant unmet medical need.

## Project aims

Neuronal voltage-gated N-type calcium channels (Ca<sub>v</sub>2.2) are strongly implicated in chronic and neuropathic pain. The ω-conotoxins are a family of calcium channel blocking cysteine knot peptides found in the venom of fish-hunting marine cone snails. The highly constrained nature of these peptides

and the availability of SAR data makes them ideal starting points for the development of peptidomimetics.

This project will follow on from previous studies where the aim is to synthesise small-molecule drug-like compounds that bind selectively to N-type calcium channels and elicit pain-blocking effects in a range of in vitro and in vivo tests.

*Relevant publications:*

- Baell, J. B.; Duggan, P. J.; Lok, Y. P. *Aust. J. Chem.* **2004**, *57*, 179.
- Baell, J. B.; Duggan, P. J.; Forsyth, S. A.; Lewis, R. J.; Lok, Y. P.; Schroeder, C. I. *Bioorg. Med. Chem.* **2004**, *12*, 4025.
- Baell, J. B.; Duggan, P. J.; Forsyth, S. A.; Lewis, R. J.; Lok, Y. P.; Schroeder, C. I.; Shepherd, N. E.; *Tetrahedron* **2006**, *62*, 7284.
- Andersson, A.; Baell, J. B.; Duggan, P. J.; Graham, J. E.; Lewis, R. J.; Lumsden, N.G.; Tranberg, C. E.; Tuck, K. L.; Yang, A. *Bioorg. Med. Chem.* **2009**, *17*, 6659.
- Duggan, P. J.; Lewis, R. J.; Lok, Y. P.; Lumsden, N. G.; Tuck, K. L.; Yang, A. *Bioorg. Med. Chem Letts*, **2009**, *19*, 2763.

### Expected outcomes

- The synthesis of drug-like organic compounds that selectively block human N-type channels.
- Publications and patents.
- PhD graduate trained in synthetic organic chemistry and medicinal chemistry.

### How will the project address the Goals of the above Themes?

Biomimicry is a sub-discipline of Biotechnology where the useful properties of a biological product are incorporated into a synthetic construct, while eliminating its less useful properties. In this project we are developing small-molecule drug-like compounds which mimic the Ca-channel blocking properties of conotoxin peptides but lack the bioavailability and toxicity issues associated with the natural peptides.

### Capabilities and Degrees Required

1. A Master of Science degree from a recognised University, majoring in **chemistry**.
2. Knowledge and the commitment to safe work practices in the laboratory
3. Demonstrated ability in the techniques of **synthetic organic chemistry**
4. Experience in chromatographic separation techniques, such as HPLC, column chromatography, and also in recrystallisation techniques
5. Experience in the use and interpretation of NMR and IR spectroscopy and mass spectrometry
6. Evidence of problem solving skills
7. Evidence of ability to co-operate and perform effectively as part of a research team
8. Demonstrated self-motivation and the ability to work independently on a given task
9. Proven ability to communicate effectively, both verbally and in writing
10. Industry experience in **synthetic organic chemistry** will be viewed favourably