Project title: Towards novel non-sedating analgesics: Identification of novel modulators targeting nicotinic acetylcholine receptors

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Project type: Computational Drug Design

Research theme: Mental Health

Project description:
Neuropathic pain (NP) is estimated to affect the lives of 7-8% of all Australians. The disease often leads to disability and early retirement and there is a need for development of novel and non-sedating analgesics. Nicotinic acetylcholine receptors have shown great promise in this respect. An example of an analgesic targeting nicotinic acetylcholine receptors is the alkaloid epibatidine. The compound is extracted from the frog *Epipedobates tricolor* from the Equadorian rain forest and local Indians have used the frog to produce poisonous arrows sufficiently potent to paralyze and kill even big animals. In low doses, epibatidine has shown analgesic effects in animal studies and it is ca. 200 times more potent than morphine without being sedative. Unfortunately, the compound also targets ganglionic nicotinic receptors and it is therefore not useful as a therapeutic agent. Our research has shown that epibatidine potently targets a unique α4α4 binding site on α4β2 nicotinic receptor and we are interested in identifying novel compounds that targets this site but are more selective. In the project you will construct a pharmacophore model for compounds targeting the α4α4 binding site. Subsequently, this model will be used in conjunction with 3D receptor models and high throughput virtual screening to identify novel lead compounds from databases of commercially available drug-like molecules.

In this project you will use professional computational drug discovery software and learn methods incl. docking, high throughput virtual screening and conformational analysis.