

Scientists discover how to design drugs that could target particular nerve cells

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(Medical Xpress) -- The future of drug design lies in developing therapies that can target specific cellular processes without causing adverse reactions in other areas of the nervous system. Scientists at the Universities of Bristol and Liège in Belgium have discovered how to design drugs to target specific areas of the brain.

The research, led by Professor Neil Marrion at Bristol's School of Physiology and Pharmacology and published in this week's *Proceedings of National Academy of Sciences (PNAS)*, will enable the design of more effective drug compounds to enhance nerve activity in specific nerves.

The team has been working on a subtype of ion [channel](#) called SK channels. Ion channels are proteins that act as pores in a cell membrane and help control the excitability of nerves.

Rather like an electrical circuit, ion channels work by allowing the flow of 'charged' potassium, sodium and calcium ions to enter or exit cell membranes through a network of pores formed by the channels, a subtype of which is the SK channel family.

The researchers have been using a natural toxin found in bee venom, called apamin, known for its ability to block different types of SK channel. SK channels enable a flow of potassium ions in and out of nerve cells that controls activity. The researchers have taken advantage of apamin being able to block one subtype of SK channel better than the others, to identify how three subtype SK channels [SK1-3] can be

selectively blocked.

Neil Marrion, Professor of Neuroscience at the University, said: “The problem with developing drugs to target [cellular processes](#) has been that many cell types distributed throughout the body might all have the same [ion channels](#). SK channels are also distributed throughout the brain, but it is becoming obvious that these channels might be made of more than one type of SK channel subunit. It is likely that different nerves have SK channels made from different subunits. This would mean that developing a drug to block a channel made of only one SK channel protein will not be therapeutically useful, but knowing that the channels are comprised of multiple SK subunits will be the key.”

The study’s findings have identified how SK channels are blocked by apamin and other ligands. Importantly, it shows how channels are folded to allow a drug to bind. This will enable drugs to be designed to block those SK channels that are made of more than one type of SK channel subunit, to target the symptoms of dementia and depression more effectively.

Vincent Seutin, one co-author of the paper, said: “Our study also shows a difference in the way apamin and nonpeptidic (potentially a useful drug) ligands interact with the channel. This may have important implications in terms of [drug design](#).”

More information: The paper, entitled ‘A crucial role of a shared extracellular loop in apamin sensitivity and maintenance of pore shape of SK channels’ by Kate Weatherall (University of Bristol), Vincent Seutin (University of Liège), Jean-Francois Liégeois (University of Liège) and Neil Marrion (University of Bristol) is published in this week's [8 Nov] *Proceedings of National Academy of Sciences (PNAS)*.
www.pnas.org/content/early/2011/11/08/10724108.full.pdf+html

Provided by University of Bristol

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