SCIENCE FOR THE BENEFIT OF HUMANITY

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A Novel Target for Modulating Ion Channel Function: The Voltage-Sensing Domain

RU 642

Technology Summary

Many cells produce electrical impulses across their surface membrane to initiate processes such as the release of neurotransmitter molecules or the contraction of muscles. The family of transmembrane protein molecules, which is referred to as the voltage-dependent cation channels, typically mediate this electrical activity. This family includes potassium (K^+), sodium (Na^+) and calcium (Ca^{2+}) selective members. The opening of a pore of a voltage-dependent ion channel, a process known as gating, is dependent upon the membrane voltage. When the pore of a voltage-dependent cation channel opens, it selectively conducts predominantly its namesake ion. Ion channels in the cell membrane allow ions to cross the membrane in a selective fashion, thus mediating the transmission of electrical impulses. This electrical signaling is how living cells transfer information over large distances rapidly.

Voltage-dependent ion channels are present in every cell and are involved in generation of electrical activity and information processing. As such, aberrant electrical activity can result in various conditions, such as heart arrhythmias, epilepsy, hypertension, etc. There is a need for methods to rapidly screen chemical compounds to determine whether the compounds bind to voltage-dependent ion channels.

Our researchers have solved the crystal structure of a number of ion channels, including the voltage-dependent calcium, potassium, and sodium channels. Their work shows the molecular basis of ion selectivity and also how the channel senses electrical signals and responds to them by opening or closing. It is therefore possible to use particular components of the ion channel, such as the voltage-sensing unit, to identify compounds that bind to that component and are most likely to affect ion channel function.

Area of Application

- Identification of compounds for the treatment of pathologies associated with ion channel dysfunction, such as neurological disorders, cardiac arrhythmia, and progressive hearing loss.

Stage of Development

- Preclinical in vitro structure-function studies.

Lead Inventor

- Dr. Roderick MacKinnon

Patent Information

- U.S. Patent 7,888,046 (calcium ion channel)
- U.S. Patent 7,405,052 (potassium ion channel)
- U.S. Patent 8,283,126 (sodium ion channel)

References

- Jiang Y., *et al*, 2003. ***Nature***, 423:33-41.
- Jiang Y., *et al*. 2003. ***Nature***, 423:42-48.