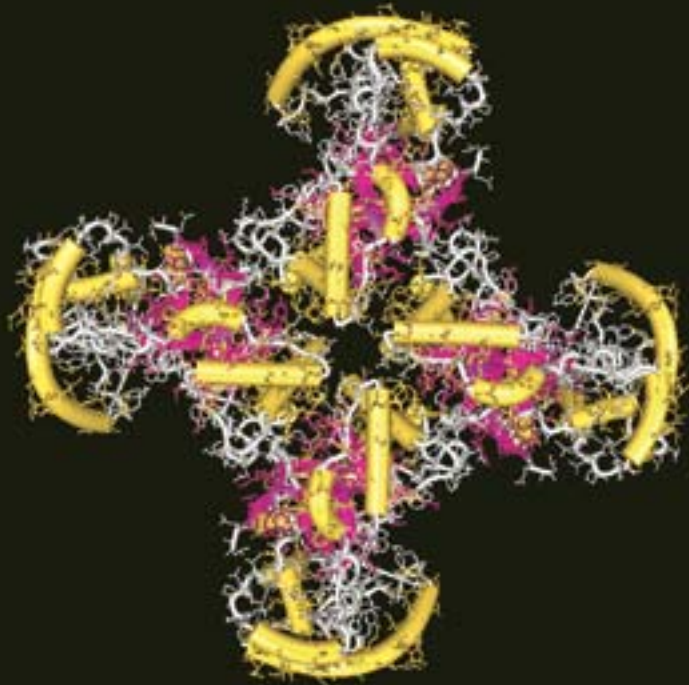


Urinary bladder disorders affect more than 200 million people worldwide. The discovery of new drugs that offer important advantages over existing therapies is being pioneered by a research agreement between emerging biopharmaceutical company Lectus Therapeutics Limited and researchers in the University's Pharmacology Department.



A potassium channel accessory protein

Ioning out health problems

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for new drugs,
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Ion channels are present in virtually every living cell. They are proteins that sit within the membrane that surrounds each cell, acting as a 'doorway' through which ions – charged atoms such as potassium (K^+), sodium (Na^+) and calcium (Ca^{2+}) – can pass. Channels differ with respect to the ions they allow through, and to the way they regulate the flow of these ions.

In the search for new drugs, ion channels have become a favourite target since they provide the ability to regulate many physiological processes – your heart beat, for example – and they could potentially be used to treat a wide range of diseases including incontinence, diabetes, epilepsy, migraine, pain, allergy and asthma, glaucoma, stroke, irregular heart beat and cancer. According to a recent report, the 28 ion channel drugs currently on the market target just five ion channel proteins, but they still generate worldwide sales in excess of \$12 billion. Given that

406 ion channel genes, representing some 1.6% of the human genome, have been identified, ion channels as a class of drug targets appear to be relatively under exploited.

Many of the research programmes currently aimed at discovering and developing ion channel drugs focus on the ability of small molecules to bind at, or close to, the opening of ion channels, thereby obstructing or restricting the flow of ions. However, the development of such drugs to treat disorders such as an overactive bladder and urinary incontinence has been limited due to undesirable side effects, like the lowering of blood pressure. This is because the drugs are not sufficiently specific about which ion channels they target. Lectus Therapeutics, a Bristol-based biotech company, was formed to address this problem since there is clearly a need for next-generation ion channel drugs that can be more selective and can target ion channels in particular cells and tissue types. →

→ Upon commencement of operations in 2003 Lectus Therapeutics entered into a research agreement with the University to fund research within the Department of Pharmacology. Under this agreement scientists funded by the company are researching the

potential to regulate the flow of ions through an ion channel. Incontinence, for example, is a problem that affects women in particular, as they grow older. It occurs as a result of the muscle in the bladder wall becoming overactive. If the relevant ion channel

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potential of new drugs to alter the function of a particular ion channel (in this case a K^+ channel), by acting on accessory proteins that regulate the function of this channel. This will be achieved through the use of technologies and tools developed by Lectus Therapeutics to study interactions between ion channel proteins and their accessory proteins.

Their system allows ion channel accessory proteins to be attached to a solid surface in a controlled and orientated manner, such that the proteins are suitable for high throughput drug screening purposes. Potential drug candidates are identified as those that can alter the binding between an ion channel accessory protein and the ion channel protein itself, since drugs that are able to alter this interaction ultimately have the

in the muscle could be kept open for longer, as a result of a new drug regulating the ion flow, the desire to urinate would be less frequent and the degree of incontinence reduced or eradicated.

The scientific team in the University has access to a series of compounds identified by Lectus Therapeutics as being potential next-generation ion channel modulators. Already the team has shown that these compounds affect ion channel function in a manner consistent with them having an improved ability to be more selective when targeting ion channels. Although there is still a long way to go, ultimately the outcome of these findings will aid the development of remedies to supplement the current paucity of pharmaceutical treatments for urinary bladder disorders.

The relationship between the University and Lectus Therapeutics is an excellent example of how the gap between industrial and academic research can be bridged to bring mutual benefit. ■

www.bristol.ac.uk/depts/Pharmacology

Lectus Therapeutics Limited

Lectus Therapeutics Limited was co-founded by Dr **Roland Kozlowski** (of the Department of Pharmacology, Bristol University, and CEO of Lectus) and Dr **V Paul Gerskowitch** (Commercial and Development Director at Lectus). In September 2003 Lectus received financial backing from the SULIS Seedcorn Fund, a fund set up to support the early-stage commercialisation of research generated by the universities of Bristol, Bath and Southampton. More recently, Lectus Therapeutics has closed on a very significant strategic deal with Takeda Research Investment, the investment arm of Takeda Chemical Industries, which is the largest pharmaceutical company in Japan.

Lectus Therapeutics possesses a proprietary proteomics platform called LEPTICSTM™ (Leveraged Enabling Proteomics Technology for Ion Channel Screening) that enables the discovery of ion channel modulators that cannot be readily identified using conventional methods. The company's vision is to become a world leader in developing ion channel therapeutics with an enhanced safety profile. To achieve this, Lectus Therapeutics will exploit the power of LEPTICSTM™ and build on its knowledge of ion channels and protein-protein interactions, to develop next-generation ion channel modulators that offer important clinical and economic advantages over existing therapies.

The company's primary focus is to relieve problems associated with urinary bladder disorders, angina and hypertension. ■

www.lectustherapeutics.com

