A cell penetrating peptide delivery platform

A cell penetrating peptide that enables delivery of functional molecules into cells that are otherwise not cell permeable.

The plasma membrane of cells is poorly permeable to both drugs and proteins (including DNA), whilst DNA is also a very inefficient translocator within cells. Thus, delivery of biologically active molecules into cells is very difficult. By attaching a cell-penetrating peptide (CPP), either covalently or non-covalently, the intracellular delivery of biomolecules and proteins can be significantly improved.

A novel CPP designated X-entry derived from the X-protein of the hepatitis B virus, which is essential for virus infection was identified by Associate Professor Geoff Krissansen at The University of Auckland. X-Entry is a platform technology that enables delivery of a variety of biological cargo molecules into cells, including therapeutic agents.

Studies to date have shown that X-entry transports functional cargoes across cell membranes, including large molecules inhibitory peptides, functional antibodies, an enzyme, oligonucleotides and siRNAs.

We have also undertaken biodistribution studies with X-entry alone, and attached to an enzyme cargo. These studies showed highest level of X-entry uptake by the heart, lung, liver, kidney, small intestine, spleen and stomach.

Applications

• Delivery of large molecules into cells to reach an intracellular target
• Delivery of small molecules that are not efficient at getting into cells
• Intracellular delivery of therapeutic agents to combat disease
• Intracellular protein replacement due to defective genes
• Delivery of imaging agents into cells
• Research Tool

Key Aspects

• It is only taken up by adherent cells, which prevents X-entry being "mopped up" by blood cells following injection, thereby enabling more efficient targeting of tissues thus improving efficacy, while limiting potential off target toxicity.
• It is small compared to other known peptides - only 7 amino acids in length therefore costs of goods are lower.
• Uptake is more controllable as uptake is specifically via syndecan-4 (and potentially other syndecans), whereas other CPPs use syndecans and a multitude of other mechanisms.
• It is taken up into the cytoplasm and nucleus of the cell.
The Molecular and Cellular Biology Research Group

The discovery of the novel CPP came out of work conducted by the Immunology, Diabetes and Cancer Research Group, led by Associate Professor Geoff Krissansen.

Associate Professor Krissansen has published over 100 papers in peer-reviewed journals and filed 20 patent applications. He has held two prestigious fellowships, the Wellcome Trust (UK) Senior Medical Research Fellowship in New Zealand, and the James Cook Associate Professorial Research Fellowship (Royal Society of New Zealand).

In 1993, Associate Professor Krissansen was awarded the Butland Distinguished Medical Science Award. His work has led to potential treatments for multiple sclerosis, cancer and asthma.

Projects in the Immunology, Diabetes and Cancer Research Group are centred on understanding and finding treatments for a variety of inflammatory diseases, including cancer.

IP Position
A family of patents have been filed, including composition of matter. Other patents include the use of novel cargoes conjugated to X-entry.

The University of Auckland

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The University of Auckland is an international centre of learning and academic excellence. It is New Zealand’s pre-eminent research-led institution and has key linkages with many of the world’s top research intensive universities.

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