PEGylated dendrimers: a novel mechanism of drug delivery

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Monash Institute of Pharmaceutical Science (MIPS) researchers, in collaboration with the biotechnology company Starpharma Holdings Ltd have developed a new method to deliver medications that may benefit thousands of patients with particular types of cancer, HIV and lymphatic conditions world-wide.

The Melbourne-based research team has shown how PEGylated Polylysine dendrimers, a new type of nano-sized drug delivery system, can be altered to target either the lymphatic system or the bloodstream.

Lead researcher at MIPS and the Associate Dean of Research, Professor Chris Porter said the discovery has particular implications for the treatment of diseases which are spread via the lymphatics and lymph nodes.

"We are excited by the possibilities that this technology may provide in the improved treatment of particular types of diseases, including metastatic cancer, lymphoma, HIV and metastitial tuberculosis," Professor Porter said.

Dendrimers are precisely defined, synthetic nanomaterials that are approximately 5-10 nanometres in diameter. They are made up of layers of polymer surrounding a central core. The dendrimer surface contains many different sites to which drugs may be attached and also attachment sites for materials such as polyethylene glycol (PEG) which can be used to modify the way the dendrimer interacts with the body.

PEG can be attached to the dendrimer to 'disguise' it and prevent the body's defence mechanisms from detecting it, thereby slowing the process of breakdown. This allows the delivery system to circulate in the body for an extended time period, maximising the opportunities for the drug to reach the relevant sites.

Professor Porter's group and Starpharma have been investigating dendrimer-based drug delivery systems for some time - but these most recent finding appear to hold particular promise.

The data, published in the Journal of Controlled Release, demonstrates that by increasing dendrimer size by increasing the chain length of attached polyethylene glycol (PEG) chains, a dramatic increase in absorption efficiency after subcutaneous injection can be achieved and transported into the lymphatic system. Conversely, a shorter PEG chain was shown to lead to rapid absorption into the blood.

"Our work suggests that careful design of the size and surface characteristics of PEGylated Polylysine dendrimers provides an opportunity to choose whether these delivery systems are absorbed and distributed via the bloodstream or the lymphatic system," Professor Porter said.

"The ability to target therapeutic treatments in this way offers the potential to maximise drug concentrations at sites of action within the lymphatic system - and importantly to minimise concentrations elsewhere, potentially reducing side effects and toxicity. It is still early days, but we're confident the potential for improved patient treatment is significant'.

Provided by Monash University