# Cancer cells' communication path blocked

October 17 2013

Lund University cancer researchers have discovered the path used by exosomes to enter cancer cells, where they stimulate malignant tumour development. They have also succeeded in blocking the uptake route in experimental model systems, preventing the exosomes from activating cancer cells.

The Lund University research team has looked at how cancer cells communicate with surrounding cells and how this encourages the development of malignant tumours. The idea is to try and inhibit tumours by disrupting this communication. The focus of their research is 'exosomes', small virus-like particles that serve as 'transport packages' for genetic material and proteins transmitted between cells.

The importance of exosomes in the tumour microenvironment has been demonstrated within the field in recent years, as it has been shown that tumour development is halted if the production of exosomes inside the cancer cell is stopped.

"However, it is very difficult to achieve this in a clinical situation with patients. A major question in the field recently has therefore been the uptake path into the cell. How do the exosomes get into the recipient cells? That is what our discovery is about", says Mattias Belting, research group leader and Professor of Clinical Oncology at Lund University.

The Lund researchers' discovery is the exosomes' journey from the sender cell to the receiver cell and how the receiver cell captures and internalizes the exosomes. They have also found a way to block the path

to uptake in the receiver cell.

"When we block the path into the cell, we also block the functional effects of the exosomes. This means that the entry route now appears to be a very interesting focus point for future cancer treatments", says Mattias Belting.

In the current study, the Lund researchers have shown that heparan sulfate proteoglycans – proteins with one or several long sugar chains connected to them – serve as receptors of exosomes and carry them into the cell. It is the proteoglycans' sugar chains, heparan sulfate, that capture the exosomes at the surface of the cell.

"Previous studies have shown that heparan sulfate plays a role in the cells' uptake of different viruses, such as HIV and the herpes simplex virus. In this way, the mechanism by which exosomes enter cells resembles the spread of viral infections", says Helena Christianson, doctoral student in Belting's research team and first author of the study.

Earlier this year, Mattias Belting and his colleagues published an article in *PNAS* that showed how they had managed to isolate exosomes in a blood sample from brain tumour patients. The analysis suggested that the content of the exosomes closely reflected the properties of the tumour in a unique way.

"Research on exosomes is exciting and relatively new. There is significant potential for exosomes as biomarkers and treatment targets of various cancers as we learn more about them", says Mattias Belting.

**More information:** Christianson, H. et al. Cancer cell exosomes depend on cell-surface heparan sulfate proteoglycans for their internalization and functional activity, *PNAS*. www.pnas.org/content/early/201 … /1304266110.abstract

Provided by Lund University