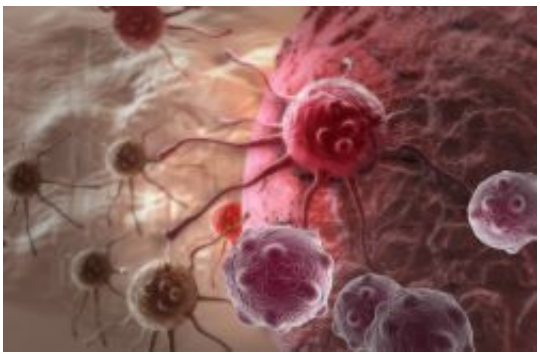
Discovery that 'size matters' in cell-to-cell communication could unlock new methods for disease diagnosis and treatment

March 27 2017, by Elizabeth Allen



Credit: University of Lincoln

Size really does matter when it comes to the mechanisms that cells use to communicate with each other, according to pioneering new nanobiotechnology research which has important implications for the diagnosis and treatment of disease.

An international team of scientists has made major strides in understanding 'exosomes' – tiny biological structures (or 'vesicles') which are used by cells in the body to transfer information. The researchers believe the findings could be significant for several fields of medical science, from personalising medical treatments to better understanding the growth and spread of cancerous tumours.

Exosomes are packed with proteins and RNA. They can be generated by one cell, taken up by another, and trigger a specific response. To date, scientific research has focused on the content of exosomes, but a new study led by scientists at the University of Lincoln, UK, focused instead on the size of exosomes and how this affects the way they work.

Led by Dr Enrico Ferrari, a specialist in nanobiotechnology, the team discovered that the smaller the exosomes are, the easier it is for target cells to pick them up. This makes communication between cells much faster.

The study examined exosomes taken from a patient with a high-grade glioma (rapidly growing brain tumour). The researchers had previously found that some stem cells within the patient's brain were producing exosomes that were responsible for supporting cancer cells and making them more aggressive.

Their latest work suggests that the level of aggression in a tumour could be determined by the size of the exosomes produced by the cancerous cells – for example the smaller the exosomes, the faster the cells can communicate and reproduce, and the quicker the cancer develops.

These initial findings could therefore have important implications for the prognosis of different cancers in the future, as doctors may be able to examine the size of the exosomes produced and more accurately predict the course of a patient's tumour.

The study was carried out by researchers from the School of Life Sciences at the University of Lincoln, UK; the Department of Medical and Biological Sciences at the University of Udine; and the Department of Neuroscience at Santa Maria della Misericordia University Hospital, both in Italy. The findings are published in the scientific journal, *Nanomedicine: Nanotechnology, Biology and Medicine*.

"Rather than looking inside the exosome, we decided to take a detailed look at the nature of the vehicle, specifically its size", explained Dr Ferrari. "If you think of an exosome as a package, regardless of the specific molecules it carries, the nature of the 'envelope' is likely to be of great importance to the delivery of the message. The larger the envelope, the more difficult it is to deliver!

"Previous research has examined how size affects the behaviour of artificial nanoparticles in a human body, and this new study found that biological particles like exosomes may act in much the same way – the smaller they are, the 'louder' their message is, as it is easier for target cells to take them up and 'hear' the message.

"Traditionally it has been difficult to observe this behaviour in exosomes because they are extremely small (well below optical resolution), very elusive, and difficult to isolate. However, our team developed a new set of techniques to overcome all of these factors and answer important questions about size-dependent uptake, which previously have not been addressed.

"The size of different exosomes has been explored in a few other studies, but never in relation to how effectively they can deliver their messages."

The new research could also have future implications for the delivery of medicine, as exosomes could potentially be used as nanocarriers for specific drugs. The scientists predict that it may be possible to manipulate the size of exosomes used in therapeutics to make them more effective, and to use the personalised exosomes produced in the human body – or particles which mimic the way they behave – to achieve more targeted and efficient drug delivery. This process is called exotherapy.

The team now hopes to pursue further research in this area to more

accurately understand the impact of exosome size on the way that cells communicate, and develop ways this knowledge can be used in the diagnosis, prognosis and treatment of individual patients.

More information: Federica Caponnetto et al. Size-dependent cellular uptake of exosomes, *Nanomedicine: Nanotechnology, Biology and Medicine* (2017). DOI: 10.1016/j.nano.2016.12.009

Provided by University of Lincoln