Cancer cells spread by releasing 'bubbles'

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A new fundamental mechanism of how tumour cells communicate has just been discovered by the team of Dr. Janusz Rak at the Research Institute of the McGill University Health Centre (MUHC) in collaboration with Dr Guha from the University of Toronto.

The cancer cells are able to communicate with their more healthy counter-parts by releasing vesicles. These bubble-like structures contain cancer-causing (oncogenic) proteins that can trigger specific mechanisms when they merge into non or less-malignant cells. These findings could change our view on how cancerous tissues work and lead to major clinical innovations. They were published on April 20 in the on-line edition of *Nature Cell Biology*.

The surface of some brain tumour cells has long been known to express a mutated version of what is called the variant III epidermal growth factor receptor (EGFRvIII). Although this factor is expressed only in a fraction of tumour cells, it has a major impact on the malignancy of the whole tumor. How could this cellular minority have such an important impact" This mechanism was still unknown… until now.

This study shows that the mutated EGFRvIII triggers production of small vesicles that project from the cell membrane and that carry mutated copies of EGFRvIII on their surfaces. They were baptised “oncosomes.” Surprisingly enough, this shows that oncoproteins are not always confined to the cell that produced them. In this case they even migrate!

Oncosomes will migrate until they fuse with another cell, either healthy

or benign tumoral. Oncogenic protein AGFRvIII then becomes integrated in the membrane of the “recipient” cell and starts stimulating specific metabolic pathways to make it act in an aberrant and malignant way. Although this may be a transient event, the changes could impact tumor behaviour by more rapid increases in cell numbers and by stimulation of blood vessel growth, hallmarks of malignant brain tumors.

“With this information we can imagine that many mutant proteins are not necessarily confined to the cells that make them, but rather can migrate and spread around as cargo of oncosomes, a process that could be referred to as formation of the “oncogenic field effect,” explained Dr. Rak. “It demonstrates that cancer is a multi-cell process, where the cells talk to one another extensively. This goes against the traditional view that a single ‘mutated’ cell will simply multiply uncontrollably to the point of forming a tumour. This discovery opens exciting new research avenues, but we also hope that it will lead to positive outcomes for patients.”

Indeed, the presence of oncosomes (containing EGFRvIII or other proteins) in blood of cancer patients could become a clinical marker, meaning that doctors could screen for a tumour’s molecular characteristics instead of having to perform invasive surgery or biopsy. Currently, in the case of brain cancer, this very precise assessment cannot be performed without removing the tumour and therefore opening a patient’s skull.

However, the assay and analysis of oncosomes would potentially only require taking a small sample of blood or cerebrospinal fluid. This would be a step in ensuring patient comfort and choosing the best therapeutic strategy for them, factors that are key in the journey towards personalized medicine in a hopefully not-too-distant future.

Source: McGill University