Extracellular vesicles: a potential way to detect cancer

Research Objectives

Dr. Lee studies the role of cancer cell-derived extracellular vesicles (EVs) in mediating drug resistance.

Detail

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Bio
Wai-Leng Lee started her research on the discovery of novel anticancer activities of plant-based therapeutic agent. After joining Monash, she has won several grants that support her research on the potential of extracellular vesicles as chemoresistance markers (markers that predict treatment outcome) for cancer management.

Funding
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Collaborators
• Prof Ian C. Paterson from the Department of Oral and Craniofacial Sciences, University of Malaya, Malaysia
• Associate Prof Bey-Hing Goh from the College of Pharmaceutical Sciences, Zhejiang University, China
• Prof Teng-Aik Ong and Dr Jasmine Lim from the Faculty of Medicine, University of Malaya, Malaysia
• Prof Bayden Wood from the Centre for Biospectroscopy and School of Chemistry, Monash University Clayton

References

• Le Yap, X. (2019). Study of cancer-derived extracellular vesicles in urine using IR spectroscopy for the detection of prostate cancer. Progress in Drug Discovery & Biomedical Science. Available at: https://doi.org/10.26180/5dd73203ec1b9

Personal Response

What sparked your interest in extracellular vesicles?

"My interest on EVs started from my observation on cancer cells’ responses to treatment in my PhD project. In the treated cancer cells, fluorescent-labelled drug compounds were found trapped in vesicular structures which were not yet characterised by that time as EVs. This observation led me to intensively follow the development of EV research around the world. Increasing evidence shown by many research teams in characterising EVs as a tool for cell-cell communication then strengthened my hypothesis on the role of EVs in regulating chemoresistance in cancers."
Extracellular vesicles

A potential way to detect cancer

Communication is essential for cells. One of the possible ways to communicate with neighbouring or distant cells is through the secretion of extracellular vesicles (EVs). All types of cells secrete EVs. The various molecules (proteins, lipids and nucleic acids) contained in EVs provide information about the originating cell and its physiological state. This is how EVs serve as a communication tool.

Depending on characteristics such as their size, density, morphology and composition, EVs are classified into different subsets which include exosomes (30–100 nm), microvesicles and late endosomes (30–1000 nm), and microparticles (100–1000 nm).

Recently, EVs have gained the attention of researchers such as Dr Wai-Leng Lee from Monash University Malaysia because EVs can provide information about health and disease, and — more particularly — about cancer progression.

A NEED FOR EARLY CANCER DIAGNOSIS

Cancer results in almost 10 million deaths per year. One in six deaths is caused by cancer and it is estimated that one in three individuals will be diagnosed with cancer in their lifetime. One of the reasons why cancer causes so many deaths is that it is diagnosed too late, at a stage where it is not responsive to existing treatments. This is why one of the aims of current clinical research is to identify tools that enable early cancer detection.

Diagnosing cancer early, even before clinical symptoms appear, would greatly increase survival rate of patients. Indeed, suitable treatments could be administered before the condition of the patient becomes irreversible and could delay or even prevent further progression of the disease.

However, diagnosing cancer at an early stage can be challenging as current methods, such as imaging techniques, often detect cancer at a late stage, when tumour mass is already visible. This is where EVs could be useful.

CANCER BIOMARKERS

A biomarker is an indicator of the severity or presence of a particular disease state. During a blood test, for example, quantities of different biological substances can be measured and, if the level of a certain substance is out of the “normal range”, it indicates the presence of a specific condition.

Cancer leads to some specific biochemical changes that could be used for early cancer diagnosis. These biomarkers could be detected with a technique known as Fourier transform infrared spectroscopy, which can be used to analyse biological materials. Blood and tissue samples are the most widely used materials to diagnose various diseases, but these biological samples are complex, composed of a high number of substances that provide excessively abundant information. EVs, however, may be convenient tools. EVs can be isolated from blood, urine, saliva or breast milk. Spectroscopy could then be used to identify the molecules contained in these EVs which reflect the condition of their originating cells and provide information about disease progression.

EV AND CANCER DETECTION

Different studies have suggested that EVs may be a useful tool in the diagnosis of various diseases including cancer, diabetes, central nervous system disorders, cardiovascular and autoimmune diseases. That is because EVs contain molecules that can be characteristic of these diseases, and thus can be used as biomarkers.

EVs are implicated in cancer progression. They act on neighbouring or distant cells and contain some cancer-specific proteins that are involved in diverse processes such as proliferation and malignancy, which are useful for cancer to spread.

By examining EVs, these cancer-specific proteins can be detected and used as biomarkers to diagnose cancer. Dr Lee and her team proved that it was possible by examining the EVs present in urines of patients with prostate cancer and of healthy participants. The EVs were analysed using FTIR spectroscopy and, from the data about EV composition obtained with this technique, they could accurately determine which EVs originated from prostate cancer patients and which came from healthy participants. This is why EVs are considered a promising tool in cancer diagnosis and treatment.

EV AND CANCER TREATMENT

Detecting EVs could be useful not only for diagnosis but also for effective cancer management. It could enable the accurate staging and grading of the disease, which is required to establish suitable treatments.

It could also help to monitor the response to treatment and detect the presence of a potential relapse, so that the treatment can be adequately adapted. In one of their studies, Dr Lee and her team discovered several EV proteins which can potentially be developed as therapeutic markers (biomarkers that can be used for both therapy and prognosis) and, if the activity of this protein is inhibited, cancer cells sense some stress.

These findings are essential for the development of personalised medicine, also called precision medicine, aiming to tailor therapy with the best response and highest safety margin to ensure better patient care.

EV AND DRUG RESISTANCE

Dr Lee and her team have studied EVs in different types of cancer, including oral cancer. They found that EVs played a role in drug resistance.

Drug resistance remains a severe problem in most chemotherapeutic treatments: chemotherapy, which is supposed to destroy cancer cells, is ineffective because cells are resistant. After it was suggested that EVs originating from cancer cells could mediate chemoresistance (drug resistance to chemotherapy), the team from Monash University Malaysia examined EVs from oral squamous cell carcinoma (OSCC) cell lines that were more or less sensitive to a chemotherapeutic drug known as cisplatin. They observed that resistant cell lines produced more EVs.

Moreover, proteins contained in EVs secreted by resistant cells were different from those found in EVs originating from sensitive cell lines, and different resistant cell lines produced EVs with different protein content. For example, EVs from resistant cells had lower levels of a protein named ATP1B3 which is involved in the transport of cisplatin into cells. As a result, less cisplatin accumulates in resistant cells.

The role of EVs in mediating drug resistance was confirmed when Dr Lee and her team inhibited EV secretion: when blocking the release of EVs by resistant cells, more cisplatin accumulated in resistant cells and decreased the viability of the cells. This suggests that inhibition of EV release could be a novel therapeutic approach to sensitize drug-resistant cells to chemotherapy.

EV AND CANCER CELL SURVIVAL

In another study, Dr Lee and her team observed that EVs originating from colon cancer cells promoted survival of neighbouring cancer cells. This observation came from an experiment in which they inhibited a protein named KRAS, which contributes to the malignancy of many cancers, can be found in EVs from cancer cells. Inhibiting the activity of this protein induced stress in colon cancer cells. In response to this stress, a high level of EVs was secreted. These EVs secreted in response to stress contained a high level of a protein known as ACSL4, which promoted the survival of the cancer cells that receive these EVs.

These findings suggest that EVs contribute to cancer survival mechanisms: as oncogenic activity is inhibited, cancer cells sense some kind of threat. This induces a stress. Cancer cells then release more EVs to communicate with neighbouring cancer cells and promote their survival.

EV FOR AND AGAINST CANCER

This is still a controversial research: is EVs and their association with cancer. Dr Lee’s work advances our understanding of how EVs help cancer progression by promoting survival of cancer cells and mediating drug resistance and uncovers ways to use EVs for cancer diagnosis and treatment.
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