Eavesdropping on cell communications to treat cancer with drug resistance

An estimated 19.3 million new cancer cases and almost 10 million cancer deaths occurred worldwide in 2020.

It’s estimated that one in three individuals will be diagnosed with some kind of cancer in their lifetime. When cancer is diagnosed at a stage where it’s not responsive to treatments, it usually becomes a fatal disease. To date, drug resistance remains a critical obstacle in most chemotherapeutic treatments for cancer patients.

It’s for this reason that there is a pressing need to identify targets for effective treatment of drug resistant cancers.

Cells can communicate with each other. They communicate with neighbouring or distant cells by secreting lipid-bound vesicles known as extracellular vesicles (EVs). All types of cells discharge EVs, which provide information about the originating cells and their physiological state.

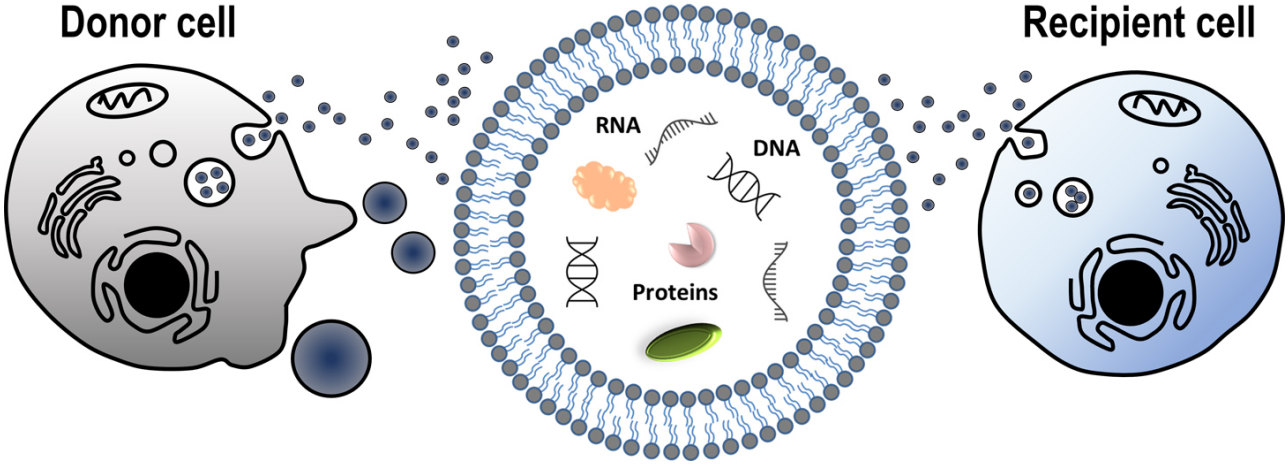

Fig. 1. EVs contain various molecules such as proteins, lipids, and nucleic acids that represent the molecular makeup of the donor cell. Uptake of EVs by recipient cells as a form of cell-cell communication.

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 (50–1000 nm), ectosomes (100–350 nm) as well as microparticles (100–1000 nm).

Recent studies found EVs contain some cancer-specific genetic materials and proteins involved in diverse processes such as proliferation and malignancy, which are useful for cancer to grow and to spread rapidly, thus making them as attractive targets for inhibiting cancer progression.

However, there's still much to learn about EVs and their association with cancer.

This study aimed to provide insights on how EVs help cancer progression by promoting cancer cells' survival and mediating drug resistance. 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), a panel of oral squamous cell carcinoma (OSCC) cell lines with more or less sensitive to a chemotherapeutic drug known as cisplatin were examined.

The resistant cell lines were observed to produce 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 similar 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.

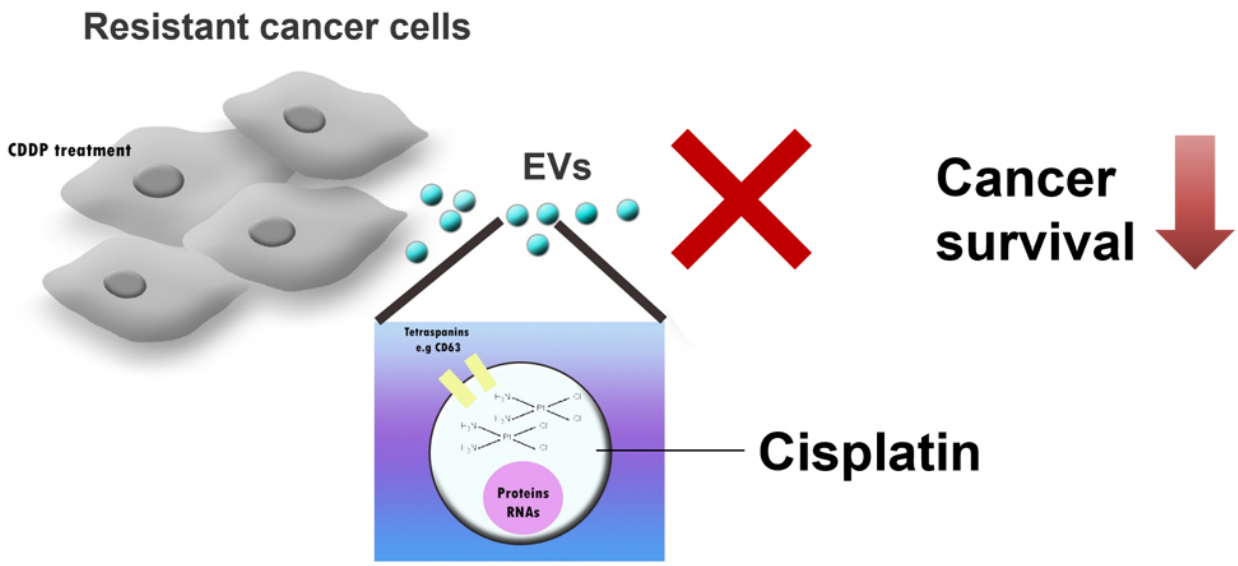

Fig. 2. Inhibition of EV secretion decreases the viability of cisplatin-resistant oral cancer cells suggesting inhibition of EV release could be a novel therapeutic approach to sensitise drug-resistant cells to chemotherapy.

The role of EVs in mediating drug resistance was confirmed when blocking the release of EVs by

resistant cells, more cisplatin accumulated in resistant cells and decreased viability of the cells were observed. This suggests that inhibition of EV release could be a novel therapeutic approach to sensitise drug-resistant cells to chemotherapy.

Xin-Hui Khoo [1], ***Ian C. Paterson*** [2], ***Bey-Hing Goh*** [3], ***Wai-Leng Lee*** [1]
[1]*School of Science, Monash University Malaysia, Subang Jaya 47500, Selangor, Malaysia*
[2]*Department of Oral and Craniofacial Sciences, University Malaya, Kuala Lumpur 50603, Malaysia*
[3]*Biofunctional Molecule Exploratory Research Group (BMEX), School of Pharmacy, Monash University Malaysia, Subang Jaya 47500, Selangor, Malaysia*

Publication

Cisplatin-Resistance in Oral Squamous Cell Carcinoma: Regulation by Tumor Cell-Derived Extracellular Vesicles
Xin-Hui Khoo, Ian C Paterson, Bey-Hing Goh, Wai-Leng Lee
Cancers (Basel). 2019 Aug 14