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Can P-glycoprotein (P-gp) be involved in the release of larger extracellular vesicles by multidrug resistant cells?

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Cancer multidrug resistance (MDR) is a major cause of treatment failure, in which cells are resistant to various drugs, being associated with the overexpression of drug-efflux pumps such as P-glycoprotein (P-gp). It was recently discovered that the drug-resistant phenotype can be horizontally transferred from drug-resistant (DR) donor cells to drug-sensitive (DS) recipient cells, through intercellular communication mediated by extracellular vesicles (EVs). These EVs include exosomes (typically smaller, with origin in the endocytic pathway) and microvesicles (typically bigger, with origin in the plasma membrane). Previous work from our group showed that MDR cells (overexpressing P-gp) released more microvesicles than their DS counterpart cells. Nevertheless, it is not known if this phenomenon is extensive to all DR cancer cells or if it is restricted to MDR cells. In this study, we aimed to verify if two pairs of DR cells (without expression of P-gp) also produce more microvesicles than their DS counterparts. EVs shed by both DS and DR cell lines were isolated by ultracentrifugation and characterized using transmission electron microscopy (TEM) for morphology analysis, dynamic light scattering (DLS) and nanoparticle tracking analysis (NTA) for analysis of size, and Western blot for analysis of the expression of EVs markers. We confirmed that the DR cells did not express P-gp and verified that the EVs shed by these cells have similar sizes to the ones released by their DS counterparts. These findings suggest that P-gp may be associated with the release of larger EVs by MDR cells. Future work will confirm this hypothesis.

Biography

M Inês Silva is currently a Master's student in the Department of Molecular Medicine and Oncology at the Faculty of Medicine, University of Porto (FMUP) and a Visiting Researcher at University of Porto, Portugal. She obtained her First degree in Biochemistry from the Faculty of Sciences of the University of Porto (FCUP) and the Institute of Biomedical Sciences Abel Salazar (ICBAS), in July 2016. She carried out her curricular internship in the Cancer Drug Resistance Group of University of Porto, Portugal.

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