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Is the dissemination of cancer multidrug resistance phenotype influenced by the shedding of extracellular vesicles by resistant tumor cells?

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Cancer multidrug resistance (MDR) is a major cause of treatment failure, being defined as a phenomenon by which cancer cells develop cross-resistance to several drugs. One of the main causes of cancer MDR is the overexpression of drug-efflux pumps, such as P-glycoprotein (P-gp). Recent studies have shown that extracellular vesicles (EVs) contribute to the dissemination of cancer MDR and interestingly, P-gp is one of the mediators which is transferred by tumor drug-resistant (donor) cells to tumor drugsensitive (recipient) cells via EVs. The present study aimed to add knowledge to the current understanding of the relevance and mechanisms of EVs-mediated dissemination of cancer MDR. Two pairs of cell lines from two different tumor models (leukemia and lung cancer) were used, consisting of a drug-sensitive cell line and its MDR (P-gp overexpressing) counterpart. The characterization of the EVs isolated from these cells was previously described by our group. The EVs released by donor cells and those captured by the recipient cells were quantified by nanoparticle tracking analysis and flow cytometry, respectively. Moreover, the ability of EVs derived from MDR cells to transfer a MDR phenotype to drug sensitive recipient cells was assessed by sulforhodamine B assay or trypan blue exclusion assay. Our results indicate that the EVs-mediated transfer of MDR phenotype seems to follow characteristic and regulated mechanisms, regarding both the release of EVs by donor cells and the uptake of EVs by recipient cells.

Biography

Diana Sousa has completed her First degree in Biochemistry from the Advanced Institute of Health Sciences North, in 2009 and Master's degree in Molecular Genetics from the School of Sciences, University of Minho, in 2011. From 2011 to 2014, she was a Research Fellow (BI) at the Cancer Drug Resistance Group of IPATIMUP. Currently, she is a PhD student at the Faculty of Pharmacy of the University of Porto carrying out her research work at IPATIMUP/i3S. She has published 16 peer reviewed publications and has presented her work in national and international meetings.

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