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EFFECT OF OUTER MEMBRANE VESICLES FROM PSEUDOMONAS AERUGINOSA ON REGULATED CELL DEATH IN MALIGNANT CELLS

Background. Triggering immunogenic types of regulated cell death (RCD) as PANoptosis can sensitise drug-resistant tumours and can rely on an efficient drug-delivery system such as outer membrane vesicles (OMVs). **Aim.** To evaluate the cytotoxic and inflammatory pro-death activities of OMVs from *Pseudomonas aeruginosa* (Pae) ATCC10145 associated with doxorubicin (DOX) in human leukaemic monocyte cells THP-1. **Methods.** Expression levels of marker genes for apoptosis, pyroptosis and necroptosis in THP-1 cells treated with Pae OMVs or OMV-DOX system were assessed by qRT-PCR. The MTT test was used to assess the OMV cytotoxicity. Lactate Dehydrogenase (LDH) release was measured by colourimetric assay. The three-dimensional excitation-emission fluorescence matrix method was used to assess the interaction between the Pae OMVs and DOX. **Results.** Pae OMVs activated both intrinsic and extrinsic apoptosis signalling pathways in the THP-1 cell line, leading to the upregulation of the CASP3 and BAX genes and downregulation of the BCL2 gene. An enhancement of necroptosis (upregulation of the RIPK3, TLR4, and MLKL genes) has been detected. The OMVs also induced pyroptotic death of monocytes via the canonical RCD pathway. The changes in fluorescent characteristics of OMV-DOX revealed the formation of complexes between them. The loading of DOX into OMVs attenuated pyroptosis (downregulating the genes NLRP3, IL-1 β and CASP1). The results of the MTT and LDH assays were consistent with the qRT-PCR data. **Conclusions.** The effect of the nanostructured OMV-DOX system on human leukaemic monocytes in vitro results in profound transcriptional reprogramming of cell death, which may indicate the launch of a coordinated PANoptosis mechanism at the gene expression level. **Funding.** The project PH/68, implemented by the Ministry of Education and Science of Ukraine, was funded via the EU Framework Program for Research and Innovation "Horizon 2020" and the Simons Foundation (2026).

Keywords: bacterial vesicles, doxorubicin, PANoptosis.

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