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Deciphering the relevance of HMGB proteins in the contribution of tumor-derived extracellular vesicles to malignant transformation of normal ovarian cells

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Ovarian cancer is one of the most lethal gynecological malignancies worldwide because it tends to be detected late, when metastasis has taken place. Early diagnosis, when the tumor is still localized in the ovaries, is a clear advantage, since this rate then increases up to 92% (1). Several studies investigated the association of high mobility group box (HMGB) proteins with cancer due to their importance and the variability functions inside and outside the cells. HMGB1 and HMGB2 proteins are the most abundant members among HMGB family and they contribute to a variety of hallmarks of cancer such as sustained proliferative signaling, cell death resistance, replicative immortality, instability in the genome and increased mutations rates, tumor-promoted inflammation, growth repressors insensibility, cellular energetics deregulation, immune destruction evasion, metastasis, and angiogenesis stimulation. Moreover, HMGB1 has been repeatedly proposed as a diagnostic and prognostic biomarker for human ovarian cancer (2). High concentrations of extracellular vesicles (EVs) are found in various body fluids, including blood, urine, saliva, and seminal plasma. The proteins and RNAs enriched in (EVs) reflect the specific physiological conditions and functions of their samples. These (EVs) and their biomolecules are ideal biomarkers for liquid biopsy. In the present work, we analyze the influence of HMGB1 and HMGB2 in the composition of extracellular vesicles derived from ovarian cancer cells, and their role in the malignant transformation of normal ovarian cells. To do that, exosomes obtained from SKOV3 and HMGB1 derivative knockout cells were used to analyze the differences in the proteomic composition by using Trapped Ion Mobility Spectrometry time-of-flight (timsTOF) technology, as well as cell proliferation, cell migration and invasion, measurements of intracellular ROS levels, or qRT-PCR and Western blotting methods for several malignancy biomarkers.

(1) Reid, BM et al. (2017). Cancer Biol. Med., 14(1), 9-32

(2) Camara-Qu?lez M et al. (2020). Cancers, 12(9), 2435