PLATELET ACTIVATION AND AGGREGATION BY BREAST CANCER EXOSOMES

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**Introduction and objectives:** Thrombosis is a major cause of mortality in cancer patients. There is increasing evidence supporting the participation of tumor-derived extracellular vesicles in cancer-associated thrombosis. Tumor-derived vesicles may carry tissue factor (TF), the clotting initiator protein, as well as to modulate platelet function. In this study, we evaluated the ability of tumor-derived exosomes in promoting platelet activation, aggregation and plasma coagulation.

**Materials and Methods:** We employed two human mammary carcinoma cell lines: MCF-7 and MDA-MB231. Exosomes were isolated from conditioned media using Exoquick\(^\text{TM}\). Particle size was confirmed on a LM10 nanoparticle tracking analyzer. Platelet/exosome interaction was evaluated by confocal microscopy and flow cytometry analyses. Platelet aggregation was measured on a Chronolog aggregometer.

**Results:** The mean size of tumor-derived extracellular vesicles ranged from 146 to 151 nm for both cell lines. The MDA-MB231-derived exosomes interacted with platelets as seen by flow cytometry and confocal microscopy. Incubation of exosomes with platelets promoted P-selectin exposure, a known platelet activation marker we observed that MDA-MB231-derived exosomes showed a more pronounced effect than in MCF-7-derived exosomes. In addition, platelet aggregation promoted by the MDA-MB231-derived exosomes was higher than with MCF-7-derived exosomes. Exosomes from MDA-MB231 cells showed a higher TF level and procoagulant activity as compared to MCF-7-derived exosomes. Accordingly, MDA-MB231-derived exosomes accelerated platelet aggregation on platelet rich plasma in a TF-dependent fashion. **Conclusion:** Our results suggest that mammary carcinoma-derived exosomes interact with platelets, mediate their activation and aggregation, also favoring plasma coagulation and platelet aggregation through TF-dependent thrombin generation.

**Key Words:** Platelets, Exosome and Breast Cancer.

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