MALIGNANT TRANSFORMATION IN MELANOCYTES INCREASES THE PRODUCTION OF PROCOAGULANT MICROVESICLES

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A correlation between cancer and procoagulant states has long been described and several evidences suggest a critical role for blood clotting molecules in tumor biology. Since phosphatidylserine (PS)-positive microvesicles (MVs) shed by murine melanoma cells display an important pro-tumoral function *in vivo*, here we investigated the procoagulant properties of MVs produced by a non-tumorigenic melanocyte-derived cell line (melan-A) and its tumorigenic melanoma counterpart Tm1. Flow-cytometric analyses showed that the rate of MVs production was considerably higher in the tumorigenic cell line. On the other hand, PS exposure was nearly identical in MVs from both melan-A and Tm-1. We further investigated the formation of coagulation multimolecular complexes whose assembly is dependent on the presence of anionic surfaces such as PS-rich membranes. As expected, both MVs supported the assembly of intrinsic tenase (FIXa/FVIIIa/FX) and prothrombinase (FVa/FXa/prothrombin) complexes, accounting for FXa and thrombin production, respectively. In support of this observation, MV-dependent zymogen activation was inhibited upon blocking of PS binding sites by annexin V. Finally, both melanocyte and melanoma-derived MVs shortened the coagulation time of murine plasma following similar concentration patterns. This result suggests that both sorts of MVs contain similar levels of the clotting initiator, Tissue Factor. Altogether, our results suggest that quantitative rather than qualitative changes in the production of procoagulant MVs accompany the malignant phenotype acquisition by melanocytes.