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1-Exosomes-Mediated Transfer of Itga2 Promotes Migration and Invasion of Prostate Cancer Cells by Inducing Epithelial-Mesenchymal Transition

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Abstract: Although integrin alpha 2 subunit (ITGA2) mediates cancer progression and metastasis, its transfer by exosomes has not been investigated in prostate cancer (PCa). We aimed to determine the role of exosomal ITGA2 derived from castration-resistant PCa (CRPC) cells in promoting aggressive phenotypes in androgen receptor (AR)-positive cells. Exosomes were co-incubated with recipient cells and tested for different cellular assays. ITGA2 was enriched in exosomes derived from CRPC cells. Co-culture of AR-positive cells with CRPC-derived exosomes increased their proliferation, migration, and invasion by promoting epithelial-mesenchymal transition, which was reversed via ITGA2 knockdown or inhibition of exosomal uptake by methyl-β-cyclodextrin (MβCD). Ectopic expression of ITGA2 reproduced the effect of exosomal ITGA2 in PCa cells. ITGA2 transferred by exosomes exerted its effect within a shorter time compared to that triggered by its endogenous expression. The difference of ITGA2 protein expression in localized tumors and those with lymph node metastatic tissues was indistinguishable. Nevertheless, its abundance was higher in circulating exosomes collected from PCa patients when compared with normal subjects. Our findings indicate the possible role of the exosomal-ITGA2 transfer in altering the phenotype of AR-positive cells towards more aggressive phenotype. Thus, interfering with exosomal cargo transfer may inhibit the development of aggressive phenotype in PCa cells.

Keywords: prostate cancer; CRPC; exosomes; ITGA2; metastasis; EMT; IHC