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Horizontal transfer of miR-23a from hypoxic tumor cell colonies can induce angiogenesis

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Abstract

Neo vessel formation by angiogenesis is an important event during many pathological conditions including cancer, where it is indispensable for tumor growth and survival. Although, various pro-angiogenic cytokines and soluble factors, secreted by tumor cells, have been reported to promote angiogenesis, recent studies have shown regulatory role of exosomes, secreted by tumor cells in the process of angiogenesis. These exosomes are capable of carrying nucleic acids, proteins, etc., as their cargo. Under the light of these facts and considering the presence of miRNAs, the non-coding RNAs capable of regulating target gene expression, as one of the major cargos in the exosomes, we investigated, whether exosomes derived from normoxic and hypoxic tumor cell colonies exhibit difference in levels of miR-23~27~24 cluster members and if so, to check the significance of their horizontal transfer on the process of angiogenesis. Results of our study showed that exosomes secreted by hypoxic tumor cell colonies possess significantly higher levels of miR23a and can induce angiogenesis. Further, we have shown that exosomes secreted by cells that ectopically over express miR23a is capable of inducing angiogenesis in different angiogenic model systems such as CAM, in ovo Xenograft and HUVEC models systems. Further, mechanistic analysis revealed that miR23a driven regulation of angiogenesis is brought about by down regulation of SIRT1 in the recipient cells. Collectively, the results presented here suggest that exosomal transfer of miR23a from tumor cell colonies can induce the process of angiogenesis by targeting SIRT1 in the recipient endothelial cells.

Keywords: SIRT1; angiogenesis; exosomal transfer; miRNA 23a.

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