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Dissecting the role of extracellular vesicles in melanoma microenvironment

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INTRODUCTION & AIM

Melanoma is an aggressive cancer characterized by a rapid metastatic process. Thus, understanding the mechanisms underlying its progression is urgently needed to improve patient outcomes. In this regard, there is consistent evidence of a tumor-sustaining crosstalk between melanoma and subcutaneous adipose tissue; however, the role of EVs in this communication still needs to be clarified.

METHOD

After isolation by SEC, EVs were characterized by NTA, TEM and Western blot analysis. The impact of these particles on melanoma cell growth was evaluated by cell proliferation and colony formation assays, and the effects on metastatic potential were assessed by transwell assay. Melanoma cell stem-like traits, including spherogenic ability, ABCG2 enrichment and vemurafenib response, were investigated by sphere formation assay, flow cytometry and cell viability assay. The metabolic consequences of EV treatment were analyzed by Western blot and cytofluorimetric assays.

RESULTS & DISCUSSION

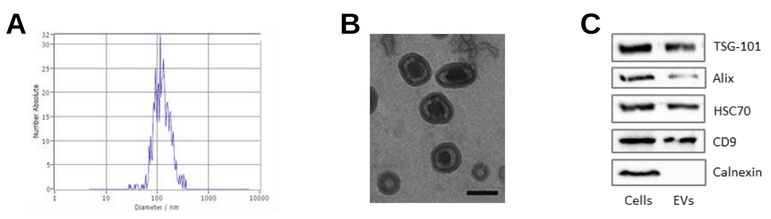


Fig. 1 Characherization of adipocyte EVs.
EVs were isolated by SEC and characterized by NTA (**A**), TEM (**B**) and WB (**C**). They were found to display the typical features of exosomes.

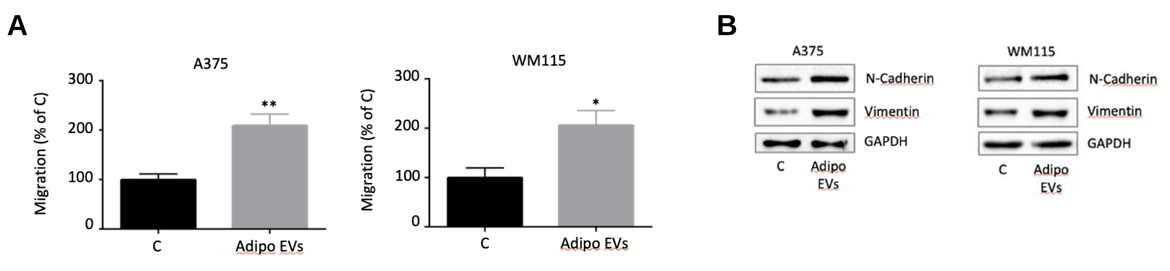
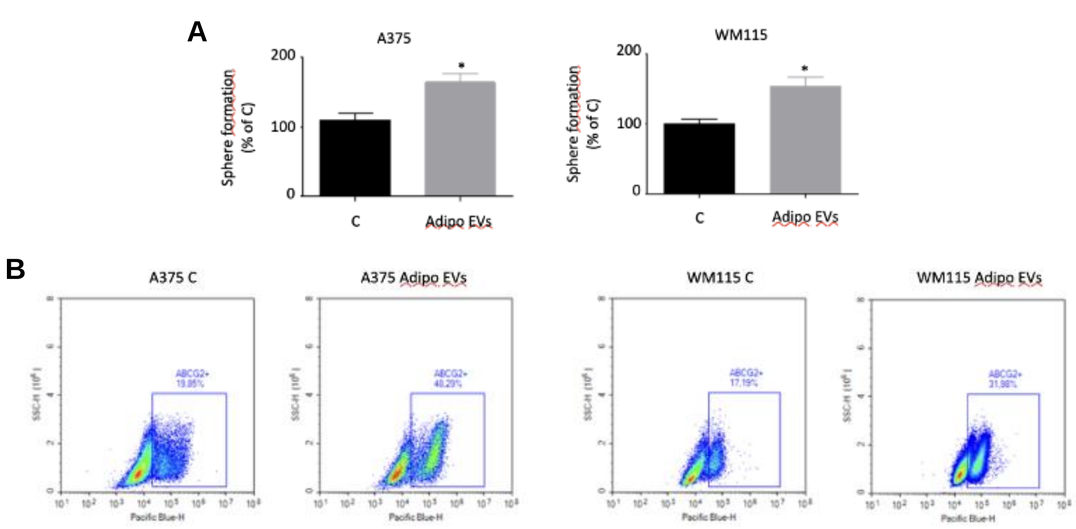


Fig. 2. Adipocyte EVs promote melanoma cell migration.
A375 and WM115 cells were treated with adipocyte EVs. In both cell lines, treatment with these vesicles led to an increase in tumor cell migration (**A**), correlating with EMT (**B**).



RESULTS & DISCUSSION

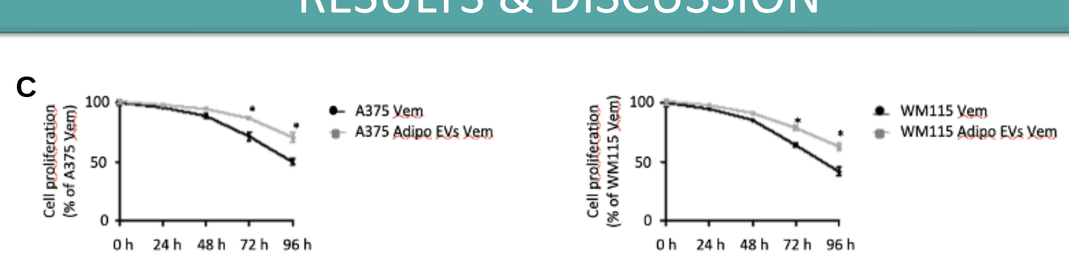


Fig. 3. Adipocyte EVs affect the stem-like features of melanoma cells.
Adipocyte-derived EVs were shown to promote the stem-like traits of melanoma cells, determining an increase in tumor cell spherogenic ability (**A**) and an enrichment in ABCG2 (**B**). This was accompanied by reduced responsivenness to vemurafenib (**C**).

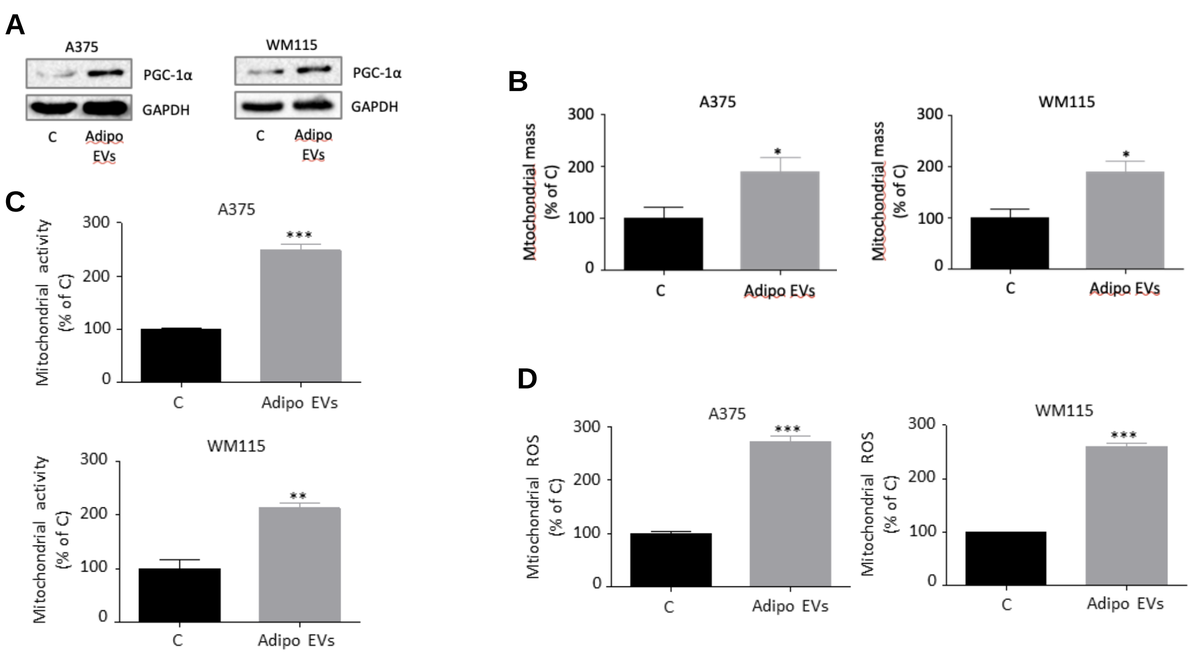
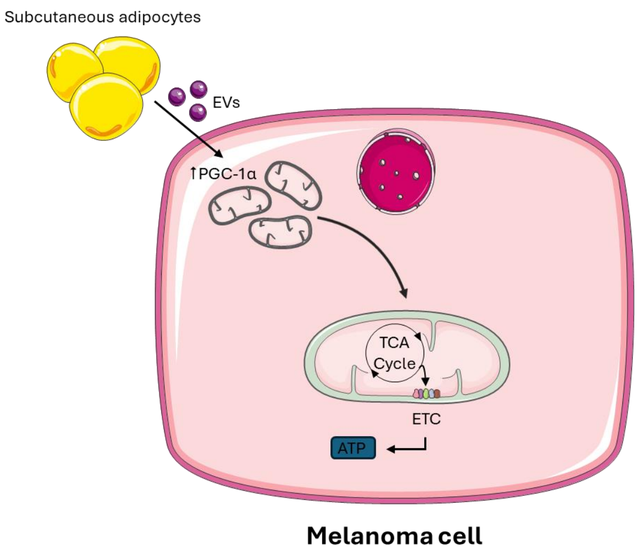


Fig. 4. Adipocyte EVs modulate melanoma cell mitochondrial metabolism.
An increase in PGC-1α protein levels was observed in melanoma cells treated with adipocyte EVs (**A**), resulting in enhanced mitochondrial mass (**B**), activity (**C**) and ROS production (**D**).

CONCLUSION

These results highlight the crucial role played by EVs in melanoma microenvironment, highlighting the ability of adipocyte-derived vesicles to sustain melanoma cell aggressiveness via PGC-1α activation.



FUTURE WORK

Future studies will be focused on the characterization of the adipocyte EV biological cargo.