Unraveling the role of extracellular vesicles in ovarian cancer stroma

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Ovarian cancer (OC) is still the most lethal gynecologic tumor, due to the rapid and silent development of omental metastasis. Thus, a deeper understanding of the mechanisms regulating OC progression may have crucial impact on the outcomes of this deadly disease.

There is consistent evidence of an association between obesity and increased OC aggressiveness. As omentum is rich in adipocytes, a key pro-tumor role for visceral adipose tissue has been postulated.

Indeed, a cross-talk between OC and omental adipose cells has been demonstrated; however, the study of this dialog has been limited to metabolites and adipokines, although recent findings point to a key role of extracellular vesicles (EVs) in the control of tumor evolution.

In the present study, we found that OC EVs could induce the production of multiple adipokines, namely interleukin 6, interleukin 1β, MCP-1 and TNFα, in adipocytes. In particular, these changes were accompanied by ERK1/2, p38 and JNK activation, which was demonstrated to modulate the release of all the above cytokines. More importantly, vesicular miR-210 seems to be deeply implicated in the pro-tumor switch of the OC EV-treated adipose cells. On the other hand, conditioned media from EV-treated adipocytes promoted OC cell migration and invasion as well as anoikis resistance; an increase in tumor stem-like traits was also observed. Finally, this media stimulated both macrophage and neutrophil recruitment, also favoring their polarization toward the pro-tumor M2 and N2 state, respectively. Overall, these data indicate that an EV-mediated bidirectional crosstalk exists between OC and adipocytes, endowing the latter with pro-inflammatory properties.