**Targeting M2-TAM via STAT3/NF-kB/AKT signaling pathway with Oxaliplatin, retinoic acid and *L. ferrea* -loaded Extracellular vesicles from Macrophages 1 down-regulates murine colon cancer metastasis.**

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**Conflict of Interest Statement:**

The authors declare no potential conflicts of interest.

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**SUPPLEMENTARY TABLES**

 **Table01**. List of antibodies used in the study.

|  |  |  |
| --- | --- | --- |
| Antibodies | Cat. Number  | Manufacturers |
| PI3K | SC-1637 | Santa Cruz Biotechnology, (Santa Cruz, CA, USA), |
| AKT-1 | 293125 | Santa Cruz Biotechnology, (Santa Cruz, CA, USA), |
| CD163 | 16646-1-AP | ProteinTech (Rosemont, IL, USA) |
| E-Cadherin | MA5-12547 | Thermo Fisher Scientific (Waltham, MA, USA) |
| VEGF-A | PB9071 | Boster Biological Technology Pleasanton, CA, USA |
| NF-KB | SC-8008 | Santa Cruz Biotechnology, (Santa Cruz, CA, USA), |
| CXCL12 | PA5-114344 | Protein Tech (Rosemont, IL, USA) |
| Vimentin | MA5-16409 | Thermo Fisher Scientific (Waltham, MA, USA) |
| MMP2 | sc-13595 | Santa Cruz Biotechnology, (Santa Cruz, CA, USA), |
| IL-4 | 214-14 | PeproTech (Rocky Hill, NJ, USA) |
| IFN-γ | 315-05 | PeproTech (Rocky Hill, NJ, USA) |
| IL-10 | PA5-85660 | Santa Cruz Biotechnology, (Santa Cruz, CA, USA), |
| PDL-1 | 66248-1-Ig | Protein Tech (Rosemont, IL, USA) |
| Alexa® Fluor 488 | A32731 | Thermo Fisher Scientific (Waltham, MA, USA) |
| Alexa® Fluor 555 | A-21428 | Thermo Fisher Scientific (Waltham, MA, USA) |
| CD163-PerCP | 46-1631-82 | Thermo Fisher Scientific (Waltham, MA, USA) |
| CD68-FITC | MA5-16676 | Thermo Fisher Scientific (Waltham, MA, USA) |

**SUPPLEMENTARY FIGURES**



**Figure 1 S -** Graphical representation of cell viability (A-B)**. OXA**: oxaliplatin, **M1EV:** M1-EVs, **M1EV1:** M1-EVs with OXA, **M1EV2**: M1-EVs with OXA+ retinoic acid, **M1EV3**: M1-EVs with OXA+*L. ferrea***.** Results are presented expressed by mean ± SD. All treated cells were compared to the CT-26 cells without treatment (\**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, and \*\*\*\**p*<0.0001).



**Figure 2 S -** Effect of M1EVs on total cell death in 24 hs and 48hs. The cell death profile was analyzed by flow cytometry (A-P). Graphical representation expresses the percentage of total death. **OXA**: oxaliplatin, **M1EV:** M1-EVs, **M1EV1:** M1-EVs with OXA, **M1EV2**: M1-EVs with OXA+ retinoic acid, **M1EV3**: M1-EVs with OXA+*L. ferrea***.** Results are presented expressed by mean ± SD. All treated cells were compared to the CT-26 cells without treatment (\**p*<0.05, \*\**p*<0.01, \*\*\**p*<0.001, and \*\*\*\**p*<0.0001).