

According to the World Cancer Research Fund colorectal cancer (CRC) is the third most common cancer in the world and in 2020 more than 1.9 million new cases of CRC were detected. The mechanisms of cancer development and progression are various, and still under investigation. One of them is the role of myeloid-derived suppressor cells (MDSCs), which accumulate locally in the tumor microenvironment, circulate in peripheral blood and are important for tumor-induced immunosuppression. MDSCs are composed of three different subpopulations, depending on their origin: granulocytic (PMN-MDSCs), monocytic (Mo-MDSCs) and early stage (e-MDSCs), which are probably progenitors of the other two. They promote tumor escape from immune surveillance, as well as stimulate its further development and metastasis formation. Although the mechanisms of their action are well known, mostly affecting T cells and their activities, the generation of MDSCs is still a matter of debate. Latest scientific reports indicate that extracellular vesicles (EVs) of tumor origin may play a certain role in this process. EVs are small cellular “droplets” stuffed with various contents which can be transported from cell to cell to transmit specific information. EVs may transport proteins, mRNA or microRNAs (miR). It appears from the literature that one of such miRs relevant for CRC may be miR-21. In our preliminary data we have shown that EVs from patients with CRC contain miR-21 and are able to induce Mo-MDSCs from normal blood monocytes. This study aims to verify what types of miR carried by EVs are altered in CRC in addition to miR-21. Using the miR inhibitors we want to verify their role in the induction of Mo-MDSCs. Additionally, following our preliminary data showing the changes in the expression of some Bone Morphogenetic Proteins (BMPs) during the MDSCs generation, we would like to determine the role of BMPs in this process. We do hope that the project will allow us to indicate the specific pathway leading to development of Mo-MDSCs in CRC patients, thus suggesting a novel target for future immunotherapy.

