Bacterial membrane carriers targeting tumor-associated microbes for advanced cancer therapy

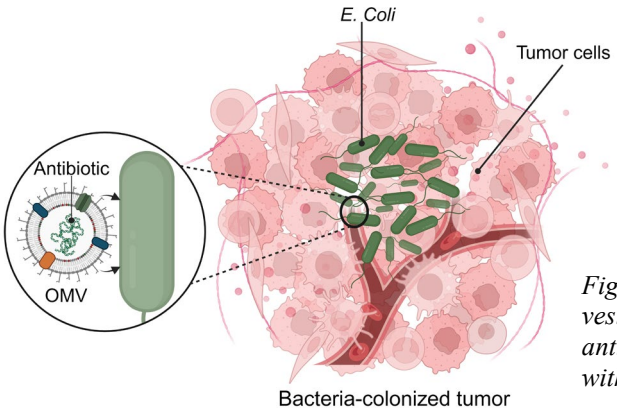

Figure 1. Illustration of outer membrane vesicles (OMVs) as drug carriers for targeted antibiotic delivery directly to bacterial cells within a tumor

Microbes are ubiquitous in human life, and their interaction with our bodies covers a wide spectrum of outcomes, from beneficial symbiosis in the guts to life-threatening infections. Recently, an important discovery showed that microbes reside also in tumors, and their presence benefits the development of cancer and confers tumors with resistance to chemotherapy. Eradication of such tumor-associated microbes could bring great benefits to many cancer patients, but targeting specifically bacteria is extremely challenging due to the bacteria innate drug resistance and limitations of current administration methods.

The project aims to create custom-designed drug carriers intended for precise interaction with and delivery of antibiotics to bacteria present in cancer sites. To achieve that, we will exploit the bacteria intercellular communication mechanism of outer membrane vesicles (OMVs), by repurposing OMVs as Trojan horses to bypass tumor and microbial barriers. We are planning to enhance OMVs' bacteria-targeting capability and load them with antimicrobial drugs to eradicate tumoral bacteria.

The project will first focus on optimizing the OMVs properties and drug-loading capabilities to create a pioneering class of OMV-based carriers, achieved via a combination of genetic manipulation and physical chemistry approaches to modify OMVs' surface and biomolecular signatures. Subsequently, we will evaluate the efficacy of these OMV-carriers in eliminating bacteria residing within the tumor microenvironment, aiming for a deeper understanding of their performance in physiologically relevant settings. To assess their effectiveness, we will start by testing these carriers using organoid in vitro model featuring co-cultured tumor and bacteria cells. Following, we plan to transition our findings from the in vitro model to an in vivo setting, using a tumor-bearing murine model mirroring clinical scenarios.

Overall, research has the potential to revolutionize cancer treatment by specifically targeting associated microbes, enhancing the effectiveness of chemotherapy, and ultimately improving patients' quality of life. We expect by the end of the project to have create a fully safe, stable, and biocompatible OMV-based carrier, loaded with antibiotics and capable of eliminating bacteria residing in tumors without causing additional adverse effects. Furthermore, the insights gained from studying the membrane interactions between OMVs and bacteria cells throughout this project will serve as the cornerstone for expanding the capabilities of our carriers in the future. This knowledge will pave the way for expanding the capabilities of our carriers in the future, enabling them to address various types of cancer, diverse bacterial strains, and colonies hosting multiple strains of bacteria.