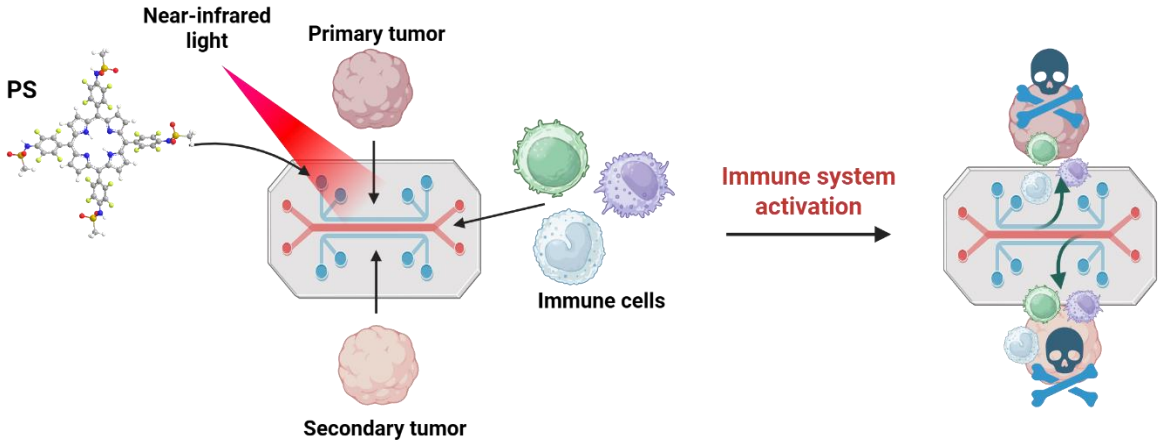
Mini-tumors, big answers: Modeling of immune system's activation with organoid-based PDT-on-Chip technology

In recent years, we have witnessed rapid advancements in modern cancer treatment strategies. One of the most dynamically developing approaches is photodynamic therapy (PDT), which involves the selective activation of specialized chemical compounds - called photosensitizers - accumulated in cancer cells, using light in the visible or near-infrared spectrum. Upon illumination, reactive oxygen species are generated, leading to the destruction of tumor cells. Interestingly, a growing body of research suggests that PDT can also stimulate the body's immune response, resulting in the elimination not only of the primary tumor but also of distant metastases - a phenomenon known as the abscopal effect.

Despite promising results from numerous studies, most newly developed photosensitizers never advance beyond the *in vitro* testing stage. The primary limitation lies in the lack of suitable research models that faithfully reproduce the complex tumor microenvironment and its interactions with the human immune system. This has created a clear need for more physiologically relevant, yet controllable and reproducible preclinical models to support the screening and development of novel therapies



The goal of this project is to develop a new organ-on-chip research model that will enable the reproduction of the tumor microenvironment and its interaction with immune cells. This model will provide an innovative tool for screening new photosensitizers for use in photodynamic therapy. The proposed system (chip) will consist of three connected chambers: one containing the primary tumor, the second containing immune system cells (e.g., T lymphocytes, NK cells), and the third simulating the secondary tumor (metastasis). To ensure a high degree of compatibility with human tumor physiology, the tumor model will be based on colon cancer organoids derived from human induced pluripotent stem cells (hiPSCs). In this model, photodynamic therapy will be carried out in the primary tumor chamber, and then the effect of PDT on the activation of immune cells, their ability to migrate, and eliminate tumor cells in the secondary chamber will be evaluated. This approach will allow the evaluation of the activity of photosensitizers along with the analysis of the phenomenon of the abscopal effect under laboratory conditions.

The project is highly interdisciplinary, combining tumor biology, immunology, microfluidic engineering, and photodynamic therapy. Its outcomes will contribute to a deeper understanding of PDT mechanisms and pave the way for the development of advanced, laboratory-based methods for testing anticancer therapies before progressing to preclinical or clinical trials. The resulting “tumor-on-chip” platform may, in the future, become a valuable tool for assessing not only the efficacy and immunogenicity of PDT but also a wide range of targeted therapies and cancer immunotherapies.