Abstract for the general public

Droplet microfluidics has advanced rapidly over the past two decades, revolutionizing analytical chemistry. A key goal in this field is the development of Lab-on-a-Chip systems for applications in experimental biology, medical diagnostics, and materials science. These systems can generate millions of uniform droplets in the pico- and nanoliter range, serving as microbioreactors for high-throughput analyses. This approach has led to breakthroughs in single-cell genomics, single-molecule DNA detection, and the assessment of the activity of millions of enzyme or antibody variants.

Building on these advances, we propose to develop a new microfluidic platform using hydrogel microbioreactors for the study of therapeutic cells. Engineered immune cells will be encapsulated together with cells in nanoliter hydrogel capsules or microgels for incubation and cultivation in tens of thousands of these microbioreactors. We will then develop methods for high-throughput selection of the most efficient variants of immune cells to better understand their mechanisms of action.

One of the most promising clinical applications of engineered cells is cancer immunotherapy. Although therapy using engineered (chimeric) T lymphocytes - so-called CAR-T has shown remarkable success in the treatment of blood cancers and several therapies have already been approved by the American and European medical agencies such as FDA and EMA, its effectiveness against solid tumors remains limited.

Challenges such as complex tumor microenvironment, poor tumor penetration and CAR-T cell exhaustion hinder its broader application. To address these limitations, our research in the second part of the project will focus on studying the activity of CAR-T cells using the developed microfluidic platform. We will screen large numbers of CAR-T cells to select the most active variants against lung and breast cancer models - both representing aggressive, genetically complex and difficult to treat types of cancer.

Understanding the mechanisms underlying cancer cell destruction and T cell depletion could lead to significant improvements in cancer therapy. By integrating microfluidic technology with single-cell analysis, our approach has the potential to become a valuable tool in biomedical and clinical research. This method could find broad applications in immunology, oncology, and infectious disease research, ultimately contributing to the development of personalized medicine.