Drug discovery and development is a long and expensive process. Despite the huge investment in drug development, the success rate of drugs reaching clinical trials is very low. It is reported that of the 250 drugs that have passed the preclinical phase and have been selected for clinical trials, only 1 drug has been finally launched on the pharmaceutical market. This is a consequence of the poor translation of results obtained in preclinical studies into clinical trials. The in vitro cell models currently used in preclinical studies are a vast simplification of conditions in the human body. On the other hand, in animal models, the process of disease formation, its development and response to the application of therapy is often different from that of the human body. Therefore, there is a great need to design and create advanced models of the preclinical research stage. The solution to this problem has somewhat become microfluidic Organ-on-a-Chip (OoC) systems. OoC technology makes it possible to obtain cellular models morphologically like in vivo (in vivo) conditions that mimic complex and specific tissue features, which is not possible under standard culture conditions. Although many advanced OoC models have been produced, it turns out that there is no gold standard specifying that a given tissue in Organ-on-a-chip systems should be modeled based on preset technological parameters, using a specific 3D cell model.

To achieve the desired goal, the geometry and microstructure fabrication technology will be selected to produce i) 2D monolayers, ii) 3D multilayers, iii) 3D aggregates/spheroids, and iv) 3D hydrogel cultures for each organ. Next, a selection of appropriate culture conditions will be made depending on the type of organ and cell model in the OoC. At this stage, the tissue microenvironment will be mimicked, and the cellular heterogeneity of the cell model will be established. In the next step, biochemical characterization of the obtained liver, lung and heart models in OoC systems will be carried out. Then, the cells will be exposed to the selected compound to investigate whether there are differences between the culture models. To answer the hypothesis analysis of the obtained results for different OoC models, macroscopic and in vivo studies will be performed. In addition, interpretation based on available clinical trial databases and consultation with clinicians may allow a conclusion to be drawn as to whether OoC technology can be used as a preclinical model. It should be noted that such complex analyses have not yet been reported in the literature.

The results obtained from the project will provide a deeper understanding of how the type of cellular model of the liver, including liver cancer, lung cancer, including lung cancer and heart cancer, affects the correct representation of the organ in vivo. In addition, the developed organ models using OoC technology can facilitate the screening and development of new drugs in the future. In addition, the approach proposed and optimized in the project (modeling and analytical methods) can be used in personalized medicine (using the patient's cells). Finally, we assume that the results obtained from the project can answer the question of whether Organ-on-a-chip systems can be useful in preclinical research.