Organ transplantation is a highly effective therapy in the treatment of various forms of end-stage organ failure. Despite the dynamic development of this area of medicine, many people do not receive their chance for a transplant or reject the graft because of the insufficiently quality of the organ. Over the past decades, because of the improved surgical techniques, immunosuppressive strategies and patient management, the number of transplant candidates has increased dramatically while the number of donors has remained unchanged. There are huge problems that modern transplantation has to face such as severe shortage of donor grafts and lack of reliable methods of organ quality assessment prior to transplantation. Many centres around the world are currently looking for ways to solve these problems by conducting research on new methods of organ preservation, which would maintain physiological condition of the grafts and enable to use so called marginal or suboptimal organs that do not initially meet the criteria for acceptance for transplantation. The other approach is to extend the panel of parameters or compounds allowing better evaluation of a true condition of the organ, because currently the primary assessment is made based on visual inspection of the graft.

The proposed research project aims to apply novel analytical approaches to assess the function and status of liver transplant during ex situ normothermic liver perfusion (NEsLP) and compare the results with hypothermic ex situ liver perfusion (hypothermic machine perfusion, HMP). A series of non-targeted organ tissue analyses, perfusate, serum, and bile (the latter only for NEsLP) will be performed using solid-phase microextraction to obtain the complete metabolic and lipidomic profile of hypo- and normothermic perfused liver transplants. Due to the non-invasive method of collecting samples for testing, these methods will allow the assessment of liver function immediately after its harvesting, during the preservation and just before transplantation. It has been proven that the production of bile by livers during NEsLP is an important indicator of the viability of this organ. However, it is believed that in addition to bile secretion, the composition of body fluids and perfusate may also be important, and that their analysis will enable understanding of the metabolic processes occurring during organ preservation, thus allowing taking full advantage of suboptimal organs. Profiling changes occurring in all small molecule compounds may contribute to finding potential biological markers of organ quality and indicators of the possible development of early liver dysfunction. Moreover, it is assumed that changes in the concentration of bile acids, which are the main organic component of bile, may correlate with changes in the transplanted organ.

The project will consist of a biological and analytical part. Regarding the former, it will be attempted to identify biochemical pathways altered by HMP and NEsLP and differentiate liver transplants from optimal donors from donors with extended criteria. Subsequently, it is planned to propose a panel of selected potential biomarkers of graft quality, which will complement tests routinely used in peri-transplant period. In the analytical part, a method for rapid and direct determination of potential biliary biomarkers of organ quality will be proposed. This method will also be used for the post-transplant monitoring of graft function based on the recipient's blood analysis.

It is believed that proposed analytical solution and its validation on the models described above will significantly contribute to the improvement of transplantation outcomes in the future by providing clinicians with more reliable tools of organ assessment and early identification of post-transplant complications.