With the increased life expectancy and prevalent incidence of vascular diseases in the Western world, chronic kidney diseases have become a worldwide public health problem with substantial morbidity and mortality. Kidney transplantation (KTx) is the best treatment option for patients with end-stage renal failure. The number of patients undergoing haemodialysis or peritoneal dialysis, which extremely reduce the patient's quality of life and are usually considered as just a bridge to transplantation, is however much higher than the number of available kidney transplants and there is increasing disparity between organ supply and demand. In order to overcome the donor shortage and to increase the number of KTx, it has become generally accepted and increasingly common to procure organs not only from so called standard criteria donors (SCDs), that are considered as healthy persons of younger age, but also from so called expanded criteria donors (ECDs), that are over 60 years of age or are over 50 years of age with two of the following: a history of hypertension, a creatinine (blood test showing renal function) greater than or equal to 1.5 mg/d or death by stroke. However, kidney transplantation from ECDs is associated with a higher risk of primary non-function (PNF), delayed graft function (DGF), early graft loss, and urinary complications.

There is currently no clinically approved available diagnostic tool to assess kidney quality before KTx, needed to guide the clinician in deciding whether to accept or decline the organ. Also predicting whether grafts will provide sufficient kidney function and long-term performance is increasingly more challenging with such donors. Most centers perform a '0' biopsy before transplantation, but the results are available a few days after the transplantation and the results are reflecting the status of only a very small part of the kidney (the site of the biopsy). This has forced the transplant community to investigate new methods of organ preservation aimed at reducing injury to the kidney before and during transplantation (tissue damage is caused when blood supply returns to tissue after a period of ischemia or lack of oxygen, called ischemia-reperfusion injury) and to develop tools to evaluate transplant kidney quality before transplantation. Furthermore, over the last several years the classical static cold storage techniques for deceased donor kidneys have been expanded towards diverse new techniques of organ preservation like hypothermic machine perfusion with or without oxygen or perfusion at sub-normothermic or near-normothermic temperatures, with debated outcomes.

The introduction of diverse perfusion fluids into the clinical practice of transplantology has opened a new valuable source of new parameters reflecting the current kidney condition, like stress markers, functional markers and damage biomarkers. We hypothesize, that one of the key markers that may reflect physiological or pathological changes in the kidney to be transplanted are the so called extracellular vesicles (EVs). EVs are small membrane vesicles that are secreted by all cell types and play and important role in intracellular communication, immune modulation, cell regeneration and activation of signaling pathways in target cells. We expect, that the kidney cells will secrete substantial amounts of EVs into the perfusion fluid during the perfusion time, as already reported in the literature. Since the rich molecular cargo of the released EVs, including proteins, lipids and nucleic acids reflect the physiological state of the parental cells, we expect that the protein composition of the kidney-derived EVs will reflect the physiological state of the whole kidney directly before transplantation as well as serve as predictor of shoer and long-term kidney function after transplantation and transplant rejection. We will perform a comprehensive analysis of the EV protein profile with modern un-targeted, comparative proteomic analysis techniques of two donor cohorts: deceased SCD and ECD donors. Since the EV samples will be analyzed at 3 timepoints during the perfusion time, the project will provide information about the dynamic changes in kidney physiology during perfusion as well as the knowledge needed to modify current organ preservation techniques, and composition of perfusion fluids to ensure optimal organ quality for a successful transplantation.