

Plasma-based liquid biopsy for minimally invasive heart transplant monitoring

Heart transplant is the current golden standard of therapy for end-stage heart failure in patients who no longer respond to any heart-preserving treatment methods. It needs to be emphasized that the recipient's body perceives the transplant as a "foreign" entity and, thus, aims to eliminate it. Immunosuppressive therapy, which is used to prevent transplant rejection, requires the optimal balance between "too much" and "not enough". Therefore, successful long-term outcomes rely on early detection of graft injury. After the surgery, organ rejection is monitored with protocol endomyocardial biopsy (9 biopsies within the first year). This procedure carries a risk of severe complications, requires hospitalisation and may not always be informative.

The aim of this project is to study liquid biopsy as a diagnostic tool for early detection of acute heart transplant rejection. Our preliminary data proved that it is possible to quantify the amount of donor-derived cell-free DNA (ddcfDNA) in recipient's plasma. We hypothesize that the level of circulating ddcfDNA is correlated with graft injury and, thus, may be considered a sign of rejection. We are going to quantify ddcfDNA in post-transplant samples and confront the results with routine histopathological assessment of endomyocardial biopsy specimens. In parallel, we are going to measure the plasma concentration of selected cytokines, aiming at defining the specific profile manifesting at the early stages of rejection. Potentially, selected cytokines may be incorporated into the algorithm of routine transplant patient management.

Our project will result in better understanding of the process of acute heart transplant rejection. We also assume that it will be possible to determine novel markers of early graft injury. Therefore, the project may contribute to a better monitoring of graft condition and improve the general management of heart transplant patients.