INTRODUCTION AND AIMS: Short-term renal allograft survival increased continuously during the last decades but the rate at which transplants are lost thereafter remained disappointingly stable at a high level. Donor organ quality affects long term outcome after renal transplantation and even though a variety of prognostic molecular markers is available their validity often remains undetermined. Study aim was to identify and validate molecular markers reflecting donor organ quality being associated with long term outcome after transplantation.

METHODS: We created a network-based molecular model reflecting donor kidney status based on transcriptomics data and molecular features reported in scientific literature to be associated with chronic allograft nephropathy. Significantly enriched biological processes were identified and representative markers were selected. An independent kidney pre-implantation transcriptomics dataset consisting of 76 organs was used to predict estimated glomerular filtration rate (eGFR) values twelve months after transplantation using clinical parameters known at time of transplantation as well as marker expression values. Clinical parameters included donor and recipient gender and age as well as last donor creatinine, cold ischemia time, transplantation number, panel reactive antibodies, and number of HLA mismatches. In addition the impact of post-transplant complications, namely delayed graft function and biopsy-confirmed rejection, was evaluated.

RESULTS: The constructed donor organ status molecular model consisted of 89 proteins with the top enriched biological processes being the neurotrophin TRK receptor signaling pathway, the Fc-epsilon receptor signaling pathway as well as the epidermal growth factor receptor signaling pathway. The best-performing regression model solely based on the clinical parameters donor age, donor gender, and recipient gender explained 17% of variance in post-transplant eGFR values. The five molecular markers EGF, CD2BP2, RALBP1, SFRP1, and DDX19B representing key molecular processes of the constructed renal donor organ status molecular model in addition to the clinical parameters significantly improved model performance (p-value < 0.0007) explaining around 33% of the variability of eGFR values twelve months after transplantation. Whereas add-on information on rejection episodes did not improve model performance, knowledge on the occurrence of delayed graft function significantly improved both models further increasing adjusted R² values from 0.17 to 0.28 (p-value < 0.0001) and from 0.33 to 0.42 (p-value < 0.0001) respectively.

CONCLUSIONS: Collectively, molecular markers reflecting donor organ status significantly improve prediction of post-transplant renal function when added to the clinical parameters.