FP7 BIOMARGIN SHOWS THAT A SMALL SET OF BLOOD MICRO-RNAS IS ASSOCIATED WITH ACUTE KIDNEY ALLOGRAFTS REJECTION.

C. Tinel, A. Benon, S. Gazut, M. Naesens, W. Gwinner, M Essig, P. Marquet, D. Anglicheau.

Background: FP7 Biomargin aimed at detecting and validating non-invasive biomarkers of kidney graft lesions. After untargeted screening of different –omics, candidate biomarkers were confirmed in independent patient groups. In this study, we investigated the diagnostic potential of microRNAs (miRNAs) in whole blood samples.

Methods/Materials: Blood samples were collected at the time of protocol or for-cause biopsies in 4 European clinical centers. Biopsies were retrospectively selected after centralized histological reading by expert pathologists, and classified into 4 groups (Normal, ABMR, TCMR or IF/TA), to build two independent case-control studies (discovery- and validation sets). Global microRNA (miRNAs) profiling was performed on blood samples from the discovery set by TaqMan® Array microRNA v3 microfluidic cards (TLDA, Life Technologies). A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify a list of biomarker candidates associated with one of the 4 groups. This list of miRNAs was quantified using custom TLDA plates on the validation set. Multivariate models were then built to define miRNAs signature of graft lesions.

Results: A total of 754 miRNAs was quantified in the discovery set that included 42 Normal, 17 TCMR, 37 IF/TA and 30 ABMR samples. Our statistical pipeline identified 141 candidates that were assessed in the validation cohort of 37 Normal, 23 TCMR, 41 IF/TA and 37 ABMR samples. The table shows the association between histological phenotypes and miR-derived statistical models in the validation cohort.

Group comparison	**Number of miRNAs in the best model**	**Mean AUC***
Rejection vs Normal	4	0.70
TCMR vs Normal	6	0.75
ABMR vs Normal	4	0.81
ABMR vs TCMR	5	0.64
ABMR vs IF/TA	5	0.72

*Estimated by resampling approaches.

Conclusion: We identified a small subset of miRNAs in the blood with a strong association with ABMR and/or TCMR, thus providing the basis for innovative non-invasive molecular tools development. Their diagnostic performance is currently being investigated in blood samples collected at time of 453 consecutive allograft biopsies in our BIOMARGIN trans-sectional study.