FP7 BIOMARGIN SHOWS THAT SMALL SETS OF INTRA-GRAFT MICRORNAS ARE STRONGLY ASSOCIATED WITH RENAL ALLOGRAFT LESIONS.

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Background: FP7 Biomargin aimed at detecting and validating 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 allograft biopsy samples.

Methods/Materials: Biopsies were collected from protocol or for-cause biopsies in 4 European clinical centers. Samples 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 miRNA profiling was performed on TaqMan® Array microRNA v3 microfluidic cards (TLDA, Life Technologies) on the discovery set. A statistical pipeline including 2 uni- and 5 multivariate analyses was applied to identify an extended list of biomarker candidates associated with one of the 4 groups. This extended list of miRNAs was quantified using custom TLDA plates on the validation set. Multivariate models were then built to define miRNA signatures of graft lesions.

Results: A total of 754 miRNAs was quantified in the discovery set that included 32 Normal, 13 TCMR, 25 IF/TA and 18 ABMR samples. Our statistical pipeline identified 140 candidates that were assessed in the validation cohort of 32 Normal, 13 TCMR, 26 IF/TA and 28 ABMR samples. The table shows the association between histological phenotypes and miRNA-derived statistical models in the validation cohort.

Group comparison	**Number of miRNAs in the best model**	**Mean AUC***
ABMR vs Normal	4	0.76
ABMR vs TCMR	3	0.90
ABMR vs IF/TA	6	0.94
TCMR vs Normal	6	0.96
Rejection vs Normal	3	0.95
Rejection vs No Rejection	4	0.86

*Estimated by resampling approaches.

Conclusion: We identified a small set of miRNAs within kidney allograft biopsies with a strong association with TCMR and ABMR. These miRNA signatures might provide useful molecular tools to improve allograft assessment. Their diagnostic performance is currently being investigated in our BIOMARGIN trans-sectional study of 312 consecutive allograft samples.