FP7 BIOMARGIN SHOWS THAT A SMALL SET OF URINARY PEPTIDES CAN DIAGNOSE ACUTE KIDNEY GRAFT REJECTION ACCURATELY.

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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, and their diagnostic performance evaluated in a larger trans-sectional study. All studies were approved by ethics committees, complied with the Helsinki declaration amended in 2008, and patients provided informed consent.
Methods/Materials: Urine samples were collected just before protocol or for-cause biopsies following a standardized procedure, and then retrospectively selected following a case-control (discovery and validation sets) or a trans-sectional (performance assessment) design. For the first two steps, untargeted screening of natural urine peptides was performed using nano-liquid chromatography – high resolution QTOF mass spectrometry, while targeted micro-LC-QTOF was used for the third. Biomarker candidates were selected if they were significantly associated ($p<0.05$ after FDR correction) with one of the 4 groups (normal, AbMR, TCMR or IF/TA), as assigned after centralized histological reading by expert pathologists, and had an AUC under the ROC curve >0.6. Finally, the most pertinent combinations of peptides were selected using SPLS-DA.

Sample distribution

	AbMR	TCMR	IF/TA	Normal	Others
Discovery set (n=133)	34	42	49	37	0
Confirmation set (n=128)	31	25	51	43	0
Trans-sectional study (n=399)	43	20	116	225	40

Results: 343 natural urinary peptides were identified. A combination of 6 showed the highest diagnostic performance with respect to AbMR in the discovery set, and yielded AUCROC=0.862 and 0.787 in the independent confirmation set and trans-sectional study, resp. Another set of 12 peptides was able to best discriminate patients with TCMR, with AUCROC=0.822 and 0.807, resp. No efficient signature was found for IFTA.
Conclusion: We identified and validated very efficient urine peptide signatures of TCMR and AbMR. Their predictive performance is now being tested in the BIOMARGIN European prospective Cohort Study.