Poster

[P25-8] P25-8: Immunosuppressive drugs (3): Biomarkers and pharmacokinetics

Chair: Hideyuki Motohashi, Japan

Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Mon. Sep 25, 2017 12:30 PM - 1:30 PM Annex Hall)

[P25-8-9] FP7 BIOMARGIN preliminary results of the investigation of a small set of urinary peptides to diagnose antibody mediated rejection

Jean-Baptiste Woillard[1], Francois-Ludovic Sauvage[2], Marteen Naesens[3], Dany Anglicheau[4], Wilfried Gwinner[5], Stephane Gazut[6], Marie Essig[7], Pierre Marquet[8] (1.CHU Limoges Univ Limoges, 2.CHU Limoges Univ Limoges, 3.KU Leuwen, 4.CHU Necker APHP, 5.Abteilung für Nephrologie, Medizinische Hochschule Hannover, Hannover, Germany, 6.CEA LIST, LIMA PC 72 91191 Gif sur Yvette, Paris, France, 7.CHU Limoges Univ Limoges, 8.CHU Limoges Univ Limoges)

Keywords: Biomargin, Antibody Mediated Rejection, Biomarker, Peptidomics, Renal Transplantation

Background

FP7 Biomargin is a European research programme 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 in all countries involved, complied with the Helsinki declaration amended in 2008, and all patients enrolled provided informed consent.

Methods

Urine, blood and biopsy sample triplets collected from 133 patients were used in the first case-control study (biomarker discovery), 128 in the second (biomarker confirmation) and 398 in the trans-sectional study with complete clinical and histological data. 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. In a first step, Mann Whitney and AUC under the ROC curve tests were performed to select biomarkers significantly ($p<0.05$ after FDR correction &AUC ROC>0.6) associated with Antibody Mediated Rejection (ABMR) in comparison to all others diagnostics as assigned after centralized histological reading by expert pathologists. Then, the most pertinent combinations of peptides were selected using SPLS-DA in the mixOmics R package (http://mixomics.org/).

Results

343 peptides naturally occurring in urine were investigated. A combination of 12 yielded the highest diagnostic performance in the discovery step (AUC ROC = 0.776) with regards to ABMR. In the confirmation set, we observed an AUC ROC=0.747 associated to a sensitivity=61.3% and a specificity=76.3%. In the trans-sectional study, the prevalence of ABMR was 10.8% and we found an AUC ROC = 0.733, with sensitivity=69.8%, specificity=76.6%, positive predictive value=26.6% and negative predictive value (NPV)=95.4%.

Conclusions

We have identified and validated an efficient urine peptide signature of ABMR with correct specificity and excellent NPV (corresponding to the probability for a patient to be free from ABMR when the test is negative).

The set of biomarkers selected exhibited better specificity than sensitivity, meaning a lower number of false positive (as expected for a diagnostic test) than negative results.