METHOD: Kidney biopsies from patients with histopathologically verified IgAN/IgA vasculitis ($n = 84$) (IgAV) [57 males, median (range) age of 39 (4–89) years] and 11 living donors (LD) [six males, median (range) age of 37 (30–65) years] were manually microdissected into glomerular and tubulointerstitial fractions. RNA was extracted with RNeasy lipid tissue mini kit (Qiagen, Valencia, CA, US) and evaluated using the Bioanalyzer 2100 (Agilent, Santa Clara, CA, US). mRNA purification, conversion to cDNA, fragmentation and double-stranded cDNA synthesis, amplification and clean-up were performed using Illumina Stranded mRNA prep ligation protocol (Illumina Inc). Paired-end RNA sequencing was performed in three different batches (Illumina Novaseq 6000).

Data pre-processing was done using Trim Galore (v.0.6.4). Reads were aligned to the Ensembl GRCh38 reference genome using STAR (v2.6.1d). Gene counts were obtained using featureCounts (v1.5.1). Quality control was made using MultiQC (v.1.7). Comparisons between groups were performed using Bioconductor package DESeq2 (v1.22.2) and gene set enrichment analysis using Bioconductor package fgsea.

The biopsies were evaluated by experienced renal pathologists using the Oxford classification [2] and the Banff classifications [3]. Clinical data at time of biopsy and 5-year follow-up was retrieved from patients' files. Co-morbidity- and mortality data was extracted from the Swedish renal registry up to 19 years after the biopsy.

RESULTS: Principal Component Analysis showed clear separation between diseased and LD kidney transcriptomes, as well as between glomerular and tubulointerstitial fractions. Top upregulated genes in glomeruli were associated with complement activation and fibrosis. In tubulointerstium, top genes were related to the immune system, including chemokines. Gene ontology enrichment analysis highlighted immune response and complement activation in both compartments. Additionally, cell membrane and mitochondrial activity were enriched in tubulointerstium. Linking bioinformatic results to clinical data at the time of biopsy, progress over time as well as to histopathological data in accordance with the Oxford classification system [2] is ongoing.

CONCLUSION: This is, to our knowledge, the most comprehensive RNA sequencing performed on paired glomerular and tubulointerstitial tissue from patients with IgAN/IgAV. Initial bioinformatical analyses highlights biologically relevant processes involving different parts of the immune system. Our project has the potential to identify molecular processes associated with rapid disease progression and specific histopathological characteristics. This enables identification of patients with a more aggressive disease and individualized treatment depending on molecular profile, which would improve kidney survival and quality of life for patients suffering from IgAN/IgAV.

REFERENCES

1. Coppo R, D'Amico G. Factors predicting progression of IgA nephropathies. *J Nephrol* 2005; **18**(5): 503–512
2. Trimarchi H, Barratt J, Cattran DC *et al.* Oxford classification of IgA nephropathy 2016: an update from the IgA Nephropathy Classification Working Group. *Kidney Int* 2017; **91**: 1014–1021
3. Roufosse C, Simmonds N, Clahsen-van Groningen M *et al.* A 2018 Reference guide to the banff classification of renal allograft pathology. *Transplantation* 2018; **102**: 1795–1814

FC048 NEW TOOL TO PREDICT THE CLINICAL COURSE AND RENAL FAILURE IN PATIENTS WITH IMMUNOGLOBULIN A NEPHROPATHY

Francesco Paolo Schena[1], Vto Walter Anelli[2], Giandomenico Cornacchia[3], Tommaso DI Noia[3], Maria Stangou[4], Aikaterina Papagianni[5] and Rosanna Coppo[6]

[1]Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy, [2]Department of Electrical and Information Engineering, Polytechnic of Bari, Italy, Bari, Italy, [3]Department of Electrical and Information Engineering, Polytechnic of Bari, Bari, Italy, [4]Department of Nephrology, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, [5]Department of Nephrology, Hippokration General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece, and [6]Fondazione Ricerca Molinette, Torino, Italy., Torino, Italy

BACKGROUND AND AIMS: Idiopathic Immunoglobulin A nephropathy (IgAN) is the most common biopsy-proven glomerulonephritis in the world. Approximately 40% of IgAN patients reach renal failure (RF) 20 years after their kidney biopsy. The high prevalence of RF shows that IgAN has a significant economic impact in the countries because renal replacement therapy is costly. Moreover, the disease's onset in the second and third decades of life represents a social challenge because patients are typically very active and highly productive in the workplace. This challenge is one more reason to move on the prediction of the clinical course and RF in IgAN patients at the time of the kidney biopsy and during the follow-up. We developed an artificial neural network (ANN) tool (DialCheck 1.0) based on seven variables and the histological score of the kidney biopsy to predict RF in IgAN patients at the time of kidney biopsy [1].

METHOD: We have recently developed a new tool which consists of a set of ANN-powered models that combine temporally accurate observations for fine-grained features and leverage state-of-the-art deep neural network techniques to forecast the patient's clinical evolution.

RESULTS: A cohort of 948 IgAN patients, of whom the clinical course of the disease was known, was used to develop the new tool that predicts the dynamics of age and disease laboratory parameters (serum creatinine, daily proteinuria), blood pressure, histological score of the kidney biopsy and the RF. The system was designed to help the physicians give a broader spectrum of information regarding the patient and the potential clinical development of IgAN and outcomes.

In detail, the model computes a latent dynamic representation of the patient and predicts a prospective clinical picture of the patient and the probability of RF. The tool with an accuracy of >80% will be tested in an independent retrospective cohort of 454 IgAN patients and in a prospective multicenter randomized clinical study in which 426 IgAN patients will be enrolled in two different groups based on the type of kidney lesions (active and chronic renal lesions).

CONCLUSION: We have a new tool (DialCheck 2.0), based on ANN, that may predict the outcome and the RF in IgAN patients. Moreover, it may help the physician to analyze the long-term response to therapy.

REFERENCE

1. Schena FP, Anelli VW, Trotta J *et al.* Development and testing of an artificial intelligence tool for predicting end stage kidney disease in patients with immunoglobulin A nephropathy. *Kidney Int Kidney Int* 2021; **99**: 1179–1188