

with end stage renal failure (ESRF) on HD and burdened with chronic viral hepatitis C (HCV).

**Methods:** Cytogenetic examination was performed in three patients groups: 23 patients with ESRF on HD; 21 patient having HCV with ESRF on HD; 29 patients with HCV without renal function disorder. Lymphocytes were cultivated according to the conventional Hungerford method for 52 hours with modifications. Selection of metaphasal plates for cytogenetic analysis, classification and method for calculation of chromosome aberrations were conventional. Multi-aberrant cells were considered those having 3 aberrations and more. Aneuploid cells were divided into hypoploid (under 42) and hyperploid ones (over 49).

**Results:** The frequency of chromosome aberrations was confidently different in all the three groups of patients examined and exceeded the norm (by 3%). The highest indexes were in patients with HCV ( $17,78 \pm 0,55\%$ ,  $P < 0,05$ ) which was the cosequence of virus-induced mutagenesis and were confirmed by the data of other authors. An intermediate result ( $10,60 \pm 1,49\%$ ,  $P < 0,05$ ) of chromosome aberrations frequency in patients having HCV with ESRF might suggest the impact of HD procedure on the chronic hepatitis flow in this patients' category. In patients with ESRF this index was confidently lower than in other patients groups ( $4,69 \pm 0,51\%$ ).

In patients with ESRF on HD a number of aneuploid cells was confidently higher ( $20,0 \pm 0,97\%$ ,  $P < 0,05$ ) and hence one may suppose the presence of oncogenic component. In patients group with HCV on HD and those without renal function disorder this index was lower and made  $14,12 \pm 1,69\%$  and  $16,32 \pm 0,53\%$  accordingly. The virus in case of a durable replicative phase is an inductor of a chain of events leading to severe and mass damages of chromosome material. This is confirmed by the highest level of multiaberrant cells  $7,71 \pm 0,38\%$  in patients with HCV. In patients with HCV on HD a number of multiaberrant cells was confidently lower and made  $2,35 \pm 0,74\%$ , which didn't differ from the indexes of patients with ESRF on HD without hepatitis. In patients with HCV the largest chromosome aberration spectrum was fixed, that included acentric rings and translocations, indicating its virus-induced damages.

A single hemodialysis procedure had no impact on the chromosome aberrations level: the frequency of metaphases with aberrations remained on pre-dialysis level.

**Conclusions:** Hemodialysis procedure has an effect on the HCV flow and neutralizes the virus impact on genetic apparatus in case of those pathologies combined. Our data allow one to explain and confirm the results of other researchers stating that the HCV flow in patients on program hemodialysis is less aggressive.

## P10

### IDENTIFICATION OF BIOMARKER CANDIDATES AND THERAPEUTIC TARGETS USING TRANSCRIPTOME-DRIVEN APPROACH

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**Introduction:** Chronic kidney disease (CKD) affects 8-16% people worldwide, with an increasing incidence and prevalence of end-stage kidney disease (ESKD). The effective management of CKD is currently confounded by the inability to identify patients at high risk of progression while still in early stages of CKD. Identifying the mechanism responsible for progression of CKD is a critical step to contain the worldwide CKD epidemic. A molecular disease definition of CKD will allow us to develop strategies for patient risk stratification to prioritize limited health care resources, to identify targeted molecular therapies for patients at high risk and to develop biomarkers to define such patients for clinical trials. Our hypothesis is that both clinical phenotypes (e.g. GFR, proteinuria) and renal tissue alterations seen in CKD are associated with, and a consequence of, the dynamic molecular mechanism reflected in the transcriptional programs of the diseased renal tissue.

**Methods:** Our work started from the identification and cross-validation of pathways and candidate intrarenal biomarkers for CKD progression in 261 kidney biopsies. We then used a sequential prioritization strategy to prioritize candidates for non-invasive biomarkers to allow broad clinical applicability. Next, intra-renal transcript levels of the top candidate biomarker were correlated with the urinary levels of the encoded proteins. Urinary protein levels were assessed for their correlation with CKD progression. Finally, the biomarker was tested for its ability to increase predictive power of established clinical marker panels for CKD progression prediction in three cohorts. We used Cox proportional hazards models to evaluate the predictive value of marker on CKD outcome, and used likelihood ratio tests, C-statistics, and Akaike information criterion (AIC) to assess the goodness of fit and improved prediction ability. Finally, we present our effort in identification the molecular disease mechanism, serving as targets, to develop novel therapies to prevent CKD progression.

**Results:** Using Epidermal Growth Factor (EGF) as a proof of principle, we could demonstrate that prediction of renal survival by eGFR and albuminuria was significantly improved by addition of uEGF to the model in diverse CKD populations with a wide spectrum of causes and stages. uEGF may contribute to the improved risk prediction as it can capture the degree of tubular differentiation and regeneration potential, mechanisms essential to retain renal function with the acute and chronic insults seen in CKD, but not be well reflected by the conventional predictors (proteinuria or baseline GFR).

**Conclusions:** uEGF shows promise as an independent risk predictor of CKD progression. Inclusion of uEGF significantly improved prediction of composite end points by eGFR and proteinuria in diverse populations worldwide with a wide range of CKD. An immediate benefit of our work can be an improved stratification of CKD patients for the selections of high-risk patients into clinical trials, addressing a critical hurdle for novel molecular target validation in CKD.

## P11

### CHARACTERIZING THE IMMUNE PROFILE OF SERIAL KIDNEY BIOPSIES DIFFERENTIATES TREATMENT RESPONDERS FROM NON-RESPONDERS IN LUPUS NEPHRITIS