enhancing TGF-β-mediated downregulation of snail and E-cadherin in HK-2.

http://dx.doi.org/10.1016/j.hkjn.2015.08.092

0104
Urinary Angiostatin: A Potential Biomarker for Diagnosis and Evaluation of Disease Severity in IgA Nephropathy

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Objective: Currently, diagnosis of IgA nephropathy (IgAN) relies on renal biopsy. Most IgAN is progressive, however, renal biopsy cannot be done frequently for its invasive property. This study is to investigate non-invasive protein biomarkers of IgAN from urine supernatant.
Methods: Urine supernatant was collected from 15 IgAN patients (Lee's grade I-II, III and IV-V, 5 in each group), 12 none-IgAN glomerular disease control (DC) patients (MCD, MN and FSGS, 4 in each group) and 5 normal control (NC). Urine sample were analyzed by Raybiotech protein array for searching differential expression of protein biomarkers. Candidate protein biomarkers were further validated in urine samples from other subjects, including 49 IgAN patients (Lee's grade I-II 8, grade III 31 and grade IV-V 10), 28 DC patients (MCD 8, MN 8 and FSGS 12) and 14 NC by ELISA method.
Results: Angiostatin was found differential expressed between IgAN group and control groups by protein array. By ELISA verification, the level of angiostatin was significantly higher in IgAN group than NC group (255.15 ± 288.43 vs 3.31 ± 5.96), but lower than DC group, including MN (579.47 ± 211.69 ng/ml) and MCD (664.56 ± 375.95 ng/ml). Angiostatin showed a significant positive correlation with SCr ($r = 0.939$), BUN ($r = 0.931$), Cys C ($r = 0.923$), proteinuria ($r = 0.784$), global sclerosis ($r = 0.718$) and crescentformation ($r = 0.588$). There was a negative correlation between angiostatin level and eGFR ($r = -0.721$). Angiostatin level in IgAN Lee's grade IV-V group was significantly higher than gradeI-II and grade III group (620.43 ± 271.47 vs 107.38 ± 83.37 vs 117.89 ± 143.84 ng/ml, $p < 0.01$). The level of angiostatin was significantly higher in IgAN group with endothelial cell proliferation change than those without (406.95 ± 336.56 vs 189.41 ± 234.70, $p < 0.01$).
Conclusion: Urine supernatant angiostatin could be used as a candidate biomarker for diagnosis of IgAN. Angiostatin level reflects the clinical and pathological features of IgAN.

http://dx.doi.org/10.1016/j.hkjn.2015.08.093

0116
Urinary Sediment miRNAs Reflect Tubulointerstitial Damage and Therapeutic Response in IgA Nephropathy

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Objective: Most of IgA nephropathy (IgAN) is chronic progressive glomerulonephritis, with different clinical and pathological features. Evaluation of the disease by repeated renal biopsy is not practical due to its invasive procedure. Urinary sediment miRNAs are hopeful to serve as non-invasive biomarkers to assess kidney injury of IgAN.
Methods: 52 biopsy-proven IgAN patients and 25 healthy controls were enrolled in this study. Urinary sediment miRNAs were extracted. Expressions of miR-34a, miR-205, miR-21, miR-146a and miR-155 were quantified by qPCR. ROC (receiver operating characteristic curve) was used to investigate the value of the miRNAs for predicting dignosis of IgAN and evaluating histopathological injury. The patients were treated according to the KDIGO guideline and followed up. The roles of miRNAs in reflecting theraputic efficacy and disease progression were analyzed.
Results: (1) The IgAN group had significantly lower urinary miR-34a, miR-205, miR-155 but higher miR-21 levels than controls. Logistic regression analysis showed that urinary miR-34a$\leq$0.047, miR-205$\leq$0.209 and miR-21$\geq$0.461 were independent factors for diagnosis of IgAN. The ROC revealed that miR-205$\leq$0.125 and miR-21$\geq$0.891 can distinguish IgAN patients with moderate and severe tubular atrophy and interstitial fibrosis from those with mild tubular atrophy and interstitial fibrosis. (2) After 21.17 months follow-up, the level of proteinuria reduction (g/24h/month) was positively correlated with baseline urinary miR-21 and inversely correlated with miR-205. The subjects who achieved a complete remission (CR) had higher baseline urinary miR-205, and lower miR-21 than those without achieveing a CR.
Conclusion: The levels of some urinary sediment miRNAs, especially baseline miR-21 and miR-205 may be used as prognostic markers for evaluating the tubulointerstitial damage of IgAN. What's more, baseline levels of urinary miRNAs may be predictors to reflect theraputic efficacy and disease progression.

http://dx.doi.org/10.1016/j.hkjn.2015.08.094

0118
Bacterial IgA Protease-mediated Degradation of aglgA1 and Its Immune Complex as a Potential Novel Therapy for IgA Nephropathy

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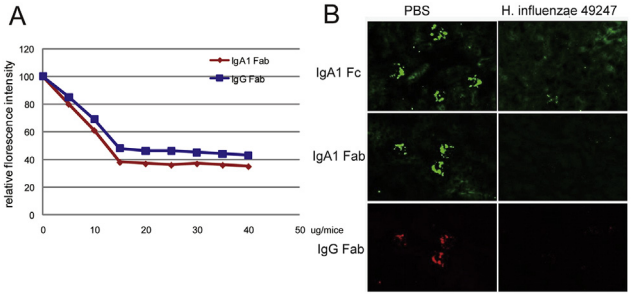
Objective: Mesangial deposition of aberrantly glycosylated IgA1 (aglgA1) and its immune complex is an initial and key pathogenic mechanism in IgA nephropathy (IgAN). The present study tested the hypothesis that bacteria-derived IgA proteases may be able to degrade the circulating and deposited aglgA1 and its immune complex locally in the mesangium and may represent a novel therapy for IgAN.
Methods: We first identified bacterial IgA proteases with high enzymatic activity by screening 14 different bacterial strains (6 species totally). Among them, 4 IgA proteases were selected and their ability to degrade aglgA1 and its immune complex was determined in vitro with artificially deglycosylated IgA1 or human IgAN biopsy and in vivo in a modified mouse model of passive IgAN.
Results: Selected bacteria-derived IgA proteases were capable of degrading serum aglgA1 and normal IgA1 pretreated with neuraminidase and β-galactosidase in vitro and also the deposited immune complex within the mesangium of renal biopsy from IgAN patients. In a modified mouse model of passive IgAN with abundant in situ mesangial deposition of the aglgA-IgG immune complex in glomeruli, a single intravenous injection of bacterial IgA protease was able to effectively degrade the deposited immune complex within the glomerulus.
Conclusion: The bacteria-derived IgA protease is a biologically active enzyme that can specifically degrade serum aglgA systemically and the deposited aglgA-IgG immune complex locally. Thus, the use of IgA protease may represent a novel therapy for IgAN.



http://dx.doi.org/10.1016/j.hkjn.2015.08.095

0122
CagA Promotes Proliferation and Secretion of Extracellular Matrix in Rat Glomerular Mesangial Cells

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