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

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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 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 644.56 ± 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 grade-I-II and grade III group (620.43 ± 271.47 vs 107.38 ± 83.37 and 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.

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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 diagnosis of IgAN and evaluating histopathological injury. The patients were treated according to the KDIGO guideline and followed up. The roles of miRNAs in reflecting therapeutic 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 < 0.047, miR-205 > 0.329 and miR-21 ≥ 0.461 were independent factors for diagnosis of IgAN. The ROC revealed that miR-205 < 0.125 and miR-21 ≥ 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 achieving 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 miR-NAs may be predictors to reflect therapeutic efficacy and disease progression.

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0118
Bacterial IgA Protease-mediated Degradation of agIgA1 and Its Immune Complex as a Potential Novel Therapy for IgA Nephropathy

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Objective: Mesangial deposition of aberrantly glycosylated IgA1 (agIgA1) 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 agIgA1 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 agIgA1 and its immune complex was determined in vitro with artificially deglycosylated IgA1 and human IgA1 biopsy and in vivo in a modified mouse model of passive IgAN. Results: Selected bacteria-derived IgA proteases were capable of degrading serum agIgA1, 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 agIgA1-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 agIgA systemically and the deposited agIgA1-IgG immune complex locally. Thus, the use of IgA protease may represent a novel therapy for IgAN.

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

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Objective: It has been reported that Helicobacter pylori infection is involved in the pathogenesis of IgA nephropathy (IgAN). However, the exact mechanism remains unclear. In this study, we set to investigate the impact of cytoxin-associated antigen A (CagA), one of the major toxins in H. pylori, on the proliferation and extracellular matrix secretion and synthesis in cultured rat glomerular mesangial cells (RGMc).

Methods: The RGMc cells were cultured in medium containing CagA of different concentration (0, 1, 2, 4 μg/ml) for different time (24, 48, 72 hours) followed by proliferation assay by CCK8 and quantitative analysis of extracellular matrix secretion (Collagen I and III). The optimal combination of CagA concentration and treatment time was chosen to stimulate RGMc cells and expression of cell proliferation associated molecules (BAX, Bcl-2, PCNA) and intracellular collagen protein synthesis (Collagen I and III) were checked by RT-PCR, western blot and immunohistochemical staining.

Results: CagA stimulated proliferation of RGMc as well as Collagen I and III secretion in culture medium in a dosage and time-dependent way. Compared with the control, 4 μg/ml of CagA significantly promoted proliferation of RGMc and Collagen I and III secretion as 10^-1 (10 ng/ml). Furthermore, immunohistochemical staining showed increased PCNA expression in RGMc upon CagA stimulation. RT-PCR and western blot also validated the elevated mRNA and protein level of BAX, Bcl-2, Collagen I and III.

Conclusion: CagA directly promotes rat glomerular mesangial cell proliferation and extracellular matrix protein synthesis and secretion, indicating an underlying mechanism for H. pylori infection associated with kidney damage in IgAN.

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0128
Clinicopathological Features and Renal Outcome Analysis of IgA Nephropathy Patients with Acute Kidney Injury
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Objective: We investigated the distinctive clinicopathological characteristics of Chinese IgA nephropathy (IgAN) population with acute kidney injury (AKI) and tried to examine the association between AKI and renal outcome.

Methods: We performed a retrospective analysis of 1512 patients who were biopsy-proven primary IgAN in the period 2006 through 2011 in our center. AKI was defined as 2012 KDIGO (Kidney Diseases: Improving Global Outcomes) criteria, we divided patients into AKI group (n = 145) and non-AKI group (n = 1367) in cross-section analysis. There were 82 AKI and 906 non-AKI patients who had been regularly followed up until December 31, 2013. The primary composite endpoint was renal progression (including doubling of serum creatinine or end-stage renal disease or start of renal replacement therapy).

Results: The prevalence of AKI in our center was 9.59% (145/1512). The clinicopathologic features were much more severe in AKI group (P < 0.05). Acute tubulointerstitial nephritis (9.7%) was the most predominant intrinsic renal injuries in Chinese IgAN population with AKI instead of macroscopic hematuria related acute tubular injury/necrosis. In multivariate logistic regression analysis, we found that older age, male gender, malignant hypertension, pre-existing impaired kidney function, proteinuria, cellular crescent, fibrocellular crescent, glomerular sclerosis ≥ 50% were possible risk factors for AKI. The cumulative survival rates without renal progression at 1-year, 3-year, and 5-year was 98.0% versus 83.4%, 93.5% versus 64.0%, 49.6% versus 33.0%, 54.5% and 6.1% respectively in patients without hypertensive crisis. Impressively, the difference of proteinuria was not statistically significant. In addition, multivariate logistic regression indicated that abnormal glucose metabolism (OR = 2.517, p = 0.049), tubular atrophy/intertstitial fibrosis (OR = 6.446, p = 0.021) and capillary thrombosis (OR = 7.266, p = 0.004) were independently associated with hypertensive crisis.

Conclusion: The incidence of hypertensive crisis was 4.2%. IgAN patients with hypertensive crisis had worse clinicopathological features. Abnormal glucose metabolism, tubular atrophy/intertstitial fibrosis and capillary thrombosis were risk factors of hypertensive crisis in IgAN patients with hypertension.

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0130
Association of Clinicopathological Characteristics and Renal Function in Patients with IgA Nephropathy
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Objective: We conducted a study to compare the clinicopathological features and to identify the potential factors associated with the renal outcome.

Methods: This was a retrospective cohort study, and a total of 1570 IgA patients were included. We evaluated the demographic, clinical and pathological characteristics of 1570 IgAN patients with different levels of kidney function. Unadjusted and adjusted logistic regression models were used to evaluate the association of clinicopathological characteristics and kidney function.

Results: Of the 1570 IgAN patients enrolled in this study, there were 1,146 patients with estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/