

β ig-h3, TGF- β -induced Protein, In Chronic Cyclosporine Nephrotoxicity

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Background: TGF- β , a key fibrogenic cytokine, is involved in the pathogenesis of chronic cyclosporine toxicity (CyAN). TGF- β inducible gene product-H3 (β ig-h3) is a TGF- β induced gene product, whose expression is highly induced by TGF- β and serves as a cell substrate through interacting with integrins. In this study, we evaluated potential roles of β ig-h3 as a urinary marker for CyAN.

Method: We measured urinary β ig-h3 in renal transplant patients who were about to undergo biopsy. Urinary β ig-h3 was determined in 9 patients with biopsy proven CyAN and 13 patients with stable renal function for control by using competitive ELISA. Biopsies were scored according to the Banff 1997 classification. Using immunohistochemical techniques, we also determined the β ig-h3 in renal tissue of patients with CyAN. In patients with CyAN, β ig-h3 urinary excretion was examined before and 1 month after reduction of CyA dosage.

Result: Urinary β ig-h3 excretion was significantly higher in the CyAN group than in the control group (173.4 ± 77.9 vs 62.6 ± 18.2 ng/mg creatinine, $p < 0.01$). In histopathological examination of the biopsies, urinary β ig-h3 levels significantly correlated with the degree of glomerular sclerosis. However, no correlation was observed between urinary β ig-h3 levels and degree of tubulointerstitial changes, such as tubulointerstitial fibrosis and tubular atrophy. In control human kidney, the β ig-h3 labeling was observed in the basement membrane of the proximal tubules and Bowman's capsule. In CyAN patients, increased β ig-h3 labeling was identified at the area of heavy infiltration of inflammatory cells and the basement membrane area of the atrophied tubules and interstitium. Whole blood trough levels of CyA decreased from 172.4 to 41.6 pg/mL at 1 month after discontinuation or the reduction of CyA dosage. Urinary β ig-h3 levels decreased from 173.4 to 64.9 ng/mg creatinine after 1 month but serum creatinine levels showed no significant change.

Conclusions: Urinary β ig-h3 levels increase in CyAN. The levels decrease with the reduction of CyA dosage. Our result suggest a possible role of β ig-h3 as a urinary marker of CyAN.