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Expression of CD71 Mesangial IgA1 Receptor Predicts Progression of IgA Nephropathy

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Objectives: The transferrin receptor (CD71) is known as a receptor for IgA1 on mesangial cells and plays a key role in the pathogenesis of IgA nephropathy (IgAN). However, little is known about the association between clinical outcomes and the level of CD71 expression.

Methods: We studied the clinical implication of mesangial CD71 in 282 patients with biopsy-proven IgAN between 2009 and 2014. Glomeruli were obtained from biopsy tissues by manual microdissection. The expression of glomerular CD71 was determined by real-time polymerase chain reaction and immunohistochemical stain. Disease progression was defined as a $\geq 30\%$ decline in estimated glomerular filtration rate. Human mesangial cells (HMCs) were cultured in medium containing sera from IgAN patients with or without silencing CD71 gene. Transcript levels of CD71 and inflammatory cytokines including IL-6 and TNF- α were compared according to disease status.

Results: During a mean follow up of 51.6 months, 40 (14.2%) patients developed disease progression. The mRNA expression level of CD71 was significantly higher in progressors than in non-progressors ($P=0.001$). Immunohistochemical study also confirmed this finding. Among the Oxford classification scores, patients with M1 had significantly higher CD71 expression levels than those with M0. In multivariable Cox model, elevated transcript levels of CD71 were significantly associated with higher risk of disease progression ($P=0.018$) and a $\geq 50\%$ increase in proteinuria from the baseline ($P=0.003$). *In vitro* study showed that the mRNA expression levels of CD71, IL-6, and TNF- α were more increased in HMCs exposed to patient's sera with the higher Oxford score (M1E1S1T0) than in those with sera from those with negative score (M0E0S0T0). Silencing CD71 significantly reduced expression levels of the inflammatory cytokine genes.

Conclusions: Our results show that glomerular CD71 expression is significantly associated with disease progression and mesangial CD71 may play a biologic role in IgAN.