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Urinary cMet can be used as a prognostic marker in immunoglobulin A nephropathy

Jung Nam An¹, Lilin Li², Jin Hyuk Kim⁵, Yong Chul Kim³, Dong Ki Kim³, Yun Kyu Oh⁵, Chun Soo Lim⁵, Yon Su Kim³, Seung Hee Yang⁴, Jung Pyo Lee⁵

¹Department of Internal Medicine-Nephrology, Hallym University Sacred Heart Hospital, Korea, Republic of

²Department of Internal Medicine-Nephrology, Seoul National University College of Medicine, Korea, Republic of

³Department of Internal Medicine-Nephrology, Seoul National University Hospital, Korea, Republic of

⁴Department of Biomedical Research Institute, Seoul National University Hospital, Korea, Republic of

⁵Department of Internal Medicine-Nephrology, SMG-SNU Boramae Medical Center, Korea, Republic of

Objectives: cMet is critical in regulating inflammation, apoptosis, and fibrosis. We investigated the correlation between urinary cMet (ucMet) levels and clinical parameters in immunoglobulin A nephropathy (IgAN). We also examined the effects of cMet agonistic antibody (cMet Ab) in an *in vitro* IgAN model.

Methods: Patients diagnosed with IgAN (n = 179) were divided into groups 1, 2, and 3, representing undetectable, below median, and above median levels of ucMet/creatinine (Cr). Stained kidney samples were graded according to cMet intensity. Primary-cultured human mesangial cells were stimulated with recombinant tumor necrosis factor (TNF)- α and treated with cMet Ab.

Results: ucMet/Cr levels were positively correlated with proteinuria ($P < 0.001$). During follow-up, patients in group 3 showed a significantly lower probability of complete remission (CR) than those in groups 1 and 2. The result remained significant after adjusting for blood pressure, estimated glomerular filtration rate, and proteinuria, which influence clinical prognosis (HR 0.61, 95% CI 0.37-0.98, $P = 0.042$). Particularly, in patients with proteinuria ≥ 1 g/day, as ucMet/Cr levels increased, the probability of CR decreased (HR 0.24, 95% CI 0.12-0.46, $P < 0.001$). ucMet/Cr levels were associated with glomerular cMet expression. After TNF- α treatment, the proliferation of mesangial cells and increased interleukin-8 and intercellular adhesion molecule-1 expression were markedly reduced by cMet Ab *in vitro*.

Conclusions: ucMet/Cr levels were significantly correlated with proteinuria, glomerular cMet expression, and the probability of CR. Inflammation and proliferation of mesangial cells were alleviated by cMet Ab treatment. ucMet could be clinically significant in treating IgAN.

Figure 1. CR probability according to ucMet/Cr level

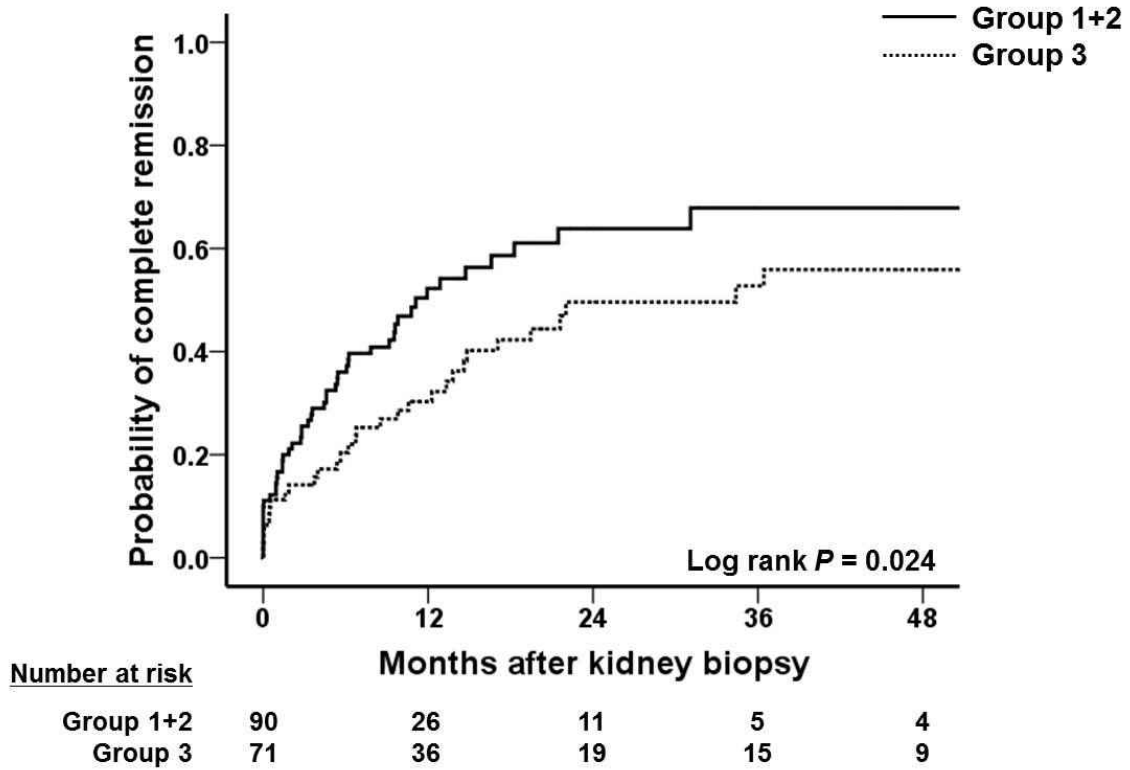


Figure 2. Proliferation of mesangial cells increased upon being stimulated with TNF- α , but was alleviated by cMet Ab treatment

