BanLec Inhibits Middle East Respiratory Syndrome Coronavirus by Binding with the S1 Subunit of the Viral Spike Glycoprotein

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Background/Objective

Middle East respiratory syndrome coronavirus (MERS-CoV) causes severe disease in human with a case-fatality rate of >30% (1). Effective anti-MERS-CoV drugs are urgently needed. We have recently shown the potent anti-MERS-CoV activity of BanLec, a jacalin-related banana lectin, in in vitro assays (2). In this study, we aimed to determine the mechanism by which BanLec inhibits MERS-CoV. As BanLec binds specifically to mannose-containing oligosaccharides and inhibits HIV-1 by binding with the glycosylated envelop protein gp120, we postulated that it also inhibits MERS-CoV by binding with the viral surface Spike glycoprotein.

Method

Bioinformatic analysis of Spike glycoprotein of MERS-CoV was performed as we have previously described (3). Potential N- and O-glycosylation sites, transmembrane domain, and the S2 heptad repeat regions were predicted using NetNGlyc, NetOGlyc, TMHMM v2.0, and MARCOIL, respectively. Cloning and purification of Flag-tagged recombinant receptor binding domain (RBD) of MERS-CoV Spike glycoprotein were performed. Antibodies against S1 of the RBD were generated. The blocking activity of BanLec was analyzed by the use of a competition ELISA.

Result

NetNGlyc and NetOGlyc analyses suggested that at least 19 and 6 potential N- and O-glycosylation sites were predicted in the MERS-CoV Spike glycoprotein. Most of the glycosylation sites were distributed in the N-terminal half of the Spike glycoprotein encompassing the RBD. In the competition ELISA, the optical density of samples containing a mixture of BanLec (180nM) and different concentrations of MERS-CoV S1 (0.0-37.5μg/ml) reduced in a dose-dependent manner. Samples containing a mixture of BanLec/PBS or MERS-CoV S1/PBS showed very high and low optical densities as expected because of the lack of binding between anti-His-tag antibodies (2o antibody) to the His-tag present on BanLec. Overall, these results suggested that BanLec inhibits MERS-CoV by binding with MERS-CoV S1.

Conclusion

BanLec inhibits MERS-CoV by binding with the S1 subunit of the viral Spike glycoprotein.