The Involvement of TLR6 in Immunopathogenesis of Dengue Virus Infection.

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Background/Objective
Toll-like receptors (TLR) are pathogen recognition receptors which are able to sense the presence of foreign microbial agents by recognizing pathogen-associated molecular patterns. The role of TLR6 in the immunopathogenesis of dengue virus infection was investigated in cell based and TLR6-/- murine model.

Method
A combinational of molecular virology, proteomics and immunological approaches are utlilized.

Result
In this study, the up-regulation of TLR6 during dengue virus (DV) infection was found in K562 cells. TLR6 and TLR2 were also found to be up-regulated in DV-infected human PBMC. IL-6 and TNF-α, cytokines downstream of TLR6 and TLR2 were up-regulated in DV-infected PBMC. Gene silencing of TLR6 in DV-infected K562 cells lowered IL-6 production compared to DV-infected K562 cells transfected with shRNA control plasmid. Similar result was obtained when TLR2/6 of PBMC was blocked during DV infection. These results suggest that TLR6 pathway is activated during dengue virus infection and its activation contributes to IL-6 production. DV NS1 protein was found to significantly increase the production of IL-6 and TNF-α when added to PBMC. The amount of IL-6 and TNF-α stimulated by DV NS1 protein was decreased when TLR2/6 was blocked, suggesting that DV NS1 protein is the viral protein responsible for the activation of TLR2/6 during DV infection. In addition, using TLR6-/- murine model of dengue virus infection, TLR6 was found to contribute to the fatality of the DV-infected mice.

Conclusion
Hence, activation of TLR6 via DV NS1 protein could potentially play an important role in the immunopathogenesis of DV infection.