Detecting Antibody Enhancement Using Dengue Reporter Viruses

Antibody Enhancement of Dengue Infection

Antibody-dependent enhancement (ADE) of Dengue virus infection occurs when non-neutralizing antibodies in serum facilitate cellular infection via Fc receptors (FcR). Because ADE results in infection of cells that would not otherwise be infected by Dengue virus, ADE is a serious risk factor for more severe Dengue pathology. Despite the importance of ADE to vaccine development and epidemiological surveys, antibodies capable of inducing ADE have been difficult to routinely monitor in serum using conventional assays such as the Plaque Reduction Neutralization Assay. A rapid, standardized assay to detect the presence of ADE-inducing antibodies in human serum would provide a strategy for early risk-assessment in vaccine trials, and for surveying epidemiological consequences of global Dengue distribution.

Dengue Reporter Viruses

Integral Molecular has developed the Dengue Reporter Virus Particle (RVP), that can be used to rapidly screen human sera for antibody-dependent enhancement of Dengue infection. RVPs combine a subgenomic replicon encoding an optical reporter, such as GFP or luciferase, with structural components from defined serotypes of Dengue virus (Figure 1). Since RVPs lack the viral machinery required to propagate infection, they are suitable for routine laboratory use. Infection of permissive cells can be readily quantified using standard optical detection platforms, allowing the RVP ADE assay to be automated for high throughput screening of sera from vaccine trials or epidemiological surveys. RVPs retain the antigenic determinants of wild-type virions, so can be used to assess ADE for all four Dengue virus serotypes. By quantifying RVP infection, both the potency and relative titer of antibodies that induce ADE can be measured.

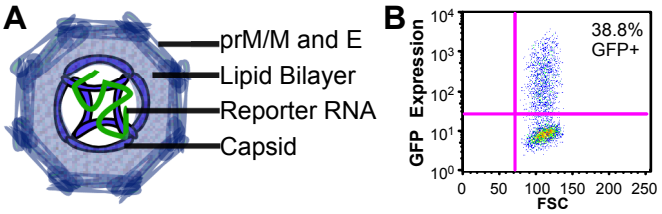

Figure 1. Dengue Reporter Virus composition and reporter expression. (A) Schematic representation of RVPs containing the viral structural proteins envelope (E), capsid, and pre-membrane/membrane proteins (prM/M), a lipid envelope, and a reporter RNA. The Reporter RNA encodes GFP or Luciferase and DENV non-structural proteins responsible for replication of the RNA. **(B)** Target cells infected by RVPs expressing GFP are easily visualized by microscopy or quantified by flow cytometry.

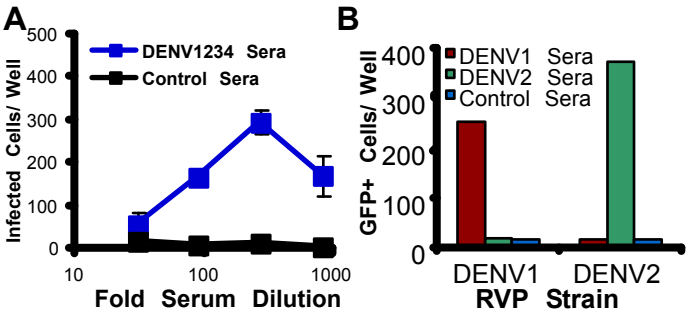

Figure 2. Detection of ADE using Dengue Reporter Viruses. (A) RVPs (serotype 1, West Pac strain) were incubated with dilutions of human tetravalent Dengue antiserum and FcR-positive human K562 cells. (**B)** RVPs from serotype 1 (West Pac) or serotype 2 (S16803) strains were incubated with 1:30 dilutions of human antisera of different serotype reactivities. Infected K562 cells were quantified by flow cytometry.

Technical Description

RVPs were used to quantify the ability of antibodies in human serum to facilitate the enhancement of infection of K562 cells, which contain the FcR but are otherwise not permissive for Dengue infection. Tetravalent (Dengue serotypes 1, 2, 3, & 4) antiserum was serially diluted to sub-neutralizing concentrations and pre-incubated with serotype 1 RVPs. Infection of K562 cells was inversely correlated with antiserum concentration, indicating the ability to detect ADE using RVPs (Figure 2A). K562 cells were not infected when there were insufficient antibodies to mediate infection of the cells. Specific enhancement of RVP infection was demonstrated by the effect of antisera of different serotype specificity. Low concentrations of serotype-specific antisera (Dengue 1 or Dengue 2) enhanced infection of FcR-positive K562 cells by RVPs of the same serotype but did not enhance infectivity of the non-reactive serotype (Figure 2B). Collectively, these data indicate that RVPs can be used to monitor not only the magnitude, but also the breadth, persistence, and specificity of the humoral response to Dengue virus antigen exposure. RVPs thus have significant potential for enabling the routine monitoring of complex immune responses, such as antibody-dependent enhancement of infection.

Contact Us

Quality controlled Dengue Reporter Viruses are commercially available from Integral Molecular with defined strains of DENV serotypes 1, 2, 3, or 4 structural proteins, and with a convenient luminescent reporter. For more information contact us at:

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