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A case study: A robust and fast fluorescent foci-based microneutralization assay using a virus expressing GFP as a key functional biomarker in support of Medimmune clinical studies for the advancement of anti-viral mAb and vaccine drug candidates

Rui Lin
MedImmune LLC, USA

Neutralizing antibodies against viruses represent a major mechanism of host protection against viral infections. Most if not all marketed vaccines elicit neutralizing antibodies. Currently, neutralizing anti-viral therapeutic monoclonal antibodies are being developed for the treatment and/or the prevention of viral diseases. Standard neutralization assays to assess the viral neutralization activities of antibodies have historically been functional plaque assays. Plaque assays are time-consuming, labor-intensive and challenging to implement in clinical studies especially those involving a large number of patients. Here we described the development and implementation of fast and robust Fluorescent Foci (FFA)-based microneutralization (MN) assays. These assays, using viruses expressing enhanced green fluorescence protein (EGFP), allow for higher throughput, better precision, and shorter assay turn-around time making them suitable for use in large clinical studies.

We will first describe the establishment of a novel FFA-based MN assay to detect and quantify neutralizing antibodies against EBV. This assay uses EBV-GFP and an engineered epithelial cell line. All assay conditions impacting assay performance were optimized and the assay was automated using liquid handling and high-content imaging systems. The robustness and precision of the optimized assay were demonstrated using serum samples from mice, rabbits and humans ($n > 600$). In addition, a companion EBV-specific IgG ELISA assay was developed. Significant correlation ($r2 = 0.89$) between both assays was demonstrated using 358 rabbit serum samples. A MN assay was similarly developed for Respiratory Syncytial virus (RSV) to support the development of MedImmune's anti-RSV therapeutic mAbs and RSV vaccine candidates. The 2-year assay control trending of RSV MN assay will be presented to demonstrate the robustness and precision of this assay.

Biography

Rui Lin received his Ph.D. from Cornell University. He completed his postdoc work in UC San Francisco and Genentech. His past work included signal transduction and anti-angiogenesis research, drug discovery and biomarker studies. He is currently a Scientist in Translational Medicine at MedImmune working on vaccine and monoclonal therapeutic antibodies.

linr@MedImmune.com