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Alternate approaches addressing variability in ADCC assay

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Monoclonal antibodies are gaining prominence as therapeutic agents to treat a wide spectrum of diseases. Several of these therapeutics antibodies mediate their action through antibody dependent cellular cytotoxicity (ADCC). ADCC assay requires peripheral blood mononuclear cells (PBMCs) or purified Natural Killer (NK) cells expressing FcγRIIIa receptor isolated from pre-screened healthy human donors as effector cells. Although *in vitro* ADCC mimics the mode of action of these antibodies in the clinic, ADCC is typically not used as a lot release assay. This is due to the extreme variability observed in the assay due to the varying response exhibited by the effector cells isolated from different donors and ethical issues with procuring blood samples, cost, logistic, and practical aspects. Therefore, this assay is limited to characterization of product during the development phase. In order to address these issues, our lab assessed several alternative approaches for performing ADCC assay. In this poster, we present data for an improved ADCC assay using cultured PBMCs, which significantly reduces assay variability. We have also generated data using a reporter-based cell line engineered to express FcγRIIIa and NFAT-RE-luc2 luciferase genes and a FcγRIIIa (CD16) binding assay as possible surrogate assays for ADCC. These assays provide alternative approaches to address the assay variability and usage of human blood associated with the traditional ADCC assay. Data obtained with cultured PBMC exhibited less variability with improved dose response, defined asymptotes and consistent slope. Whereas data obtained with reporter based bioassay and binding assay not only addressed the variability but also exhibited good precision and broader working window with low background and have the potential to become a robust lot release assay.

Biography

Prabhavathy Munagala is a cell biologist with 12 years of extensive experience in the development and validation of potency assays (cell based and cell free). She also has hands-on experience in upstream and downstream processing. Academically, she holds Master, MPhil and PhD degree in Biotechnology. She joined USP–India in May 2011 as Senior Manager (Cell Biology) in Biologics and Biotechnology laboratory at the USP facility in Hyderabad, India. At USP, she leads the Cell Biology team and is responsible for the overall functions of the cell biology group. Before joining USP, she worked in leading biopharmaceutical companies such Dr. Reddy's Laboratories, INTAS Biopharmaceuticals, Vivo Biotech Limited etc.

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