

## Cell-Based Bioactivity Assays

Our Cell and Tissue Services Department analyzes and compares various substances for their potency and mode-of-action in cell-based activity assays also as stand-alone services.

A cell-based assay is an analytical procedure to measure the biological activity of a test substance based on a specific, functional, biological response of a cellular test system.

The use of *in vivo* bioassays is diminishing, given disadvantages associated with cost, low throughput, practical, and ethical considerations.

Cell-based assays are pivotal tools for activity testing in batch release and for mode-of-action analysis of drug candidates and new compounds.

### Our services comprise:

- Cell-based assays using primary cells & cell lines
- Cell line development for new cell-based assays
- Establishment of fully characterized target cell banks according to Good Cell Culture Practice (“GCCP”) principles
- Optimization of cell based assays for mode-of-action analysis and batch release testing
- Generation of full dose-response curve or potency estimation in high throughput assays
- Establishment and validation of international standard derived internal standard banks
- Validation of batch release assays according to international guidelines
- Standardized FMEA-based risk assessment
- Statistical data analysis

### Our assay portfolio covers:

- Anti-viral assays (AVA), according to the European Pharmacopoeia
- Anti-proliferation assays (e.g. for Interferons and other cytokines)
- Cell proliferation assays (e.g. growth factors)
- MHC-I up-regulation assays for immuno-modulating substances
- Commercial and proprietary reporter gene assays for type I Interferons

- Antibody-dependent cellular cytotoxicity assays (ADCC)
- Complement-dependent cytotoxicity assays (CDC)
- Antibody-dependent cellular phagocytosis assays (ADCP)
- Dendritic cell (DC) assays
- T cell assays
- Induced lymphocyte assays (ILA) to investigate cytokine responses (bead array) and expression of cellular markers (flow cytometry)
- Cell-based assay for follicle-stimulation hormone (FSH) activity
- Apoptose assays
- Cell cycle analysis
- Human Artificial Lymph Node (HuALN) model to predict drug-related effects on the human immune system *in vitro*

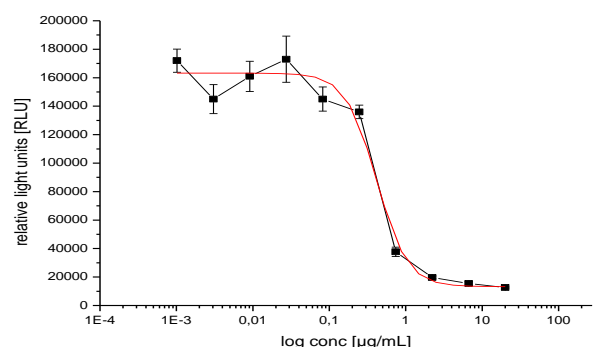
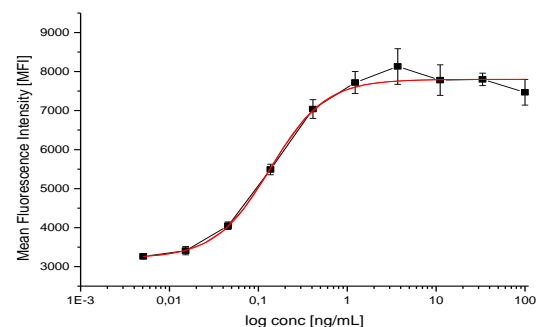
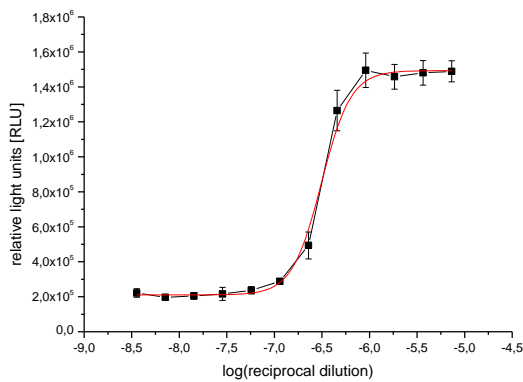
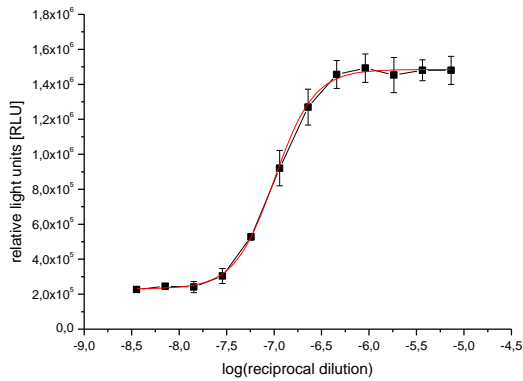
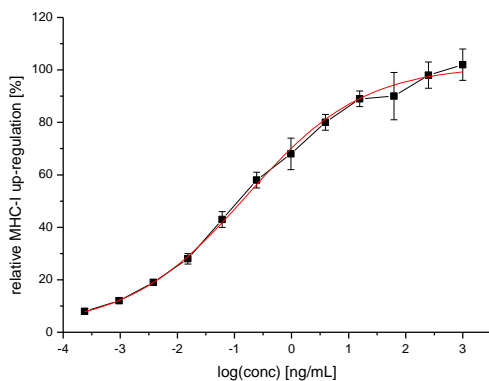


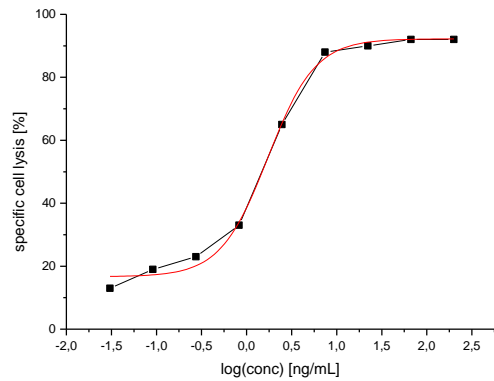
Figure 1: Proliferation / anti-proliferation assays. GM-CSF proliferation (top diagram) and antibody-induced inhibition (bottom diagram) of TF-1 cell line.



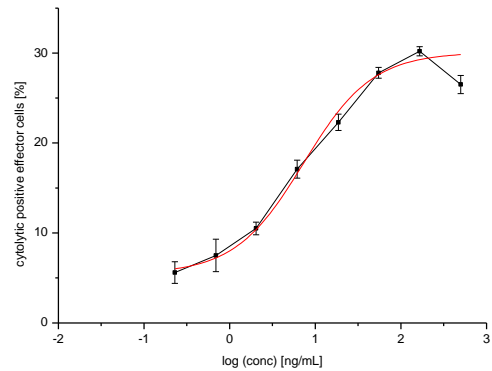
**Figure 2: Anti-viral assay (AVA).** The assay was conducted according to the EP using EMC virus in combination with the cell line A549 (survival of cells, luminescence based ATP detection). Comparison of a second generation IFN- $\beta$  with a commercial IFN- $\beta$  product. The decreased slope in the inflexion point (top diagram) shows lower IFNAR1 affinity of the second generation IFN- $\beta$ .



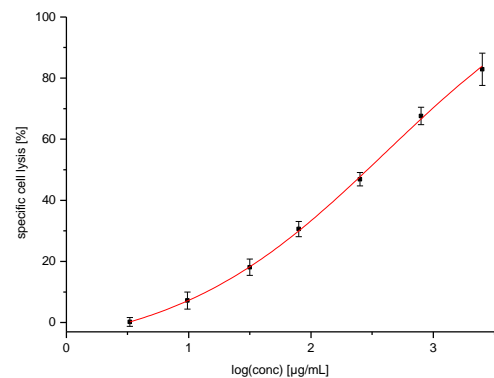
**Figure 3: Immuno-modulating effect (MHC-I up-regulation) of a commercial IFN- $\beta$  product analyzed by flow cytometry.**



**Figure 4: Antibody-dependent cytotoxicity assay (ADCC) of Adalizumab (MabCampath<sup>®</sup>, Genzyme) using primary NK cells in combination with CD52 positive target cells.**



**Figure 5: Antibody-dependent cellular phagocytosis assay (ADCP).** For this assay, SK-BR-3 cells were treated with Trastuzumab and stained with PKH26. The labelled target cells were then exposed to in vitro differentiated macrophages for phagocytosis. Phagocytotic frequency was quantified by double positive macrophages (CD14- and PKH26) (FACS).



**Figure 6: Complement-dependent cytotoxicity assay (CDC).** Human complement serum induced cytotoxicity of Alemtuzumab treated CD52 positive target cells.