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# Immunotoxicity Services

Traditional preclinical models often fail to fully recapitulate the complexity of the human immune response and may not adequately reflect the safety of candidates entering the pipeline. As part of our early de-risking strategy, Cyprotex has developed a battery of *in vitro* assays using primary human cell models to assess the immunogenic and cytotoxic potential of various drug modalities such as biologics, oligonucleotides and small molecules. Our on-site biobank of HLA-typed immunocompetent cells allows both inter-individual and population wide responses to be evaluated.

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- ▶ **PBMC Cytokine Storm Panel:** measures release of pro-inflammatory cytokines (TNF, IFN- $\gamma$ , IL-6 and IL-10) by human PBMCs after 72 hr exposure.
- ▶ **T-Cell Immunogenicity Risk Panel:** measures cytokine release (IL-2 and IFN- $\gamma$ ) by human PBMCs after 6 day exposure.
- ▶ **PBMC Proliferation Assay:** measures drug-induced PBMC proliferation and corresponding increase in cellular ATP after 24–72 hr exposure.
- ▶ **PBMC Cytotoxicity Assay:** measures drug-induced cellular ATP depletion and LDH release in human PBMCs after 24–72 hr exposure.
- ▶ **Dendritic Cell Activation Assay:** measures pro-inflammatory cytokine release (TNF, IL-6 and IL-10) and cellular ATP in monocyte derived dendritic cells after 24 hr exposure.

## Related Skin Sensitization Services

- ▶ Direct peptide reactivity assay (DPRA) according to OECD TG 442C
- ▶ KeratonoSens™ assay according to OECD TG 442D
- ▶ U-SENS™ assay according to OECD TG 442E



## Your Partner in Immunotoxicity Assessment

- ▶ **Extensive experience.** Our team of experts have decades of combined industry experience in immunotoxicology to plan optimal screening strategies and assist with data interpretation and future project planning.
- ▶ **On-site biobank.** Our biobank houses a wide diversity of HLA-types cell types isolated from the blood of healthy human donors allowing inter-individual and population-wide immune responses to be evaluated.
- ▶ **Diverse Modalities.** We have experience working with a range of diverse modalities covering biologics, oligonucleotides and small molecules.
- ▶ **Project support.** Dedicated study managers are assigned to your project and are on hand to support you with logistics, data delivery and any technical questions.
- ▶ **Comprehensive range of services.** We offer a wide range of flexible services which can be specifically designed for your needs.
- ▶ **Secure high quality data delivery.** Our laboratories based in the USA and Europe follow strict quality procedure to ensure your data is the highest quality and is stored and delivered securely.

## Representative Data from Dendritic Cell Activation Assay

	Immunogenic <i>in vivo</i>	IL-6	TNF	IL-10	Cellular ATP
<b>Biologics</b>					
LPS EK	Yes	↑<0.4 ng/mL	↑1 ng/mL	↑4 ng/mL	No response
MDP	Yes	↑10 ng/mL	↑140 ng/mL	No response	No response
<b>Oligonucleotides</b>					
ODN2395 (Class C)	Yes	↑0.85 µM	↑0.91 µM	↑5.95 µM	No response
ODN1668 (Class B)	Yes	↑2.29 µM	↑1.40 µM	No response	No response
ssRNA40/LyoVec™	Yes	↑130 ng/mL	↑330 ng/mL	No response	No response
<b>Small Molecules</b>					
Resiquimod (R848)	Yes	↑50 ng/mL	↑290 ng/mL	↑1430 ng/mL	No response
CL075	Yes	↑60 ng/mL	↑50 ng/mL	↑320 ng/mL	No response
Pindolol	No	No response	No response	No response	No response
Lapatinib	No	No response	No response	No response	↓4.65 µM

Dendritic cells were exposed to the test articles for 24 hr before supernatants were harvested for cytokine analysis and cell viability assessment. The table displays minimum effective concentration values for a range of different modalities.

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