



MHC-associated Peptide Proteomics (MAPPs) Strategies for Immunogenicity Risk Assessment and Vaccine Design

Unwanted immunogenicity — when a biologic unintentionally activates the patient's immune system — often affects therapeutic efficacy and safety of new drug candidates. To complement conventional MHC class I and II strategies, IQVIA Laboratories In Vitro Immunology offers MAPPs solutions using a multiplexed setup to provide improved throughput and generate high-quality datasets that can inform in silico models and machine learning tools.

MAPPs assay

The MAPPs assay is a mass spectrometry-based method to identify peptides that are naturally processed and presented by major histocompatibility complex (MHC) molecules.

- **MHC-II pathway:** Exogenous protein fragments — such as biotherapeutic candidates — are processed by antigen-presenting cells (APCs) and presented to CD4⁺ helper T cells via MHC-II
- **MHC-I pathway:** Peptides derived from intracellular sources — including viral proteins, tumor antigens and vaccine components — are presented on MHC class I molecules to CD8⁺ cytotoxic T-cells on nearly all nucleated cells

MHC-II-presented peptides can activate CD4⁺ T cells and initiate an immune response. The MAPPs assay allows you to:

- Assess the immunogenicity risk of biotherapeutic candidates by identifying naturally presented epitopes
- Improve your de-immunization efforts and the development of safer biotherapeutics
- Evaluate candidates that act directly on dendritic cells or T cells, where standard in vitro T cell immunogenicity assays often fail due to assay interference

MHC-I presented peptides can activate CD8⁺ T-cells and elicit direct killing of infected/cancer cells.

The MAPPs assay helps you:

- Identify endogenous peptides, including ones from non-canonical sources, to assess anti-viral/anti-tumor immunity
- Assess unwanted immunogenicity of advanced therapeutic modalities
- Provide insight into immune-targeting mechanisms, supporting (cancer) vaccine development

Our MAPPs workflow

- 1. Donor derived cells:** Monocytes are isolated from peripheral blood mononuclear cells (PBMCs) of healthy donors with diverse HLA class I and/or class II backgrounds and differentiated into immature dendritic cells (iDCs)

MHC-II complexes using optimized antibody cocktails (anti-HLA DR, DP, DQ, and/or pan HLA class I antibodies)
- 2. Antigen loading and maturation:** iDCs are loaded, incubated or transfected with biotherapeutic candidates and subsequently matured
- 3. MHC complex isolation:** Cells are harvested, lysed, and pre-cleared prior to affinity purification of MHC-I complexes, MHC-II complexes, or sequential MHC-I/

4. Peptide identification: MHC-associated peptides are eluted and identified using LC MS/MS
- 5. Data analysis:** Advanced bioinformatics workflows identify and characterize presented peptides, map them back to source proteins, enabling comparative and semi-quantitative analyses across donors, conditions or candidates

Fit-for-purpose donor selection via our in-house biobank

Our quality-controlled biobank of HLA-typed PBMC samples supports robust and representative study design. Our capabilities include:

- Post-thaw viability and recovery assessment
- Subpopulation analysis via flow cytometry
- Selection by HLA typing, donor gender, ethnicity and year of birth
- Functional assessments (polyclonal and naïve antigen responses)
- Recall antigen reactivity assessment (CMV)
- Customized pre-screening/reactivity assessment

Multiplexing to increase throughput and generate high-quality data sets

Traditional MAPPs assays require large numbers of dendritic cells per candidate, limiting assay throughput and increasing costs. By multiplexing selected candidates into single DC samples, we increase assay throughput and provide a cost-efficient solution. This approach is particularly useful in generating high-value datasets suitable for training machine-learning models on immunogenicity risk at the peptide-presentation level.

Through our thoughtful design of candidate pools, individual peptides can be confidently traced back to the originating candidate

Design your pools with support from the expert mass spectrometry team from ImmuneSpec and/or other in silico experts.



The IQVIA Laboratories difference

Our seasoned In Vitro Immunology team delivers scientifically rigorous, regulatory-ready MAPPs solutions, tailored to each project. Our team brings years of expertise in recommending the most appropriate assays and optimizing them for your needs. Our scientists are leaders in global immunogenicity working groups that evaluate and establish industry standards for regulatory submissions.

Our agile approach ensures that we connect with customers after each stage to determine the next step. Our In Vitro Immunology lab holds a Belgian Biobank License and houses >1300 quality-controlled PBMC samples from healthy donors with 4-digit HLA typing, immunophenotyping and antigen response assessment. Customized reporting is available for regulatory submissions.

Whether you need a standardized assay or a fully custom solution, IQVIA Laboratories will collaborate with you to reduce immunogenicity risk and accelerate confident decision-making.



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