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Immunogenicity Risk Assessment in Drug Candidate Selection

Introduction

Early in development, understanding whether a candidate drug might induce an unwanted anti-drug immune response can make or break a project. The sooner you spot and deal with these risks, the better. If a candidate drug is likely to trigger an immune response, it can lead to wasted time and resources. By spotting these risks early in development, it enables you to focus on molecules with lower immunogenic potential or redesign your molecule to keep your drug on a successful development path. Getting ahead of this issue can make all the difference in achieving success in the clinic – allowing you to start smart, and finish fast.

Why We Need Immunogenicity Testing

The immune system determines whether a therapeutic protein is foreign based on several factors, including the protein's amino acid sequence, structure, post-translational modifications (PTMs), and formulation. If the protein differs significantly from the body's natural proteins, the immune system sees it as foreign and mounts a response. This reaction can lead to anti-drug antibodies (ADAs) that neutralize the drug, diminishing its efficacy and potentially causing adverse side effects, especially when the ADAs cross-react with the body's own proteins.

Immunogenicity refers to a molecule's ability to trigger an unwanted immune response. When antigen-presenting cells (APCs) process the protein and display peptide fragments on major histocompatibility complex (MHC) class II molecules, CD4+ T cells recognize these fragments via their T cell receptors (TCR). They then initiate an immune response, which can lead to the production of anti-drug antibodies (ADAs). These antibodies can reduce the drug's efficacy and cause adverse effects.

Screening for Immunogenicity

To determine a drug candidate's immunogenic potential, we can use a variety of screening methods—these primarily include a combination of in silico and in vitro/ex vivo approaches.

In Silico

In silico tools, such as Abzena's iTope-AI platform, use sophisticated algorithms to predict T cell epitope binding to MHC class II molecules, covering a broad range of human leukocyte antigen (HLA) alleles. This means you can identify immunogenic 'hotspots' within a protein early on so they can subsequently be modified to reduce immunogenicity. These predictions are based on extensive known T cell epitope datasets and their corresponding HLA binding motifs, which allow the algorithm to identify patterns that might be missed through other experimental methods.

While in silico tools are great for early-stage high throughput screening, they do have their limits, in particular around an algorithm's capacity to model the complex interactions between peptides and the immune system. As described above, generating a T cell response is a multi-stage process: antigen processing followed by peptide presentation, TCR recognition and T cell activation. Almost all in silico algorithms look at the middle part—putative peptide binding to HLA-molecules. While this stage is absolutely necessary, not all peptides that are predicted to bind will actually be presented or recognized by TCRs and so in silico approaches can be over-predictive. This is why in silico predictions must also be validated through experimental approaches.

In Vitro/Ex Vivo

In vitro assays are used to back up in silico predictions and give a clearer picture of how a drug candidate interacts with immune cells. These assays can simulate the human immune response and typically involve human peripheral blood mononuclear cells (PBMCs) or dendritic cells (DCs) and assess T cell activation in response to the therapeutic protein.

In vitro tests aim to replicate the conditions a therapeutic protein would face in the immune system, which can give you a better prediction of immunogenicity risks than in silico models alone.

Applying Phase-Appropriate Solutions

The best way to overcome the limitations of each testing method is to integrate multiple approaches into one smart strategy. By combining computational predictions with empirical data and biological observations, we can achieve a comprehensive understanding of a therapeutic protein's immunogenic potential. This integrated approach enables the identification and mitigation of immunogenic risks at multiple stages of development, from early candidate selection to late-stage clinical trials.

Once you find candidates with lower immunogenicity risk, you can focus on making those molecules better in terms of efficacy, safety, and manufacturability, which underpins the overall developability of a drug candidate. Furthermore, the identification of specific immunogenic regions within a candidate protein allows for targeted de-immunization efforts, such as modifying T cell epitopes to make them less recognizable by the immune system by reducing their binding avidity to HLA molecules. Taking this proactive approach can help stop ADAs from developing and extend the therapeutic window for biologic drugs. Ultimately, this integrated strategy helps you make smarter decisions early on in development, saving time and money by avoiding late-stage failures.

Challenges in Predicting Immunogenicity

Even when you combine different screening methods, predicting immunogenicity isn't easy. The immune system's response is influenced by multiple factors, including genetic differences between patients, especially in HLA class II molecules. On top of that, aspects such as past exposure to similar antigens and the patient's overall health can also affect how their immune system reacts.

Genetic Variability and Immune System Diversity

One of the main obstacles in predicting immunogenicity comes from the variability within the human immune system. HLA molecules are highly polymorphic, which results in genetic diversity across the human population. As a consequence, a therapeutic protein may be presented differently depending on an individual's specific HLA type, which can trigger varying immune responses. A peptide that is non-immunogenic in one person could elicit a strong immune response in another due to these HLA differences. This genetic diversity makes it tough to predict immunogenicity, as you need to consider a wide range of HLA alleles.[1]

In silico tools are particularly useful here. They can predict T cell epitope binding across many HLA alleles to help account for patient diversity. When you combine in silico predictions with in vitro tests that use immune cells from donors with different genetic backgrounds, you get a more representative picture of immunogenicity risks.

Adding further complexity, the immune history of an individual's past exposures to pathogens, vaccines, or biologic therapies, shape how someone's immune system responds to new therapeutic proteins[1]. If two people have the same HLA type, their immune responses can still be very different because of their unique immune histories. Prior immune responses can make the system more likely to produce ADAs when exposed to new biologic drugs. While these antibodies might not last long, they can still cause hypersensitivity reactions and reduce the drug's efficacy.[2]

Structural and Biophysical Factors

The structure and physical characteristics of a therapeutic protein also influence its immunogenicity. Considerations like protein aggregation, glycosylation patterns, and the presence of neoepitopes (new epitopes created by modifications or mutations) can increase the chances of an immune response. Protein aggregation (typically associated with higher concentrations), in particular, is known to boost immunogenicity by creating new immunogenic epitopes and increasing the likelihood of T cell activation.[3] However, by contrast, it may be possible that higher doses can promote tolerance and reduce immunogenicity, whereas lower or inconsistent doses may increase the chance of an immune response.[4]

Glycosylation, a common PTM, can affect immunogenicity by altering protein folding, stability, and recognition by the immune system.[5] In some cases, non-human glycan structures introduced during biologic production in non-human cell lines can trigger an immune response. Additionally, changes in the protein structure that lead to the exposure of normally buried epitopes can create neoepitopes that are recognized as foreign by the immune system.

You can tackle these issues using protein engineering techniques, such as optimizing glycosylation patterns or reducing aggregation to lower immunogenicity with the help of optimal buffer conditions and formulations. Techniques like MHC Class II Associated Peptide Proteomics (MAPPs) can also help identify hotspots in the amino acid sequence and subsequently modify specific regions to reduce their immunogenic potential without affecting the protein's therapeutic function.

Lack of Standardization Across Testing Methods

An issue that has long been a challenge in immunogenicity and other biological assessments is a lack of standardization. Differences in assay design, reagents, and detection methods make it hard to compare studies and draw clear conclusions about a protein's immunogenicity.

Thankfully, in response to these challenges, there's a growing recognition of the need for regulatory agencies and the scientific community to develop unified guidelines for immunogenicity testing. Working groups such as the European Immunogenicity Platform (EIP) and HESI/AAPS[6] have been formed to bring together experts in immunogenicity testing and regulatory bodies to harmonize assay requirements and standards to ensure consistency in pre-clinical immunogenicity testing.

Abzena's EpiScreen® 2.0: A Comprehensive Approach to Immunogenicity Testing

Abzena's EpiScreen® 2.0 platform integrates multiple immunogenicity testing methods by using an array of ex vivo assays designed to evaluate the immunogenic potential of biologic drug candidates. The platform's strength lies in providing detailed insights into CD4+ T cell responses, MHC class II peptide presentation, and cytokine release.

We developed the original EpiScreen® platform over 20 years ago and it has served as a key tool in many drug development programs. In 2024, we launched the upgraded EpiScreen® 2.0, which improves on the original by offering more advanced immune response measurements. It provides the improved sensitivity needed, along with detailed insights into specificity and mechanism of action (MoA), to help better understand immunogenicity risks and how to reduce them through protein engineering and formulation.

Time Course Assay

Using flow cytometry, EpiScreen® 2.0's whole PBMC Time Course Assay delivers levels of sensitivity comparable to traditional assays using [3H]-thymidine for proliferation but also allows you to characterize the responding immune cells by multiplexing the readout with T cell activation markers—without the need for radioactive compounds (Figures 1-4). This results in a data-rich readout showing both T cell activation and proliferation to give confident immunogenicity risk assessment.

Different numbers of donors can be used but by using a minimum cohort of 50 donors, the assays are not only able to generate statistically significant data but also provides the opportunity to tailor the distribution of HLA-DR allotypes to reflect the population of interest.

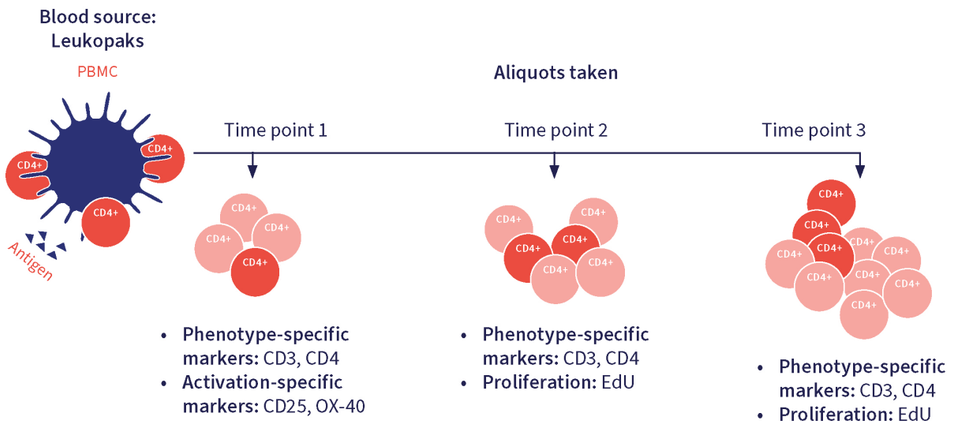

Figure 1. Schematic showing Episcreen® Time Course Assay Overview

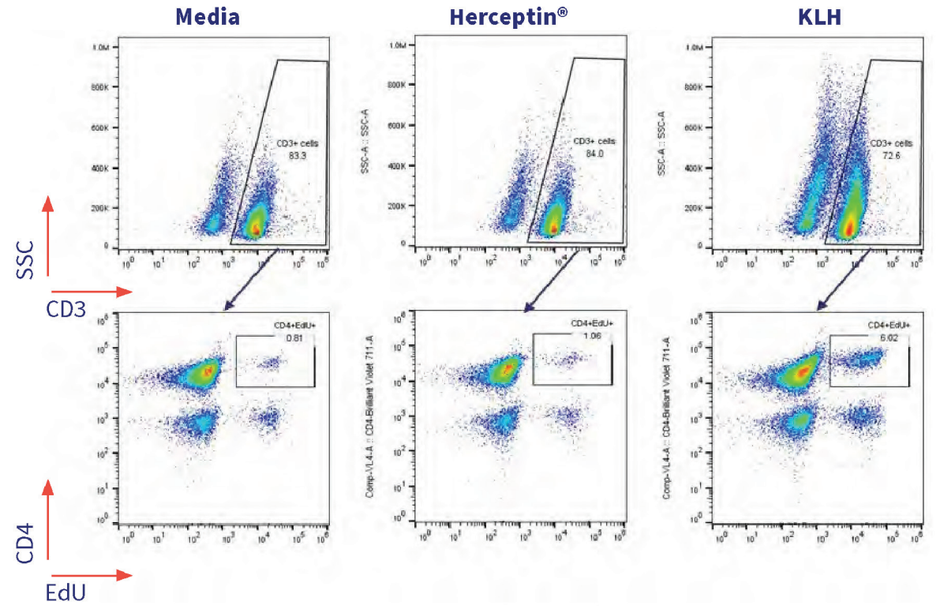

Figure 2. EpiScreen® looks at CD4+ T cell proliferation. Flow cytometry gating strategy to determine EdU+ cells in response to Media, Herceptin® (low immunogenicity control), and KLH (high immunogenicity control).

Monitoring CD4+ and CD8+ T Cell Behavior

As well as the improved sensitivity and the ability to assess CD4+ T cell proliferation via flow cytometry, EpiScreen® 2.0 (Figure 3) can optionally provide information on CD8+ activation if required. This gives insights into the MoA, which is especially helpful for gene therapies where vectors can be cross-presented on MHC-I.

DC:T Cell Assay

The EpiScreen® 2.0 DC:T cell assay is a variation of the Time Course assay specifically designed to assess the potential immunogenicity of antibodies and proteins that directly modulate T cell activation. In this assay, monocytes are purified from PBMCs (again typically from 50 individual donors with a pre-determined distribution of HLA-DR allotypes (coverage and frequency)) and allowed to differentiate into immature moDCs. The DCs are then challenged with the test biotherapeutics and, following maturation, incubated with autologous CD4+ T cells prior to assessing T cell proliferation.

This assay is particularly valuable for molecules that modulate T cell function as the therapeutic does not come into direct contact with T cells, rather it is processed by dendritic cells prior to T cell addition.

Cytokine Release Evaluation

The production and release of cytokines forms part of the innate inflammation and infection response and can, in certain circumstances, be detected in the serum of patients within minutes to hours after infusion. There are well documented examples where elevated cytokine levels have been observed in patients but where in vitro and in vivo animal studies have failed to be predictive of such severe reactions (see the TGN1412 case study below).

The EpiScreen® 2.0 Cytokine Screen™ assay assesses the potential for cytokine release syndrome—a severe immune reaction that can occur when T cells are excessively activated. It measures cytokine levels in response to the drug candidate, helping to spot and assess the likelihood of a cytokine storm.

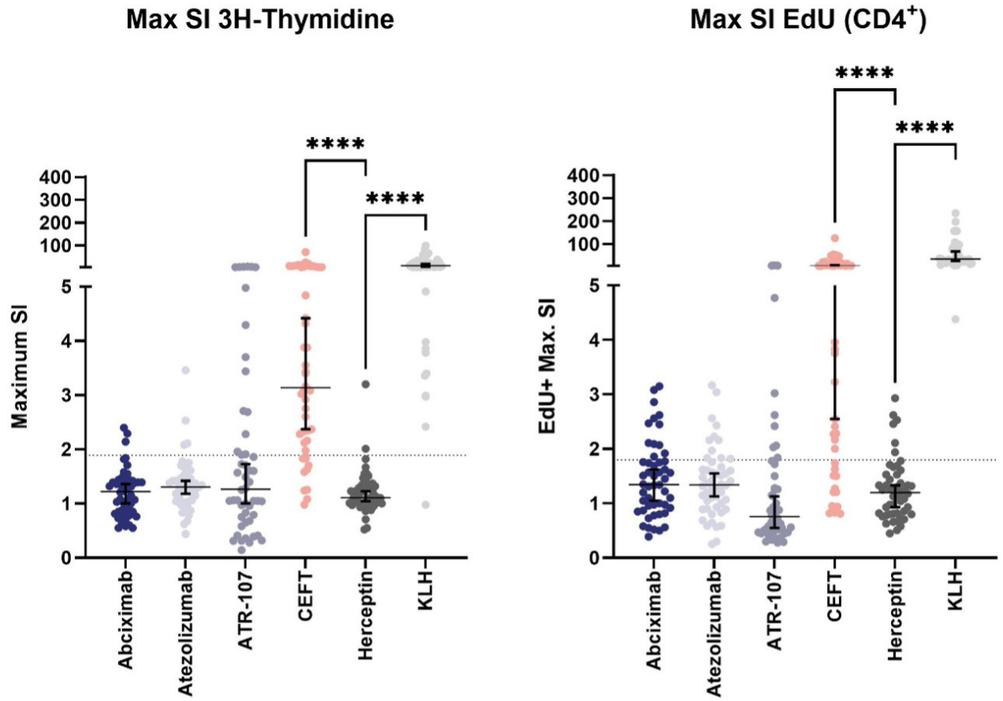

Figure 3. Box and whisker plot showing maximum proliferation SI obtained on PBMC (non-CD8+ depleted) over the Episcreen® 2.0 Time Course assay in response to test samples. Left, 3H-Thymidine readout. Right, EdU readout on CD4+ T cells. One-way ANOVA, followed by Friedman's post-test was used for statistical analysis. ****p <0.0001 (n=50). The dotted lines represent the threshold for a positive response (SI ≥1.9 for 3H-Thymidine; SI ≥1.8 for EdU).

Table 1. Proliferation and activation response in PBMC (non-CD8-depleted)

Sample	% Response 3H-Thy	% Response EdU	% Response AIM	Expected ADA (%)
Abciximab	6	24	14	6-44
Atezolizumab	8	22	12	13-36
ATR-107	32	20	32	76 (37.5*)
CEFT	80	76	82	70-90+
Herceptin®	4	12	10	10
KLH	98	100	100	90-100+

* Reported response in vitro

+ Expected assay response rates are reported for CEFT and KLH

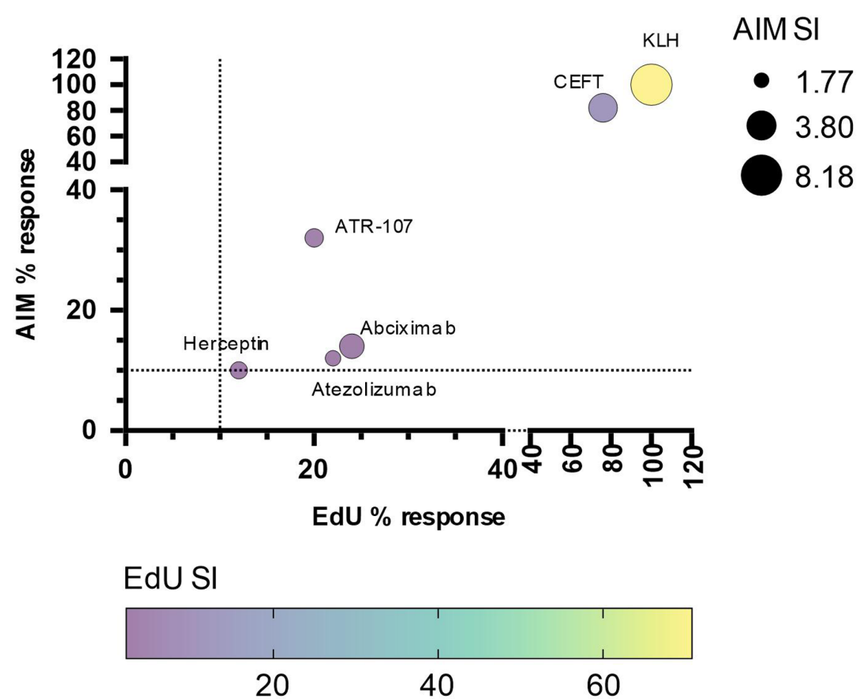

Figure 4. Multiple variable analysis bubble plot: AIM response rate (Y axis), EdU response rate (X axis), SI from AIM positive responses (dot size) and SI from EdU proliferation positive responses (color).

MHC-Associated Peptide Proteomics (MAPPs)

EpiScreen® 2.0 MAPPs detects and identifies MHC Class II bound peptides processed and presented by DCs from therapeutic proteins. When combined with our ex vivo T cell epitope mapping assay, it helps pinpoint peptides recognized by CD4+ T cells with the potential to trigger an immune cascade, leading to T cell proliferation and subsequent ADA formation.

These tools give you a way to design biopharmaceutical candidates with a lower risk of immunogenicity. They're especially useful for:

- Evaluating new product candidates with known ADA inducers.
- Pharmacologically active products that have a direct positive or negative impact on T cell function.
- Large or complex candidates, helping guide ex vivo T cell epitope mapping.
- Acting as a pre-filter for potential T cell epitopes, offering more accurate predictions than in silico methods.

We've worked with the US Food and Drug Administration (FDA) using MAPPs assays to study the immunogenicity of the Factor VIIa analogue Vatreptacog Alfa (see the case study below). MAPPs assays are also available for MHC Class I presentations.

In Silico Screening with iTope-AI and TCED™

To complement the ex vivo assays, we use iTope-AI, a proprietary in silico tool that applies computational algorithms to predict peptide-MHC binding and find potential T cell epitopes (Figure 5). iTope-AI models how amino acid side chains of a peptide interact with specific binding pockets in the grooves of 46 human MHC class II alleles (DR, DP, and DQ), with an optional human proteome filter.

iTope-AI can analyze how each amino acid contributes to peptide binding for each allele, giving precise information on the location of the core 9-mer sequences that interact with the MHC class II binding groove. It's a helpful first step for evaluating the immunogenic potential of antibodies and proteins. However, as with other in silico algorithms, iTope-AI tends to over-predict CD4+ T cell epitopes, so it's best used as a rapid, high throughput screening tool prior to testing with e.g. EpiScreen® 2.0.

Once immunogenic amino acid sequences have been identified using T cell epitope mapping, iTope-AI can be applied to find the core 9-mer sequences. Once identified, these sequences can then be used to design non-antigenic variants, which disrupt MHC Class II binding and reduce immunogenicity.

iTope-AI can also be used in conjunction with TCED™, a database of T cell epitopes built from over a decade of EpiScreen® 2.0 T cell epitope mapping studies. Antibody and protein sequences can be quickly checked against this database for homology to known epitopes to give fast and accurate immunogenicity assessments.

Together, TCED™ and iTope-AI are often used to rapidly analyze multiple sequences, such as therapeutic antibody candidates, to find a lead sequence with a lower risk of immunogenicity.

PDB	Allele	Peptide + core motif	iTope-AI
	Anchor Position	P1 4 6 9	
2FSE	DRB1*01:01	AGFKGEQGPKGEPG	FKGEQGPKG
1FYT	DRB1*01:01	PKYVKQNTLKLAT	YVKQNTLKL
3L6P	DRB1*01:01	APPAYEKLSAEQSPP	YEKLSAEQS
2IPK	DRB1*01:01	XPKWVKQNTLKLAT	WVKQNTLKL
1SJH	DRB1*01:01	PEVIPMFSALSEG	VIPMFSALS
3OXA	DRB1*01:01	PVSKMRMATPLLMQA	MRMATPLLM
3PGD	DRB1*01:01	KMRMATPLLMQALPM	MRMATPLLM
3PDO	DRB1*01:01	KPVSKMRMATPLLMQALPM	MRMATPLLM
1AQD	DRB1*01:01	VGSDWRFLRGYHQYA	WRFLRGYHQ
1PYW	DRB1*01:01	XFVKQNAAALX	FVKQNAAAL
1KLG	DRB1*01:01	GELIGTLNAAKVPAD	IGTLNAAKV
4OV5	DRB1*01:01	GSDARFLRGYHLYA	ARFLRGYHL
1SJE	DRB1*01:01	PEVIPMFSALSEGATP	VIPMFSALS
1T5X	DRB1*01:01	AAYSDQATPLLLSPR	YSDQATPLL
4I5B	DRB1*01:01	VVKQNCLKLATK	VKQNCLKLA
4AEN	DRB1*01:01	MPLAQMLLPTAMRMKM	MLLPTAMRM
1A6A	DRB1*03:01	PVSKMRMATPLLMQA	MRMATPLLM
1J8H	DRB1*04:01	PKYVKQNTLKLAT	YVKQNTLKL
4IS6	DRB1*04:01	WNRQLYPEWTEAQRLD	LYPEWTEAQ
4MD4	DRB1*04:01	ATEYRVRVNSAYQDK	YRVRVNSAY
2SEB	DRB1*04:01	AYMRADAAAGGA	YMRADAAAG
4MCZ	DRB1*04:01	GVYATRSSAVRLR	YATRSSAVR
4MCY	DRB1*04:01	SAVRLRSSVPGVR	VRLRSSVPG
4MDI	DRB1*04:02	SAVRLRSSVPGVR	VRLRSSVPG
4MD5	DRB1*04:04	SAVRLRSSVPGVR	VRLRSSVPG
1BX2	DRB1*15:01	ENPVVHFFKNIVTPR	VHFFKNIVT
1YMM	DRB1*15:01	ENPVVHFFKNIVTPRGGGSGGGGG	VHFFKNIVT
2Q6W	DRB3*01:01	AWRSDEALPLGS	WRSDEALPL
4H1L	DRB3*03:01	QHIRCNIPKRISA	IRCNIPKRI
3C5J	DRB3*03:01	QVILNHPGQISA	ILNHPGQI
4H26	DRB3*03:01	QWIRVNIPKRI	IRVNIPKRI
4H25	DRB3*03:01	QHIRCNIPKRIGPSKVATLVPR	IRCNIPKRI
1H15	DRB5*01:01	GGVYHFVKKHVHES	YHFVKKHVH
1ZGL	DRB5*01:01	VHFFKNIVTPRTPGG	FKNIVTPRT
1HQR	DRB5*01:01	VHFFKNIVTPRTP	FKNIVTPRT
1FV1	DRB5*01:01	NPVVHFFKNIVTPRTPPPSQ	FKNIVTPRT
1JK8	DQ8	LVEALYLVCGERG	EALYLVCGE
3LQZ	DP2	RKFHYLPFLPST	FHYLPFLPS

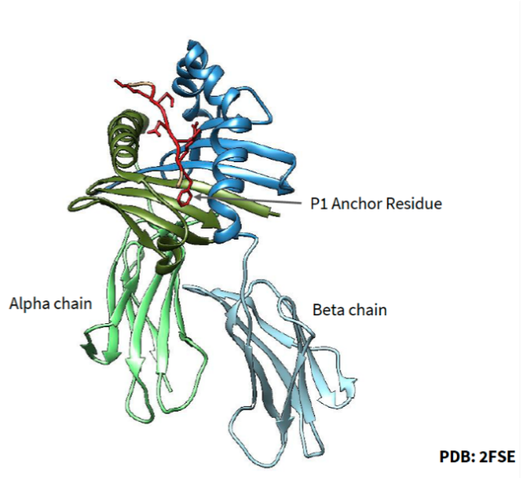

Figure 5. iTope-AI predicts 95% of peptide binding core motifs identified by 3D structure from X-ray crystallography. Table shows a comparison of known protein binding cores from a protein database (PDB) with the resulting iTope-AI predictions.

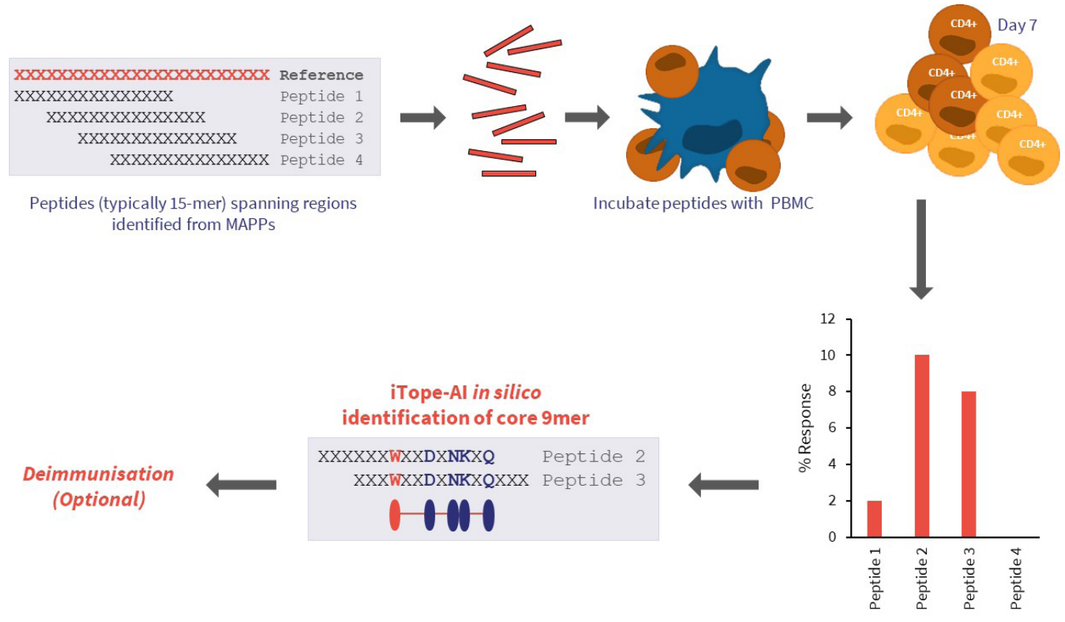

Figure 6. EpiScreen™ T Cell Epitope Mapping. iTope-AI identifies key residues contained within T cell response-inducing peptides.

T Cell Epitope Mapping

T Cell Epitope Mapping is a targeted assay that identifies specific immunogenic hotspots, picking out the precise location, number, and magnitude of T cell epitopes in toxins, protein scaffolds, and both human and non-human proteins. This allows you to pinpoint regions the immune system is likely to recognize.

In CD4+ T cell epitope mapping studies, 15-mer peptides, with a 12 amino acid overlap, are synthesized to span the sequence of the test sample (Figure 6). These peptides are tested against PBMCs from 50 donors with over 80% DRB1 allotypic coverage of the global population. Peptides can either displace those already bound to MHC class II or be taken up by DCs, processed and presented as linear peptides bound in the MHC class II groove. When CD4+ T cells bind to these MHC class II/peptide complexes, it can trigger an activation cascade that leads to T cell proliferation. T cell activation is measured by EdU uptake.

The data from these assays can then guide deimmunization efforts and lower the risk of immunogenicity in clinical settings.

Case Studies: Insights from Immunogenicity Testing

Here we'll take a look at some examples of immunogenicity testing in action.

TGN1412 in PBMC Cytokine Screen

The disastrous outcome of the TGN1412 clinical trial in 2006 highlights why strong immunogenicity testing is essential. TGN1412, a CD28-specific monoclonal antibody designed to treat autoimmune diseases, caused a severe cytokine storm in all six healthy volunteers during a Phase I trial. The extreme release of pro-inflammatory cytokines led to life-threatening conditions, including multiple organ failure and disseminated intravascular coagulation, putting all participants in intensive care.[7]

Standard preclinical safety tests, including those done on cynomolgus macaques, didn't predict this outcome, highlighting the potential deficiencies of animal models. The key reason was that the macaques' CD4+ effector memory T cells didn't express CD28, which is required for the cytokine release seen in humans. Human CD4+ effector memory T cells, on the other hand, express high levels of CD28, making them vulnerable to TGN1412's agonistic activity.

Subsequent investigations showed that traditional in vitro assays, which used soluble forms of TGN1412, didn't mimic the real in vivo environment where the drug interacts with T cells through direct cell contact. However, when TGN1412 was immobilized on tissue culture plates, mimicking localized receptor engagement, the assays triggered massive lymphoproliferation and pro-inflammatory cytokine release, much like what happened in the clinical trial. This finding led to the development of more predictive in vitro assays, like the PBMC cytokine screen in our EpiScreen® 2.0 platform, which better predicts cytokine release risks from therapeutic antibodies (Figure 7).

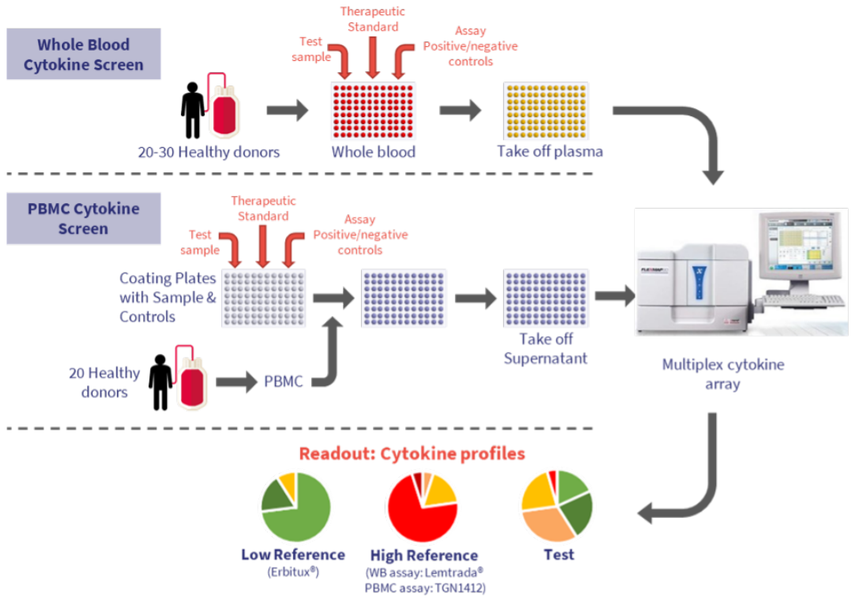

Figure 7. EpiScreen™ Cytokine Screen. Schematic showing overview of whole blood and PBMC Cytokine Screen Assay

iTope-AI and Natalizumab

Natalizumab (NZM), a humanized monoclonal antibody used to treat multiple sclerosis, provides a strong example of how predictive tools like iTope-AI can be powerful. NZM caused the formation of neutralizing ADAs in some patients, which significantly reduced its effectiveness.[8] Researchers identified a single dominant T cell epitope within the FR2-CDR2 region of NZM's light chain. This epitope was predicted to bind with high affinity to a wide range of HLA-DR alleles, which clinical data later confirmed.

iTope-AI's predictions were validated through ex vivo assays, which demonstrated that this specific epitope drove the immunogenic response in multiple sclerosis patients. The accuracy of iTope-AI in identifying these immunodominant regions shows its value in early drug development. By identifying and modifying these epitopes, you can mitigate the risk of ADA formation and improve the safety and efficacy of therapeutic antibodies.

MAPPing Immunogenic Regions

MAPPs was used to lower the risk of a therapeutic protein that had shown immunogenic potential in early clinical trials. Native rFVIIa has been used successfully for over 20 years with no reports of immunogenicity in congenital hemophilia patients. Vatreptacog Alfa (VA), an rFVIIa analog with 3 amino acid substitutions, was designed to be more effective but was discontinued after Phase 3 trials due to ADA development. In a paper co-authored with the FDA, we evaluated the MAPPs assay's ability to predict the immunogenicity of VA. Our results showed that VA triggered stronger T cell responses than wild-type rFVIIa and had high MHC-II affinity in 100% of patients with ADAs. In comparison, only 44% of patients without ADAs showed similar affinity.[9]

Two de-immunized VA variants, DI-1 and DI-2—designed to reduce MHC-II binding affinity—showed significantly lower T cell responses. The MAPPs assay identified ten clusters of peptides from FVIIa molecules, with mutations E296V and M298Q in VA linked to higher immunogenicity. iTope-AI was also able to identify a cluster of neoepitopes containing strong MHC class II binding motifs (Figure 8).

The MAPPs assay, along with in silico assessments and T cell proliferation tests, effectively evaluated the immunogenicity risks of these therapeutic proteins. MAPPs identified protein-derived peptides presented by MHC-II, which helped guide de-immunization efforts. Our cluster frequency analysis further confirmed that the DI-1 and DI-2 variants had lower immunogenicity compared to VA.

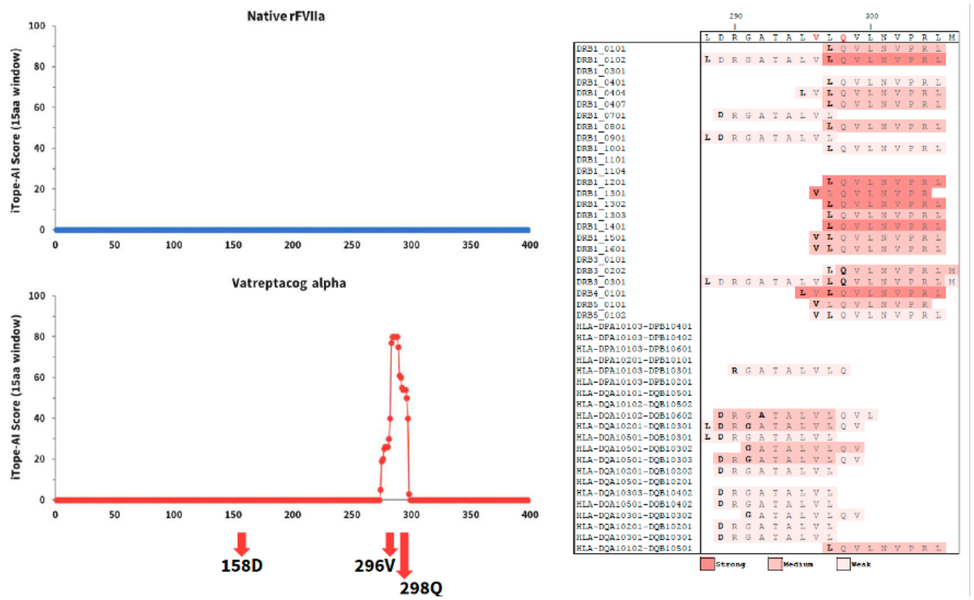

Figure 8. Changes in the amino acid sequence of a factor Vatreptacog are associated with clinical immunogenicity. iTope-AI identifies a cluster containing strong MHC class II binding motifs.

Integration of Immunogenicity Testing in Drug Development

Immunogenicity testing shouldn't be a separate step in drug development but rather integrated from the very start. Abzena's approach ensures that immunogenicity is considered throughout every phase of biologic development, from lead selection and optimization to clinical trials and beyond. This strategy helps identify potential immunogenic risks early, so you can design and select safer, more effective candidates to progress forward.

From discovery through to lead selection stages, we use tools like iTope-AI to screen candidates for immunogenic epitopes. This gives an early look at potential immunogenic risks for each candidate. By doing this early assessment, you can prioritize molecules with lower predicted immunogenicity, helping streamline the process by focusing on the most promising candidates.

One major benefit of early immunogenicity testing is that it lets you optimize drug candidates over time. Instead of waiting until late in development to assess immunogenicity, when changes can be expensive and complicated, our approach involves continuous testing and optimization. This allows you to refine candidates in real time, using feedback from immunogenicity assays to make adjustments that lower risks while keeping or even improving the drug's efficacy.

Regulatory Compliance and Risk Mitigation

A well-rounded immunogenicity testing strategy improves both the safety and efficacy of biologic therapies and helps with regulatory compliance and risk management. Agencies like the FDA and European Medicines Agency (EMA) stress the importance of immunogenicity assessment throughout the drug development process. By building immunogenicity testing into the development strategy early and keeping it going, Abzena helps customers meet regulatory expectations, cutting down on the chances of delays or setbacks during approval.

Moreover, the insights gained from these tests provide a solid foundation for regulatory submissions, including Investigational New Drug (IND) applications and Biologics License Applications (BLA). Detailed immunogenicity data can be crucial for showing that a new therapy is safe, especially for complex biologics, where immune responses are a bigger concern. By tackling these issues early, you can reduce the risks in your development program and improve your chances of regulatory approval.

Tailored Immunogenicity Strategies for Complex Modalities

As biologic therapies become increasingly complex the need for tailored immunogenicity testing strategies has grown. Our platform is designed to handle these challenges, providing customized testing solutions that fit the specific therapy and context.

For monoclonal antibodies (mAbs), our Composite Human Antibody™ (CHAb™) technology combines iTope-AI predictions with humanization and de-immunization strategies to lower the risk of ADAs without affecting the antibody's function. From bioconjugates and peptides to fusion proteins, the platform evaluates the immunogenic risk of the biotherapeutic and any linker technologies to de-risk the components. Cytotoxic payloads can be problematic to assess for immunogenicity in vitro and currently immunogenicity of the antibody-drug conjugate (ADC) is performed during clinical trials, however with the rise in ADCs there is a growing need for innovation here. For newer therapies like cell and gene therapies, we offer a range of assays to assess the specific immunogenic challenges they face. Whether it's checking the immunogenicity of viral vectors in gene therapy or looking at the risk of immune rejection in cell therapies, our tailored approach ensures these innovative treatments are as safe and effective as possible.

Abzena's Vision for the Future

Abzena is a leader in immunogenicity assessments, providing expertise across the full spectrum of biologic development. With a deep understanding of how to predict and manage immunogenicity, we give customers the tools and insights they need to develop safer and more effective biologic therapies. This leadership is built on a commitment to scientific rigor, innovation, and a thorough approach to risk assessment.

Our expertise goes beyond traditional biologics like monoclonal antibodies (mAbs)—it also covers the rapidly growing areas of cell and gene therapies, bioconjugates, and other complex treatments. This wide range of capabilities means we can handle the unique challenges of each type of therapy, offering customized solutions to meet every customer's specific needs.

As the field of biologics evolves, so does our vision for the future. Whether we're developing new technologies, exploring novel therapies, or advancing personalized medicine, Abzena is committed to leading the way in biologic drug development. This forward-thinking approach means we will continue offering the most advanced tools and insights, helping bring the next generation of biologic therapies to patients worldwide. By staying true to our values of scientific excellence, innovation, and collaboration, we plan to remain a leader in immunogenicity assessments and biologic drug development for years to come.

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