myNEO Therapeutics

myEPITOPE

Next-level immunogenicity prediction

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Executive summary

"Is this peptide sequence immunogenic?" or "Should immunogenicity be promoted or avoided?" are central questions across vaccine, T-cell therapeutic, and biologics development. Whether the goal is to maximize immune activation or to avoid unintended immune responses, this question is critical — yet today, it too often remains unanswered or requires costly, time-intensive laboratory assays such as ELISpot.

Current computational methods have mostly limited themselves to predicting peptide–MHC binding affinity, capturing only a fraction of the biological determinants of T-cell activation. **myEPITOPE** is based on neoIM which is a **first-in-class**, state-of-the-art immunogenicity prediction engine that actually **quantifies antigen immunogenic potential and prioritizes highly actionable epitopes** (Pfitzer et al., 2025).

In oncology, for example, as personalized cancer vaccines move into clinical practice, selecting truly immunogenic targets has become essential. Yet even in recent clinical studies, only about half of computationally selected neoantigens induce detectable T-cell responses in patients. In retrospective analyses of personalized cancer vaccine datasets, myEPITOPE increased the proportion of selected epitopes that elicited detectable $CD8^+$ T-cell responses by 25-40% substantially improving epitope selection efficiency in that setting.

More broadly myEPITOPE, which is designed to work in **MHC class I and MHC class II** contexts, supports both (1) immunogenicity maximization workflows (e.g., vaccines and T-cell therapeutic target selection) and (2) immunogenicity risk assessment workflows (e.g., biologics development).

myEPITOPE delivers what current tools cannot: accurate, scalable, biologically grounded immunogenicity prediction — enabling better immunotherapies and safer biologics.

The critical need for accurate epitope prediction

Accurate epitope-level immunogenicity prediction is a core requirement across multiple therapeutic modalities. For vaccines, developers seek epitopes that reliably induce protective or therapeutic T-cell responses. For T-cell therapeutics, developers need to prioritize immunologically actionable targets in the relevant biological context and for biologics, developers aim to identify and reduce peptide regions that may trigger unwanted immune responses. In all of these settings, the quality of epitope prioritization directly affects efficacy, safety, development time, and experimental burden.

Despite years of algorithmic innovation, many computationally prioritized peptide candidates turn out to be non-immunogenic in practice. This **suboptimal antigen actionability** increases immune escape, limits therapeutic potency, and potentially augments relapse incidence. In other contexts, inaccurate prediction can also increase development risk by failing to flag immunogenic liabilities early. Accurate selection and prioritization of antigen targets is highly **challenging due to the chain**

of sequential process steps required for an antigen to be presented and immunogenic: the source protein must be successfully transcribed and translated, correctly processed by the proteasome, transported into the endoplasmic reticulum, loaded onto MHC class I or II molecules with sufficient binding affinity and stability, presented on the cell surface, and ultimately recognized by a cognate TCR with appropriate avidity. The complexity of this process increases the **computational challenge of correctly prioritizing truly actionable epitopes**. Indeed, ligandomics studies have shown that as few as 2-6% of computationally predicted neoantigens elicit detectable T-cell reactivity.

Correct prioritization is therefore of paramount importance, with the downstream decision criteria depending on the application:

- In vaccine formulation design, epitope payload is limited by formulation constraints, so each slot should be filled with the most appropriate targets.
- In biologics development, candidate liabilities should be identified early enough to inform sequence optimization and de-risking.
- In T-cell therapeutic target prioritization, ranking should enrich for epitopes that are not only presented but also immunologically actionable.

Therefore, optimal epitope prioritization requires context-aware ranking: maximizing desired immunogenicity where immune activation is the goal, and minimizing immunogenicity risk where immune activation is undesirable, while accounting for platform-specific design constraints.

myEPITOPE: a paradigm shift in immunogenicity prediction

Epitope prioritization is increasingly performed through computational approaches, where candidate peptides are screened in silico for their likelihood of triggering a relevant immune response. This reliance on in-silico methods is primarily due to the considerable costs in both time and resources of other validation methods, which preclude them from being used in any practical therapeutic pipeline.

Computational state-of-the-art algorithms for antigen prediction have **historically focused primarily on MHC binding affinity and stability**. These are necessary but **insufficient** for determining CD8+ T-cell activation.

myNEO introduces myEPITOPE based on neoIM – **a first-in-class, high-precision immunogenicity prediction tool** – that **goes beyond binding** to estimate the likelihood that MHC–presented epitopes elicit T-cell responses (Pfitzer et al., 2025). In evaluations, it **reduces false positives and improves target selection efficiency, with ≥30% higher predictive power versus publicly available tools**.

Retrospective validation across two clinical trials

To further investigate the potential clinical impact of myEPITOPE, a retrospective study was performed on two recent personalized cancer vaccine trials, both with reported clinical benefits:

- BioNTech pancreatic cancer phase I trial (19 patients, 20 targets/patient)
- Evaxion melanoma phase I trial (12 patients, 10 targets/patient)

This retrospective validation is going to demonstrate the practical value of improved epitope-level immunogenicity ranking in a high-stakes translational setting and provide a strong basis for broader deployment across additional workflows.

Methodology

In a first step, for each patient, the exact set of selected epitopes was gathered. Next, the percentage of epitopes that tested positive was calculated for each patient's vaccine (as evaluated by ex vivo ELISpot assays in both trials).

In a second step, for each patient epitope selection was repeated based on the same mutation set used in the original study: candidates were prioritized with myEPITOPE, and the top N epitopes were then chosen by myEPITOPE score—with N equal to the number of epitopes in that patient's original vaccine to allow side-by-side comparison. Finally, the percentage of ELISpot-positive epitopes was calculated for the selected set.

Results: myEPITOPE significantly improves epitope selection

Despite the high quality of both pipelines and the clinically favorable setting, many selected epitopes appeared to be non-immunogenic in both trials:

- BioNTech pancreatic cancer trial: 43% of the administered epitopes failed to raise any type of CD8+ immune response.
- Evaxion melanoma trial: 53% of the administered epitopes failed to raise any type of CD8+ immune response (see Figure).

In contrast, an epitope prioritization by myEPITOPE would have significantly increased the actionability of the personalized vaccine formulations in both trials. Indeed, myEPITOPE improves the proportion of actual immunogenic epitopes in a vaccine design from 47% to 70% in the melanoma study and from 57% to 72% in the pancreatic cancer study (**Figure 1**). This demonstrates a **25–40% absolute improvement in selecting epitopes** that generate detectable T-cell responses.

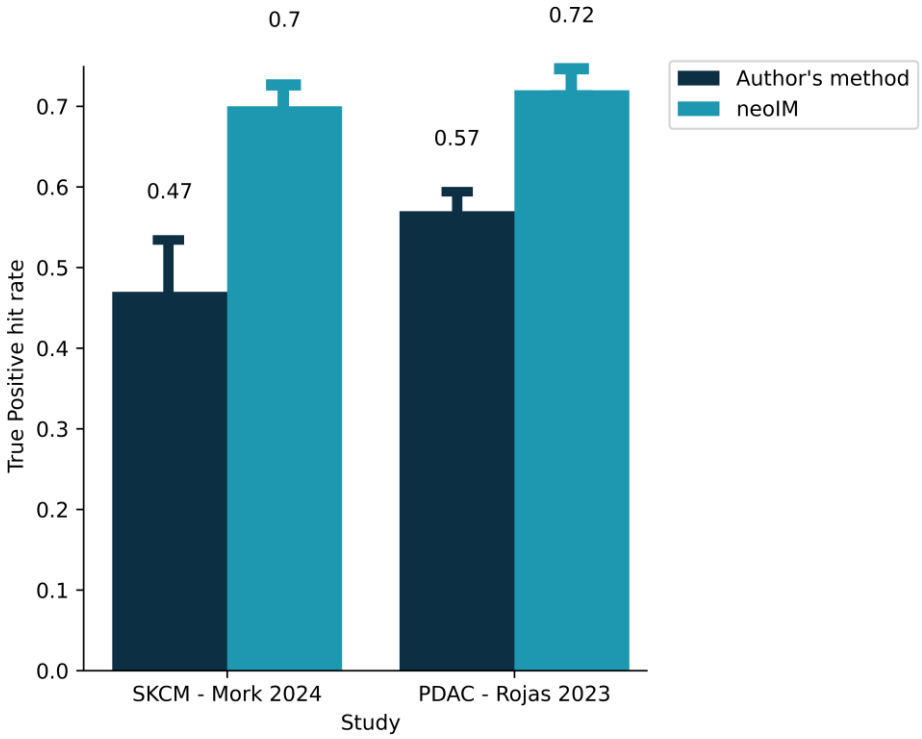

Figure 1. Proportion of clinically actionable epitopes. The exact, patient-specific vaccine designs were extracted from two recent studies, and the proportion of selected epitopes yielding a positive CD8 immune response, according to the authors' method of selection, was thus computed (dark blue bars). In comparison, the same proportion as would be obtained exclusively by myEPITOPE-driven selection is shown. Asterisks indicate $p < 0.05$ (z-test).

Conclusion

myEPITOPE provides a transformative improvement in neoantigen immunogenicity prediction and increases the "quality per epitope" in settings where target payload is limited.

With the representative oncology use case highlighting the practical impact of improved immunogenicity ranking, myEPITOPE strengthens target prioritization workflows from discovery through translational decision-making.

By improving epitope prioritization quality and reducing false-positive burden, myEPITOPE helps teams make better use of limited experimental and development capacity.

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