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NEW PEPTIDE-BASED VACCINES TO TARGET MELIOIDOSIS

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Introduction

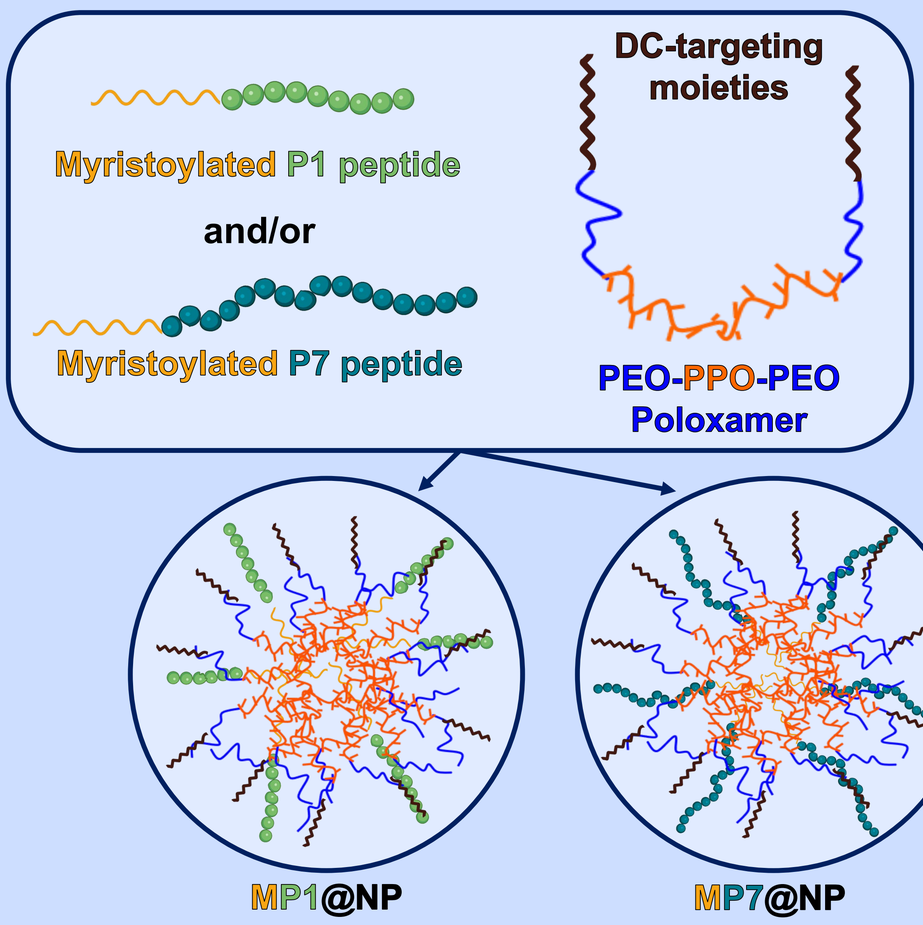
Melioidosis, which is caused by *Burkholderia pseudomallei*, was originally considered as a relatively rare human disease, however recent studies estimate approximately 165.000 cases per year, with up to 45% fatality rate. To make matters worse, comorbidities, like diabetes – which increases the risk factor by 12-fold – or climate change and severe weather events – which promotes the spread of *B. pseudomallei* geographically beyond the tropical and subtropical regions where it is endemic – increase future outbreaks. Due to these factors, over the next decade, the number of cases will increase globally, and *B. pseudomallei* will spread from the original Asian region even to Europe.[1]

Recently, two new proteins have been discovered, the protective BpOmpW[2] and BpPhbB, which are promising in vaccine research, because they stimulate relevant immune responses to combat melioidosis infection[3]. Epitope peptides were subsequently identified from the above-mentioned proteins (**P1** and **P7**), that can trigger IFN-γ responses in CD4+, CD8+ and NKT cells. Compared to expressed proteins, peptides have several advantages for vaccine antigens, as they can elicit a more precise immune response, thus making them safer with wider applicability, and they can be produced more efficiently without potential bio-contamination and do not require refrigerated transport.

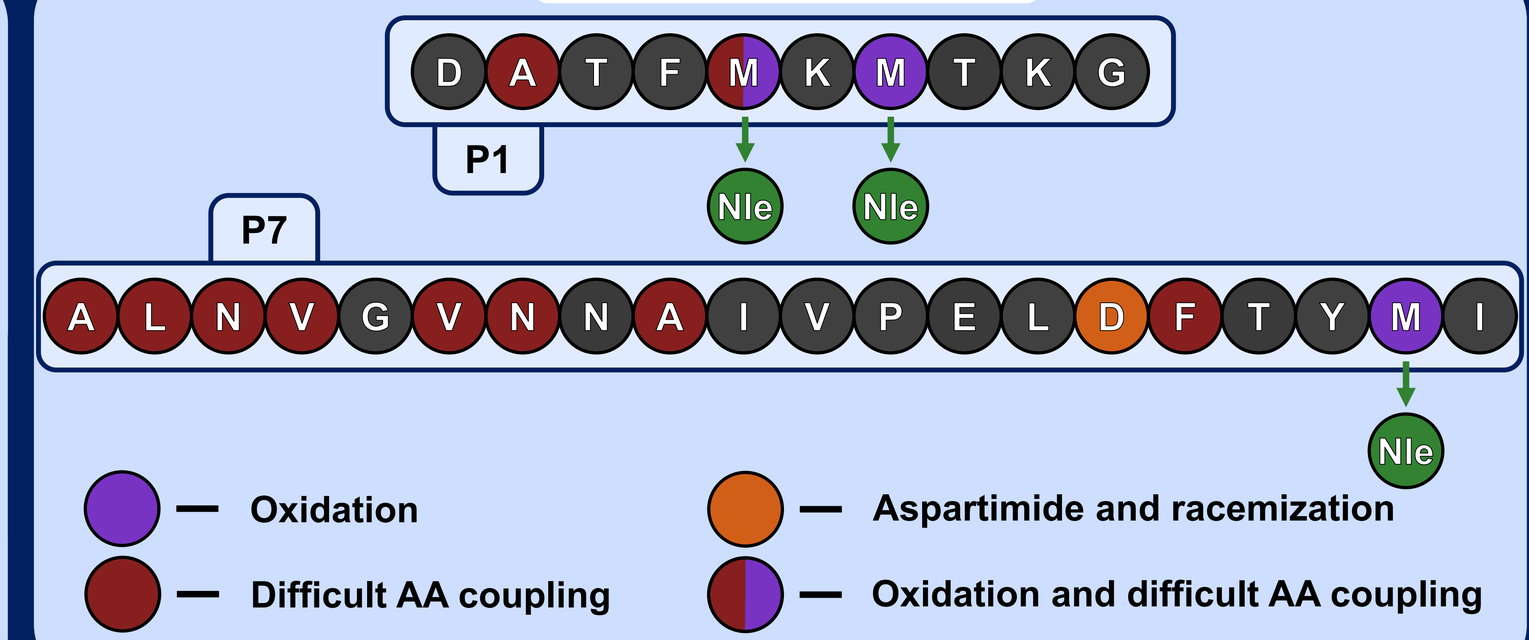
Aims

Develop vaccine candidates from P1 (DATFMKMTKG) and P7 (ALNVGVNNAIVPELDFTYMI) peptides

Apply nanovaccine design strategies[4]



Synthetic challenges

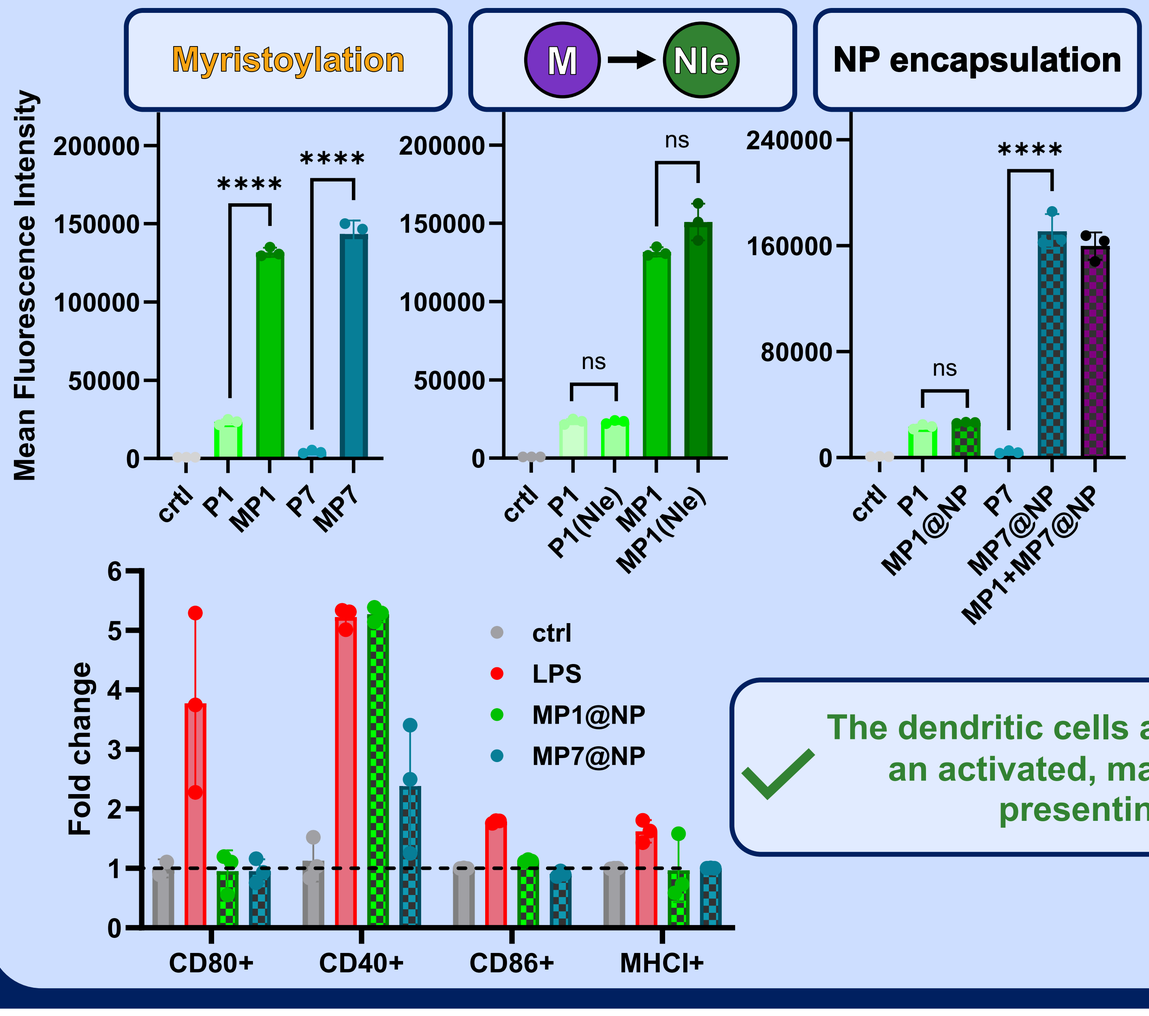


Synthetic solutions – P7 peptide

Classical „batch" type SPPS automated synthesizer - RevoPSy[5]	Continuous flow SPPS synthesizer[6]
Difficult AA coupling	Difficult AA coupling
✓ Double coupling	✓ Heat assisted single coupling
Aspartimide and racemization	Aspartimide and racemization
✓ 0.1M HOBt 2-2% DBU-pip Fmoc deprotection, RT 3x5 min	✓ Fmoc-Asp(OBno)-OH and Fmoc-(Dmb)Gly-OH
40.3% crude purity	58.5% crude purity

However, same desired product amount / mg crude peptide!!!

Nanovaccine design - step by step improvements



✓ **Improved cellular uptake**

✓ **The dendritic cells are shifted toward an activated, mature, antigen-presenting state**

Summary

We have demonstrated that the selected peptides can be produced with good purity using improved synthetic methods both with classical „batch" and with continuous flow SPPS.

From the perspective of cell recognition, the replacement of Met with a non-oxidizable Nle is permitted.

Moreover, we have shown that myristoylation provides a self-adjuvating property, and the DC-targeting poloxamer (PEO-PPO-PEO) encapsulation further improved the *in vitro* efficacy of the modified peptides.

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This work was supported by the Lendület (Momentum) Programme of the Hungarian Academy of Sciences (LP2021-28), NKFIH, 2024-1.2.9-NETWORKING-2024-00005 and the COST Action CA2311-SNOOPY 'Searching for Nanostructured or pOre fOrming Peptides for therapY' and VALIDATE Pump-Priming Grant (March 2019) led by Julen Tomás-Cortázar.