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Platform for peptide vaccine sequence optimization

Stanford researchers have developed methods for optimizing peptide vaccines, with candidate peptides against EGFPvIII-expressing glioblastoma and SARS-CoV-2.

Synthetic peptide vaccines are inexpensive, easy to administer, and can be leveraged against both cancer and pathogens. Improved peptide sequences could boost vaccine effectiveness, but sequence optimization methods are currently limited to painstaking cell-based screens and poorly validated *in silico* prediction. These efforts are limited by a lack of understanding of the proteosome processing step that occurs before peptides are presented as extracellular antigens.

To address this need, researchers in the Wong lab have developed design principles and screening methods that produce peptides with enhanced proteosome processing and cancer immunization. One improvement in sequence optimization comes from the inclusion of proteasome catalyzed peptide splicing (PCPS), which has been previously overlooked as a major determinant of proteosome activity.

Stage of Development Pre-clinical. Using novel design and screening methods, the researchers have identified EGFRvIII and SARS-CoV-2 peptide vaccines with improved proteosomal processing. In a mouse glioblastoma model, the EGFRvIII vaccine yields increased survival over the non-optimized peptide. The screening method, which includes *in vitro* and *in silico* steps, is ready to use for any intended target.

Applications

- Improved peptide vaccines against:
    - EGFRvIII-expressing cancer, such as glioblastoma
    - SARS-CoV-2
- Development of peptide vaccines with enhanced proteosome processing

- Diagnostic reagents to assess vaccine effectiveness using patient PBMCs

Advantages

- Improved anti-glioblastoma efficacy due to increased proteosome processing
- More accurate and rapid identification of T cell epitopes
    - Identifies large pool of PCPS products (ignored in previous methods)
    - *In vitro* and *in silico* combined method is faster than cell-based approach

Patents

- Published Application: WO2022165426
- Published Application: 20240066115

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