Novel T cell Epitopes and Biomarkers for HPV-immune Therapy

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Technology description

Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide and cervical cancer is the fourth most common cancer in women worldwide. Human papillomavirus subtype 16 (HPV16) is the primary cause of most HPV-associated HNSCCs, as well as cervical cancer, making the virus a major global health threat. While there are HPV vaccines that effectively prevent HPV-related cancers, the impact of vaccination on the incidence of HNSCC and cervical cancer may not occur until 2060 due to slow vaccine uptake in boys and time between infection and diagnosis. Thus, over 600,000 new cases are predicted to occur in that interim, providing strong rationale for the development of new therapeutics against HPV-associated malignancies.

Researchers at the Biodesign Institute and their collaborators have identified 16 strong and 29 moderately immunogenic cytotoxic T cell epitopes from specific HPV16 antigens. Further, they have identified that there is high T cell infiltration and dysfunction in HPV+HNSCC and that HPV antigen expression in cancer cells correlates with T cell exhaustion and dysfunction. The novel HPV16 CTL-epitopes identified can serve as immune biomarkers for monitoring immune therapy and can be used to develop targeted immunotherapies against HPV-associated malignancies. Additionally, candidate epitopes from the entire HPV16 genome have been predicted from existing patient databases with <500nM affinity and can be used in future studies to define more immunogenic HPV16 T cell epitopes. This expanded repertoire of HPV-specific T cell epitopes has broadened the number and applicability of HPV therapeutic targets and provides predictive biomarkers to immunotherapies in HPV cancers to significantly advance research and therapeutic development in the HPV+ cancer space.

Application area

- Immune biomarkers for monitoring immune therapy
- Targets for designing personalized precision based immunotherapies
- T cell therapies against HPV-malignancies
- CAR T cell therapies against HPV-malignancies
- Therapeutic vaccines against HPV

• Develop fluorescent tetrameric molecules for detecting HPV-associated diseases
• Immune monitoring HPV-specific T cells in any individual

Advantages

• Significantly broadened the number and applicability of HPV therapeutic targets
• Immunogenicity of each epitope is shown in several patients, as opposed to binding
• CTL dysfunction can be reversed by targeted T cell expansion and synergistic inhibition of specific immune dysfunction genes
• Novel strategies are used that enhance the success rate of detecting immunogenic T cell epitopes from low sample numbers
o Can enhance the detection of low frequency T cells such as T cells against tumor antigens or chronic viruses
• The identified epitopes can be used to identify, clone and express the T cell receptor (TCR) responsible for immune response and the TCRs can be used to develop therapies against HPV-malignancies

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