Docket #: S20-371

Direct Detection of T cell Mediated Immune Responses Using Peptide MHCs (pMHCs) Displayed on Multimeric Protein Scaffolds

The recognition of peptide-MHC (pMHC) complexes by T cells is the cornerstone of cellular immunity, enabling the elimination of infected or tumoral cells. pMHC can thus be leveraged as a detection tool for T cells. The molecule naturally exists in a monomeric form, which impedes easy detection of T cells due to their weak equilibrium dissociation with the lymphocyte. To overcome this limitation, inventors at Stanford have developed a flexible pMHC display system on a self-assembling protein scaffold. Termed a spheromer, the platform has high compatibility with currently available pMHC molecules and streptavidin reagents that are routinely used for T cell analysis. Due to its increased specificity and sensitivity, the pMHC-spheromer platform overcomes the current limitations of existing T cell detection platforms. The platform is a valuable tool that can be used for the detection, isolation, and activation of antigen-specific T cells, enabling the successful tracking and modulation of the adaptive immune response.

Stage of Development
Research in vitro

Applications

- Detection and quantitation of disease-relevant T-cells
- Disease tracking, such as immunity in vaccinated individuals
- Induction of antigen-specific immunological tolerance to treat autoimmune conditions

Advantages

- Greater detection efficiency than any commonly used pMHC multimer reagents
- Customizable system enabling addition of co-stimulator molecules
- Modulation of anti-tumor/anti-viral immunity by inducing antigen-specific responses

Publications

- Yogeshwar, S. M., Muñiz-Castrillo, S., Sabater, L., Peris-Sempere, V., Mallajosyula, V., Luo, G., ... & Mignot, E. (2024). HLA-DQB1* 05 subtypes and not DRB1* 10: 01 mediates risk in anti-IgLON5 disease. *Brain*, awae048.
- Gao, F., Mallajosyula, V., Arunachalam, P. S., van der Ploeg, K., Manohar, M., Röltgen, K., ... & Davis, M. M. (2023). Spheromers reveal robust T cell responses to the Pfizer/BioNTech vaccine and attenuated peripheral CD8+ T cell responses post SARS-CoV-2 infection. *Immunity, 56*(4), 864-878. DOI: 10.1016/j.immuni.2023.03.005
- Mallajosyula, V., Ganjavi, C., Chakraborty, S., McSween, A. M., Pavlovitch-Bedzyk, A. J., Wilhelmy, J., ... & Davis, M. M. (2021). CD8+ T cells specific for conserved coronavirus epitopes correlate with milder disease in patients with COVID-19. *Science immunology, 6*(61), eabg5669. https://doi.org/10.1126/sciimmunol.abg5669
- Goldman, B., (2021). Stanford study ties milder COVID-19 symptoms to prior run-ins with other coronaviruses. *Stanford Medicine News*.

Patents

- Published Application: WO2022133347
- Published Application: 20240076356

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