Website address:
https://www.gesundheitsindustrie-bw.de/en/article/press-release/neue-t-finder-plattform-liefert-tiefe-einblicke-t-zell-antwort-auf-neuartigen-krebsimpfstoff

New T-FINDER Platform Provides Deep Insights Into T Cell Responses Against Novel Cancer Vaccine

BioMed X and the Universitätsmedizin Mannheim announced today the publication of two manuscripts in the field of cancer immunology in the journal Science Advances. The work is based on a collaboration bet- ween both institutions and researchers at the German Cancer Research Center (DKFZ), the Heidelberg Uni- versity, and the Helmholtz Institute for Translational Oncology (HI-TRON). The main objective of the colla- boration was to understand the role of specific T cell responses in a patient with an aggressive subtype of diffuse glioma who showed sustained remission after receiving a neoepitope peptide vaccine at the Univer- sity Hospital Mannheim.

T cells are critical for maintaining human health by eli- minating tumor cells from the body - a process which is driven by the specific interaction of unique receptors on the surface of T cells (T cell receptors or TCRs) to mutant peptides (antigens) on the surface of tumor cells. The identification of such cancer-specific anti- gens, and the TCRs that bind them, underlies current efforts to develop targeted cancer therapies. Until now, functionally robust high-throughput approaches to this challenge were lacking.

Dr. John M. Lindner and his research team at the Bio- Med X Institute in Heidelberg designed the T-FINDER platform to solve this problem. The platform, published now in Science Advances, is capable of rapidly screening thousands of potential interactions between TCRs and antigens on the surface of potential target cells for their ability to activate T cells. Driven by a trio of lead scientists (Miray Cetin, Dr. Veronica Pina- monti, and Dr. Theresa Schmid), the team first gene- rated a highly sensitive reporter cell line for T cell acti- vation. This reporter lies at the heart of T-FINDER, which can sensitively read out the specificity of any number of T cell-activating receptors (for example, CAR-T receptors in addition to classical TCRs) and ligands. For the latter, Dr. Pinamonti provided solu- tions to key aspects of enabling the detection of class II HLA-presented peptides during her PhD thesis work, leading to the development of novel strategies for boosting antigen processing and presentation by the target cell. This class of ligand was until now very chal- lenging to investigate experimentally, and together with its superior sensitivity form the foundation of T- FINDER's advantages in the field.

In a companion manuscript also appearing today, the team collaborated with a research team led by Dr. Ed Green from the Clinical Cooperation Unit Neuroimmu- nology and Brain Tumor Immunology (Head: Prof. Michael Platten) at DKFZ and University Hospital Mannheim. The researchers applied T-FINDER to decode the immune response of two diffuse midline glioma patients vaccinated against the H3 mutation which was driving their cancer. Patients receiving the H3-vaccine have shown promising but heterogeneous results, and with the aid of T-FINDER, the two groups could precisely map the functional immune response of a patient in remission to TCRs binding HLA class II-presented epitopes of mutant H3. This work pro- vides key insights into the mechanism of anti-tumor T cell responses in these patients, and will support ongoing vaccination studies.

"We are excited about the publication of the results of our collaboration with Ed Green, Michael Platten, and colleagues," said John Lindner, Head of Immunology Discovery at the BioMed X Institute. "Our joint research demonstrated the unique sensitivity, flexibility, and overall performance of our new T-FINDER platform, especially for class II HLA-presented targets, which have always been a challenge in the past."

"Previously, we have been limited in the tools we could use to study class II-presented epitopes such as mutant H3. The T-FINDER platform has enabled us to identify and benchmark dozens of H3-reactive TCRs, allowing us to track patient responses to vacci- nation today, as well as benchmark TCRs for the auto- logous cell therapies of tomorrow," said Ed Green, Head of the ImmunoGenomics team in Michael Plat- ten's lab at the DKFZ.

Publications:

Cetin et al. T- FINDER: A highly sensitive, pan- HLA platform for functional T cell receptor and ligand discovery
Science Advances. 2 Feb 2024, Vol 10, Issue 5. DOI: doi.org/10.1126/sciadv.adk3060

Boschert et al. H3K27M neoepitope vaccination in diffuse midline glioma induces B and T cell responses across diverse HLA loci of a recovered patient. Science Advances, 2 Feb 2024, Vol 10, Issue 5. DOI: doi.org/10.1126/sciadv.adi9091.

Press release

06-Feb-2024
Source: Universitätsklinikum Mannheim GmbH

Further information

- Universitätsmedizin Mannheim
- BioMed X
  Institute