Jun Huang, J Clin Cell Immunol 2023, Volume 14

Jun Huang
University of Chicago, USA

Direct observation of T cell receptor ligand discrimination

A major unanswered question is how a T Cell Receptor (TCR) discriminates between foreign and self-peptides presented on the Major Histocompatibility Complexes (pMHCs) of antigen presenting cell surfaces. Here, we used in situ Fluorescence Resonance Energy Transfer (FRET) to measure the lengths of single TCR-pMHC bonds and the conformations of individual TCR-CD3ζ receptors at the membranes of live primary T cells. We found that a TCR discriminates between closely related peptides by forming single TCR-pMHC bonds with different lengths and the most potent pMHC forms the shortest bond. The bond length dictates the degree of CD3ζ dissociation from the inner leaflet of the plasma membrane to precisely control the accessibility of CD3ζ ITAMs for phosphorylation. We further developed Lattice light-sheet microscopy Multi-Dimensional Analyses (LaMDA), an end-to-end pipeline comprised of publicly available software packages that combines machine learning, dimensionality reduction and diffusion maps to predict different cell signaling states by surface molecular dynamics. LaMDA reliably discriminates between structurally similar pMHC ligands by analyzing 3D TCR dynamics at the T cell membrane. Our data revealed the mechanism by which a TCR deciphers the structural differences among peptides via the TCR-pMHC bond conformation and TCR surface dynamics.

Biography

Jun Huang is a tenured professor at the University of Chicago. His lab performs basic and translational research with the objective of developing effective vaccines and cell immunotherapies for the treatment of cancer, infection and autoimmunity. He carries out basic immunological research, focusing on molecular mechanisms of T cell recognition and signaling at the single-molecule level. He performs systems immunology, studying the differentiation of T cells at the single-cell level. He engineers CAR-T cells, aiming at the treatment of cancer and autoimmunity. He develops new biomaterials, enabling the detection, profiling and manipulation of T cells for diagnosis and treatment.

Received: March 08, 2023; **Accepted**: March 13, 2023; **Published**: April 17, 2023