INSTITUTE SEMINAR

16TH OCTOBER, 2017 | 04:00 PM | FERMION HALL

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TITLE

Direct Observation of T Cell Receptor Conformation Dynamics

ABSTRACT

T cell receptor (TCR) antigen recognition determines the selection, development, differentiation, fate and function of a T cell. However, it is still unclear how T cells are able to sense a small number of foreign antigens among a large abundance of self-antigens and subsequently trigger a specific immune response against an infection. The molecular mechanism of TCR antigen recognition and it's conformation change remains a central question in immunology. Numerous studies have been performed and various models have been proposed to explain this key question. However, a common problem of these studies is that they are unable to directly measure and visualize the dynamic TCR-pMHC (peptide histocompatibility complex) interactions at the single-molecule level under physiological conditions. Our in situ single-molecule measurements have provided important insights into the biochemical basis of TCR antigen recognition, and we have found that TCRs can specifically and sensitively recognize even a single agonist pMHC with fast TCR-pMHC binding kinetics.1-2 These data suggest that TCRs may serially engage with a small number of agonist pMHCs in order to maximize TCR signaling and sensitivity. More importantly, we found the origin of the conformation change in the TCR-CD3 complex during the physiological interaction.1,2 Finally, I will also discuss the downstream signaling kinetics of T cell by measuring intracellular calcium imaging. We have developed various model systems, molecular biology assay, microscopy imaging techniques which are interesting to discuss.

Reference:

1. D. K. Sasmal, … and J. Huang. "Direct Observation of T Cell Receptor Conformation Dynamics in Live Cell" (Under Revision)

2. E. Hui, J. Cheung, J. Zhu, X. Su, M. J. Taylor, H. A. Wallweber, D. K. Sasmal, J. Huang, J. M. Kim, I. Mellman and R. D. Vale "T cell co-stimulatory receptor CD28 is a primary target for PD-1-mediated inhibition" Science 2017, 355, 1428.