第十一分会场
生物力免疫学

Session 1：生物力免疫学

Mechanoimmunology of β_2-intergrin-induced adhesion of hepatic cells

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Liver microcirculation is unique in human body due to the complicated structure of sinusoidal nodes, in which multiple types of hepatic and/or hemapoietic cells interact with each other under blood flow. Adhesion of flowing peripheral leukocytes to liver sinusoidal endothelial cells (LSECs) or Kupffer cells (KCs) is crucial in liver immune responses. While it is known that two b_2 integrins LFA-1 and Mac-1 plays distinct functions in the most of organ-specific microcirculations, Mac-1 seems to be predominant in neutrophil (PMN) adhesion and crawling in localized inflammation while the role of LFA-1 is controversial in liver. To address this issue, we first compared the binding kinetics of LFA-1 and Mac-1 coupled on human RBCs to ICAM-1 expressing on mouse LSECs or KCs in quiescent or activated cases using various mechano-biological approaches. It was found that the binding kinetics between these two integrin molecules is different when their ICAM-1 ligands were expressed on distinct cells, supporting that Mac-1 predominantly mediates the adhesion between leukocytes and LSECs and KCs. Next, we tested the flow-induced crawling of mouse PMNs on LSEC monolayer. It was indicated that PMNs tend to migrate along the direction of shear flow and yield high crawling velocity and moving displacement than those under static condition, which is aggravated by TNF-α stimulation for both static and shear conditions. This work provides an insight for quantifying the intrinsic binding kinetics and the blood flow-induced crawling features between PMNs and LSECS or KCs, from a new viewpoint of mechanoimmunology.

Structural mechanism of TCR/pMHC catch bonds

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T-cell Receptors (TCR) interact with peptide conjugated major histocompatibility complex (pMHC) and trigger adaptive immune responses. Previous studies indicated that TCR/pMHC bonds show catch bonds at smaller forces and transit to slip bonds at higher forces. We perform molecular dynamics (MD) simulations and mutagenesis studies to investigate the structural mechanism of catch bond. MD simulations indicated that mechanical forces weaken the interaction between