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TCR signaling initiated by CD3 stimulation under acidic conditions

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The extracellular pH drops below 7 in some diseased areas, such as inflammatory loci, solid cancer nests, and infarction parts. Immune systems have to work under such acidic areas, but the immune cell functions under acidic condition are largely unknown. In this study, we found that the phosphorylation levels of CD3-zeta, ZAP-70, and PLC-γ1 induced by OKT-3, anti-CD3 antibody, were higher at pH 6.3 than those at pH 7.6. The activation of PLC-γ1 was further increased by the co-stimulation with CD28.6, anti-CD28 antibody, at pH 7.6, but not at pH 6.3. The level of cytosolic free calcium ions was increased to a higher level by OKT-3 at pH 6.3, but further addition of CD28.6 decreased the level of cytosolic free calcium ions induced by OKT-3 at pH 6.3. The calcium ion mobilization at pH 6.3 was dependent on ZAP-70 and LAT, but not SLP-76. The expression of IL-2 and IL-25 was not induced significantly by OKT-3 or OKT-3 plus CD28.6 at pH 6.3. These results suggest that the TCR signaling initiated by CD3 stimulation is more active at acidic pH and induces calcium ion mobilization but not the expression of IL-2 and Il-25. L-plastin was activated by OKT-3 at acidic pH in the LAT dependent manner, suggesting the possibility that the internal matrix participates in the activation of TCR signaling under acidic conditions. We are now investigating calcium ion mobilization and interleukin expression under acidic conditions with T cells isolated from human blood

Biography

Hiroshi Kobayashi has completed his Ph.D (1974) in biochemistry from Tokyo University in Japan. After his postdoctoral training at Colorado University Medical Center in USA, he started to study adaptation strategies of living cells to acidic environments at Chiba University in 1978. His research is now focused on immune cell functions under acidic conditions from 1996 at Graduate School of Pharmaceutical Sciences, Chiba University. He retired in March 2012 and continues his research as a Professor Emeritus at Chiba University. He has published more than 20 papers in reputed journals in the recent 10 years

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