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TCR signaling under acidic conditions in human peripheral blood T cells

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Abstract

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 conditions are largely unknown. We found with Jurkat cells derived from human T cells 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. Calcium ions were mobilized to a high level by OKT-3 at pH 6.3, but the co-stimulation with CD28 decreased the level of cytosolic free calcium ions 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 was not induced by OKT-3 in pH 6.3 medium. In human peripheral blood T cells, the addition of OKT-3 induced the phosphorylation of CD3-zeta, ZAP-70, and PLC-γ1, but no calcium ion mobilization was observed upon the addition of OKT-3 under acidic conditions. The CD3 stimulation activated ERK but not p38 at acidic pH. These results suggest that TCR signaling initiated by CD3 stimulation in acidic diseased area is different, at least in part, from that examined until now in conventional alkaline medium. We are now investigating the downstream pathway(s) of the TCR signaling operating at acidic pH in human peripheral blood T cells.

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.