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Molecular mechanisms of TLR2-mediated antigen cross-presentation in Dendritic Cells

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Cross-presentation is an important function of Dendritic Cells (DCs), which present exogenous antigens on MHC class I molecules to prime Cytotoxic T Lymphocyte (CTL) responses. The effects of Toll-Like Receptor (TLR) 2 triggering on the cross-presentation of exogenous antigens by DCs remain unclear. Here, we used synthetic di-palmitoylated peptides and TLR2 agonist-conjugated peptides as models to elucidate the mechanisms of TLR2-mediated cross-presentation. We observed that the internalization of di-palmitoylated peptides by Bone Marrow-Derived DCs (BMDCs) was promoted by TLR2 via clathrin-mediated endocytosis. The administration of these di-palmitoylated peptide-pulsed BMDCs eliminated established tumors through TLR2 signaling. We further investigated that the induction of antigen-specific CTL responses and tumor regression by di-palmitoylated peptides was transporter associated with antigen processing (TAP) independent. Moreover, presentation of di-palmitoylated peptides by MHC class I molecules were inhibited in the presence of an endosomal acidification inhibitor (chloroquine) or a cathepsin S inhibitor (Z-FL-COCHO). The endocytosed di-palmitoylated peptide also passed rapidly from early endosome antigen-1 (EEA1)-positive endosomes to RAS-related GTP-binding protein 7 (Rab7)-associated late endosomes compared with their non-lipidated counterparts. Furthermore, we found that di-palmitoylated peptide-upregulated Rab7 expression correlated with antigen presentation via the TLR2/MyD88 pathway. Both JNK and ERK signaling pathway are required for upregulation of Rab7. In summary, our data suggest that TLR2-mediated cross-presentation occurs through the upregulation of Rab7 and a TAP-independent pathway.

Biography

Kuan-Yin Shen has received his PhD from Graduate Institute of Life Science of National Defense Medical Center in 2014. He accepted Post-doctoral fellowship in National Health Research Institutes in 2016. He has his expertise in the flied of Tumor Immunology to explore the mechanism of antigen processing for tumor vaccine development. To establish novel approach for immunotherapeutic tumor vaccines, he investigates the immune responses induced by lipo-immunogens, recombinant lipoproteins and lipo-peptides.

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