

The Midwinter Conference of Immunologists

Name: Chie HOTTA

E-mail: chie@yokohama-cu.ac.jp

I approve that this abstract appears on the MCI web page.

ABSTRACT

MHC class I pathway to present extracellular exogenous antigens to CD8⁺ T cells for the induction of cytotoxic T lymphocyte immunity. Dendritic cells (DCs) are defined as the only antigen-presenting cells that are able to do cross-presentation and prime both naive CD8⁺ T and CD4⁺ T cells. Although DCs trigger immune responses via cross-presentation, the intracellular antigen processing pathway of cross-presentation and its regulatory mechanisms have not been defined. Here I show that immature DCs can internalize the abundant volume of exogenous soluble ovalbumin (OVA) antigen by macropinocytosis and prepare the potential antigenic peptides to be loaded onto MHC class I molecules, which results in the efficient cross-presentation. In contrast, intermediately mature DCs which are less mature than lipopolysaccharide-stimulated fully mature DCs, have no cross-presentation ability even though they possess the capacity for endocytosis. Immature DCs temporarily maintain weakly acidic pH in the phagocytic compartments even after uptake of OVA antigens, in contrast to the rapid acidification in the phagocytic compartments in intermediately mature DCs. After endocytosis of exogenous OVA antigens into the phagocytic compartments, the internalized exogenous antigens move into the cytosol from the phagocytic compartments in immature DCs, but not in intermediately mature DCs. Intermediately mature DCs treated with 20 mM NH₄Cl which efficiently neutralized the acidity in the phagocytic compartments, recovered the ability of cross-presentation in intermediately mature DCs. Intermediately mature DCs treated with leupeptin and pepstatin A, lysosomal protease inhibitors, does not recover the cross-presentation ability in them. Furthermore, immature DCs treated with diphenylethylideneiodonium chloride which acidify the phagocytic compartments, fail to do both antigen trafficking into the cytosol and cross-presentation. These data suggest that the intracellular antigen processing pathway for cross-presentation depends on the transport of the antigen cargo into the cytosol from the phagocytic compartments. Thus, immature DCs with the capacity for antigen uptake and antigen trafficking into the cytosol develop into intermediately mature DCs which have the capacity for antigen uptake but not for trafficking of the antigen into the cytosol. The intermediately mature DCs further develop into mature DCs that have no capacity for antigen uptake. Also, our data suggest that the transport of the cargo into the cytosol from the phagocytic compartments may be dependent upon the pH in the phagocytic compartments.

Chie HOTTA

Department of Immunology and Parasitology

Yokohama City University School of Medicine

3-9 Fukuura, Kanazawa-ku, Yokohama 236-0004, Japan

Fax: +81-45-787-2509 Tel: +81-45-787-2612

E-mail: chie@yokohama-cu.ac.jp