

*Antigen cross presentation by dendritic cells: control of
phagosome maturation and acidification*

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Dendritic cells initiate CD8⁺ T cell immune responses. To do so, dendritic cells take up antigens in the periphery and generate proteolytic peptides which are on MHC class I molecules. These peptide-MHC complexes are exposed on the surface of dendritic cells, where they engage cognate T cell receptors upon establishment of tight physical contacts between the dendritic cells and the T lymphocytes. In the last few years, we have analyzed the intracellular event that lead to MHC class I loading with peptides from phagocytosed antigens. We showed dendritic cells have developed number of specialization of their phagocytic pathway that allow them to be the most efficient antigen cross presenting cells. These specializations include the ability of DCs to export internalized proteins to the cytosol (1), the capacity of dendritic cell phagosomes to recruit ER resident proteins (2) and a remarkable lack of acidification that probably protects phagocytosed antigens from complete degradation (3). The mechanisms of pH regulation in dendritic cells are being analyzed in more detail. In particular, we show that Rab27a, a small GTPase present on lysosome-related organelles, controls the recruitment of the NADPH oxidase NOX2 to phagosomes. In Rab27a-defective dendritic cells, phagosome acidification is increased and cross presentation is less efficient than in wild type cells.

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(2) Guermonprez P, Saveanu L, Kleijmeer M, Davoust J, Van Endert P, Amigorena S. ER-phagosome fusion defines an MHC class I cross-presentation compartment in dendritic cells. *Nature*. 2003 Sep 25;425(6956):397-402.

(3) Savina A, Jancic C, Hugues S, Guermonprez P, Vargas P, Moura IC, Lennon-Dumenil AM, Seabra MC, Raposo G, Amigorena S. NOX2 controls phagosomal pH to regulate antigen processing during crosspresentation by dendritic cells. *Cell*. 2006 Jul 14;126(1):205-18.