Année de publication : 2004

Pierre Guermonprez, Sebastian Amigorena (2004 Sep 17)
[An export-reimport model for cross presentation of particulate antigens by MHC class I molecules in dentritic cells].
Journal de la Société de biologie : 121-2

Résumé

Federica Benvenuti, Stephanie Hugues, Marita Walmsley, Sandra Ruf, Luc Fetler, Michel Popoff, Victor L J Tybulewicz, Sebastian Amigorena (2004 Aug 25)
Requirement of Rac1 and Rac2 expression by mature dendritic cells for T cell priming.
Science (New York, N.Y.) : 1150-3

Résumé

Upon maturation, dendritic cells (DCs) acquire the unique ability to activate naïve T cells. We used time-lapse video microscopy and two-photon imaging of intact lymph nodes to show that after establishing initial contact between their dendrites and naïve T lymphocytes, mature DCs migrate toward the contacted lymphocytes. Subsequently, the DCs tightly entrap the T cells within a complex net of membrane extensions. The Rho family guanosine triphosphatases Rac1 and Rac2 but not Rho itself control the formation of dendrites in mature DCs, their polarized short-range migration toward T cells, and T cell priming.

Nicolas Blanchard, Maud Decraene, Kun Yang, Francesc Miro-Mur, Sebastian Amigorena, Claire Hivroz (2004 Aug 24)
Strong and durable TCR clustering at the T/dendritic cell immune synapse is not required for NFAT activation and IFN-gamma production in human CD4+ T cells.
Journal of immunology (Baltimore, Md. : 1950) : 3062-72

Résumé

The exact function of TCR clustering and organized macromolecular patterns at the immune synapse between APCs and T lymphocytes is unclear. Using human immature or mature dendritic cells (DCs) and autologous CD4(+) effector T cells, we demonstrate that, within a given conjugate, mature DCs induce strong and long-lasting TCR clustering and protein kinase C-theta translocation in a superantigen dose-dependent manner. Moreover, mature DCs promote CD43 exclusion in a dose-independent manner. In contrast, immature DCs are less potent at inducing these molecular rearrangements. Using these models to correlate T cell functions with the frequency, the intensity, and the duration of TCR clustering, we show, in Jurkat T cells, that weak and transient TCR clustering is sufficient to promote TCR down-modulation, protein kinase C-theta translocation at the synapse, and substantial NFAT

transcriptional activation. Moreover, we show, in CD4(+) T cell blasts, that strong TCR clustering is required for neither TCR down-modulation nor optimal IFN-gamma production. Together, our results demonstrate that some CD4(+) functional responses, such as cytokine production, are independent of central supramolecular activation cluster formation.

Beatriz C Gil-Torregrosa, Ana Maria Lennon-Duménil, Benedikt Kessler, Pierre Guermonprez, Hidde L Ploegh, Doriana Fruci, Peter van Endert, Sebastian Amigorena (2004 Feb 10)
Control of cross-presentation during dendritic cell maturation.
European journal of immunology : 398-407

Résumé

The initiation of most cytotoxic immune responses requires MHC class I-restricted presentation of internalized antigens to CD8(+) T lymphocytes, a process called cross-presentation. In dendritic cells (DC), the only antigen-presenting cells that activate naive T cells, cross-presentation is particularly efficient after internalization of opsonized antigens or immune complexes, which are cross-presented through a proteasome- and transporter associated with antigen processing (TAP)-dependent MHC class I antigen presentation pathway. We now show that FcgammaR-mediated cross-presentation is tightly regulated during DC maturation. Cross-presentation increases soon after activation by lipopolysaccharides, and it is then inhibited in fully mature cells. The initial induction of cross-presentation results from an increase of both antigen internalization and delivery to the cytosol, and from a slight rise in the activity of the proteasome and TAP. The subsequent block of cross-presentation in mature DC is a consequence of the selective down-modulation of antigen internalization and cytosolic delivery, while proteasome and TAP activities continue to rise. Therefore, FcgammaR-mediated cross-presentation is regulated during DC maturation by the selective control of antigen internalization and transport to the cytosol.

Année de publication : 2003

Federica Benvenuti, Cecile Lagaudrière-Gesbert, Isabelle Grandjean, Carolina Jancic, Claire Hivroz, Alain Trautmann, Olivier Lantz, Sebastian Amigorena (2003 Dec 23)
Dendritic cell maturation controls adhesion, synapse formation, and the duration of the interactions with naive T lymphocytes.
Journal of immunology (Baltimore, Md. : 1950) : 292-301

Résumé

The initiation of adaptive immune responses requires the direct interaction of dendritic cells (DCs) with naive T lymphocytes. It is well established that the maturation state of DCs has a critical impact on the outcome of the response. We show here that mature DCs form stable conjugates with naive T cells and induce the formation of organized immune synapses. Immature DCs, in contrast, form few stable conjugates with no organized immune synapses. A dynamic analysis revealed that mature DCs can form long-lasting interactions with naive T

cells, even in the absence of Ag. Immature DCs, in contrast, established only short intermittent contacts, suggesting that the premature termination of the interaction prevents the formation of organized immune synapses and full T cell activation.

Pierre Guermonprez, Loredana Saveanu, Monique Kleijmeer, Jean Davoust, Peter Van Endert, Sebastian Amigorena (2003 Sep 26)

ER-phagosome fusion defines an MHC class I cross-presentation compartment in dendritic cells.

Nature : 397-402

Résumé

Induction of cytotoxic T-cell immunity requires the phagocytosis of pathogens, virus-infected or dead tumour cells by dendritic cells. Peptides derived from phagocytosed antigens are then presented to CD8+ T lymphocytes on major histocompatibility complex (MHC) class I molecules, a process called « cross-presentation ». After phagocytosis, antigens are exported into the cytosol and degraded by the proteasome. The resulting peptides are thought to be translocated into the lumen of the endoplasmic reticulum (ER) by specific transporters associated with antigen presentation (TAP), and loaded onto MHC class I molecules by a complex « loading machinery » (which includes tapasin, calreticulin and Erp57). Here we show that soon after or during formation, phagosomes fuse with the ER. After antigen export to the cytosol and degradation by the proteasome, peptides are translocated by TAP into the lumen of the same phagosomes, before loading on phagosomal MHC class I molecules. Therefore, cross-presentation in dendritic cells occurs in a specialized, self-sufficient, ER-phagosome mix compartment.

Christine Sedlik, Daniel Orbach, Philippe Veron, Edina Schweighoffer, Francesco Colucci, Romina Gamberale, Andrea Ioan-Facsinay, Sjef Verbeek, Paola Ricciardi-Castagnoli, Christian Bonnerot, Victor L J Tybulewicz, James Di Santo, Sebastian Amigorena (2003 Jan 9)

A critical role for Syk protein tyrosine kinase in Fc receptor-mediated antigen presentation and induction of dendritic cell maturation.

Journal of immunology (Baltimore, Md. : 1950) : 846-52

Résumé

Dendritic cells (DCs) are the only APCs capable of initiating adaptive immune responses. The initiation of immune responses requires that DCs 1) internalize and present Ags; and 2) undergo a differentiation process, called « maturation », which transforms DCs into efficient APCs. DC maturation may be initiated by the engagement of different surface receptors, including certain cytokine receptors (such as TNFR), Toll-like receptors, CD40, and FcRs. The early activation events that link receptor engagement and DC maturation are not well characterized. We found that FcR engagement by immune complexes induced the phosphorylation of Syk, a protein tyrosine kinase acting immediately downstream of FcRs. Syk was dispensable for DC differentiation in vitro and in vivo, but was strictly required for

immune complexes internalization and subsequent Ag presentation to T lymphocytes. Importantly, Syk was also required for the induction of DC maturation and IL-12 production after FcR engagement, but not after engagement of other surface receptors, such as TNFR or Toll-like receptors. Therefore, protein tyrosine phosphorylation by Syk represents a novel pathway for the induction of DC maturation.

Année de publication : 2002

Clotilde Théry, Livine Duban, Elodie Segura, Philippe Véron, Olivier Lantz, Sebastian Amigorena (2002 Nov 12)
Indirect activation of naïve CD4+ T cells by dendritic cell-derived exosomes.
Nature immunology : 1156-62

Résumé

Dendritic cells (DCs) secrete vesicles of endosomal origin, called exosomes, that bear major histocompatibility complex (MHC) and T cell costimulatory molecules. Here, we found that injection of antigen- or peptide-bearing exosomes induced antigen-specific naïve CD4+ T cell activation in vivo. In vitro, exosomes did not induce antigen-dependent T cell stimulation unless mature CD8alpha- DCs were also present in the cultures. These mature DCs could be MHC class II-negative, but had to bear CD80 and CD86. Therefore, in addition to carrying antigen, exosomes promote the exchange of functional peptide-MHC complexes between DCs. Such a mechanism may increase the number of DCs bearing a particular peptide, thus amplifying the initiation of primary adaptive immune responses.

Clotilde Théry, Laurence Zitvogel, Sebastian Amigorena (2002 Aug 3)
Exosomes: composition, biogenesis and function.
Nature reviews. Immunology : 569-79

Résumé

Pierre Guermonprez, Jenny Valladeau, Laurence Zitvogel, Clotilde Théry, Sebastian Amigorena (2002 Feb 28)
Antigen presentation and T cell stimulation by dendritic cells.
Annual review of immunology : 621-67

Résumé

Dendritic cells take up antigens in peripheral tissues, process them into proteolytic peptides, and load these peptides onto major histocompatibility complex (MHC) class I and II molecules. Dendritic cells then migrate to secondary lymphoid organs and become competent to present antigens to T lymphocytes, thus initiating antigen-specific immune

responses, or immunological tolerance. Antigen presentation in dendritic cells is finely regulated: antigen uptake, intracellular transport and degradation, and the traffic of MHC molecules are different in dendritic cells as compared to other antigen-presenting cells. These specializations account for dendritic cells' unique role in the initiation of immune responses and the induction of tolerance.

Sebastian Amigorena (2002 Jan 10)
Fc gamma receptors and cross-presentation in dendritic cells.
The Journal of experimental medicine : F1-3

Résumé

Année de publication : 1983

R E Hinson, S Siegel (1983 Oct 1)
Anticipatory hyperexcitability and tolerance to the narcotizing effect of morphine in the rat.
Behavioral neuroscience : 759-67

Résumé

The role of Pavlovian conditioning in tolerance to the narcotizing effect of a high dose of morphine in the rat was examined. Initially, two groups received nine injections of morphine (40 mg/kg), and two groups received nine injections of saline. One group administered each substance was injected in one of two distinctive environments: the animal colony or a distinctive room. Subsequently, rats in all groups received five morphine injections in the distinctive room. Analyses of videotape records of postinjection behavior indicated that rats tested in the presence of the usual predrug cues were more tolerant to the narcotizing effect of morphine than rats tested with cues different from those previously associated with morphine. In addition, rats tested with the usual predrug cues exhibited more anticipatory « hyperexcitable » behavior than rats tested in the absence of the usual predrug cues. These results provide further evidence that compensatory pharmacological conditional responses partially mediate tolerance, and they suggest that these drug-anticipatory responses contribute to so-called « withdrawal symptoms. »

Année de publication : 1982

P Plat (1982 Dec 1)
[Health in the life of adolescents. Some biologic aspects. I. Report. II. Role of public authorities].
L'Infirmiere francaise : 13-20

Résumé

F H Ruddle (1982 Jan 1)
Reverse genetics as a means of understanding and treating genetic disease.
Advances in neurology : 239-42

Résumé