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Chapter 1 : Plasmacytoid dendritic cell - Wikipedia

Dendritic cells (DC) are professional antigen-presenting cells (APCs) that modulate the outcome of the immune response toward immunity or tolerance. There are a large variety of DC subsets according to surface phenotype, function, and tissue distribution. Murine plasmacytoid DC (pDC) represent a.

This article has been cited by other articles in PMC. Abstract Dendritic cells DCs play a significant role in establishing self-tolerance through their ability to present self-antigens to developing T cells in the thymus. DCs are predominantly localized in the medullary region of thymus and present a broad range of self-antigens, which include tissue-restricted antigens expressed and transferred from medullary thymic epithelial cells, circulating antigens directly captured by thymic DCs through coticomedullary junction blood vessels, and peripheral tissue antigens captured and transported by peripheral tissue DCs homing to the thymus. When antigen-presenting DCs make a high affinity interaction with antigen-specific thymocytes, this interaction drives the interacting thymocytes to death, a process often referred to as negative selection, which fundamentally blocks the self-reactive thymocytes from differentiating into mature T cells. Alternatively, the interacting thymocytes differentiate into the regulatory T Treg cells, a distinct T cell subset with potent immune suppressive activities. The specific mechanisms by which thymic DCs differentiate Treg cells have been proposed by several laboratories. Here, we review the literatures that elucidate the contribution of thymic DCs to negative selection and Treg cell differentiation, and discusses its potential mechanisms and future directions. Upon recognition of microbes, DCs internalize and digest them into small peptides, which are subsequently loaded onto the antigen-presenting molecules major histocompatibility complex MHC classes I and II and displayed at cell surface. While immunity is beneficial when it develops against foreign antigens, it is detrimental when it develops against self-antigens as it results in unnecessary and potentially harmful host cell damages. Not surprisingly, our immune system has evolved to ensure such harmful autoimmunity not to arise. One fundamental system created is to interfere the development of self-reactive T cells in the thymus. Each of developing T cells thymocytes expresses a TCR molecule by a process of random gene rearrangement, which creates a diverse repertoire of T cell compartment that can recognize pathogens of an enormous diversity. However, this random process unwantedly but inevitably accompanies a generation of TCRs that react to self-antigens at a high affinity. Thymocytes expressing such self-specific TCRs, if they develop into mature T cells, are likely to cause the harmful autoimmunity. To prevent this from happening, self-specific thymocytes are either routed to cell death, a process named negative selection or clonal deletion, or differentiated into regulatory T Treg cells, a distinct T cell subset equipped with immune suppressive activities 3 , 4 , 5. These two processes will be referred to as central tolerance in this review. Central tolerance is crucially dependent on thymic antigen presenting cells APCs including cortical thymic epithelial cells cTECs and medullary thymic epithelial cells mTECs. Similarly, mTECs negatively select thymocytes of strong self-reactivity, and also mediate positive selection of Treg cells. Notably, mTECs uniquely express a transcription factor named AIRE AutoImmune REgulator , which causes transcription of a wide selection of tissue-restricted genes that are usually only expressed in peripheral tissues. Accordingly, a broad array of tissue-restricted antigens are expressed and presented in mTECs, and this presentation mediates negative selection and Treg cell differentiation of thymocytes specific for the tissue-restricted antigens 9 , 10 , 11 , However, not every tissue-restricted antigen is expressed in mTECs 13 , and even among those expressed, some are not effectively presented by mTECs Thus, additional mechanisms are likely to operate that complement mTECs, and fulfill central tolerance. While the role of DCs in immunity has been well recognized, their role in central tolerance has not been firmly established until recently. Here, we will review the literatures that addressed the role of DCs in central tolerance following a brief description of the subset and origin of thymic DCs. Early studies have suggested that there are common T-myeloid precursors that can differentiate into either T cells or myeloid cells including DCs. For example, thymic lymphoid precursor cells,

when transferred into irradiated thymus, formed progenies of both DCs and T cells 16 , Furthermore, T cells and DCs were generated in the thymus by an identical kinetics One study performed a fate mapping study using the reporter of IL-7 receptor, a key marker of lymphoid lineages, and showed that the reporter was never expressed in thymic cDCs while it was expressed in T cells More recently, a new strategy named retroviral barcoding was used to determine lineage relationship between thymic DCs and T cells This study revealed a high similarity between thymic DCs, splenic DCs, and bone marrow-derived progenitors, but a marked difference between thymic DCs and mature T cells. Notably, this study also showed that T-lineage progenitors differentiate into DCs under certain circumstances such as lymphopenic or DC-depleted condition. Thus, DC development in the thymus appears to entail plasticity, which is likely to help homeostatic maintenance of the cells. Both DC subsets home to the thymus through blood vessels, but the specific tissues that they originated from has not been comprehensively determined. First, they acquire antigens from mTECs. These antigens include tissue-restricted self-antigens expressed under the control of AIRE, and span a broad range of subcellular origins such as the membrane, nucleus, and cytosol 14 , 29 , Secondly, thymic DCs acquire antigens from the blood. Similarly, when mice were painted on the skin with a small molecule fluorophore, the fluorophore was found in thymic DCs These findings suggest that DCs in the circulation, skin, heart, and possibly other peripheral tissues, migrate to the thymus and present the peripheral tissue antigens. Table II Open in a separate window n. In contrast, mTECs presented the antigens at much high levels and played a sufficient role in deleting those thymocytes 29 , It is not clear understood what determines DC-dependency vs. Interestingly, Aichinger et al. This finding suggests that mTEC may focus presentation of antigens processed by autophagosomes while the rest of antigens are given to DCs to share the burden. However, this possibility has not been tested. Mice that are deficient in DCs from birth or in adult life had the number of Treg cells similar to mice sufficient in DCs 36 , These findings led to a claim that DCs are not necessary for Treg development. However, this claim was not readily consented in the field because DCs could positively select Treg cells specific for the antigens that they present Table II. The same mice also produced ova-specific Treg cells when they were injected with ova iv, the route by which injected antigen is exclusively taken up and presented by DCs among thymic APCs Recently, Perry et al. First, they assessed the contribution of bone marrow-derived APCs to Treg cell development by injecting MHCII-deficient bone marrows into irradiated wild type mice and determining Treg cell TCR repertoire in comparison to that of control mice. Next, they closely examined 15 TCR clones that are most abundant in wild type mice for their dependency on bone marrow-derived APCs. For this examination, thymocytes were transduced with the retrovirus that encode each of the frequent TCR clones, injected into the thymus of the mice that lacked DCs, and examined whether they differentiated into Treg cells. Many of the clones failed to differentiate into Treg cells, indicating that these clones are completely dependent on DCs for Treg cell development Table II. For example, thymocytes should receive strong TCR-signaling to differentiate into Treg cells However, relatively little is known what molecules need to be expressed and what cellular events have to occur in DCs for them to select Treg cells. An early study suggested that thymic stromal lymphopoietin TSLP -mediated maturation of thymic DCs plays an important role in Treg cell development CD70 in DCs has been suggested to play an important role in Treg development Genetic ablation of either CD70 or CD27 reduced the number of Treg cells in the thymus, while CD27 signaling rescued developing Treg cells from apoptosis. These findings suggest that DC interaction with thymocytes through CDCD27 costimulatory molecules plays a significant role in Treg development. This binding enhances the ability of the Treg cell progenitors to compete for limiting amounts of IL-2 and secure the developmental niche for Treg cells in the thymus. These mice also failed to produce ova-specific Treg cells when ova was injected iv or expressed in mTECs. Moreover, DCs from these mice poorly generated antigen-specific Treg cells in vitro. This reduction may rescue some of the high affinity self-reactive T cells from being negatively selected and help them differentiate into Treg cells. Although there are numerous questions that remain to be answered, here we picked three outstanding questions that we believe warrant the highest priority.

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Dendritic cells (DC) are professional antigen-presenting cells (APCs) that modulate the outcome of the immune response toward immunity or tolerance.

Flt3 or CD signaling induces differentiation and proliferation of pDCs, although their mechanisms are not entirely understood. Phosphoinositide 3-kinase PI3K -dependent activation of rapamycin mTOR is believed to regulate this signaling pathway. Transcription factor E has also been found to play a key role in influencing the lineage commitment of a common DC progenitor on its course to becoming a pDC. Plasmacytoid dendritic cells are also distinguished from cDCs because of their ability to produce significant amounts of type-1 interferon. CCR7 expression prompts the matured pDC to migrate to a lymph node where it will be able to stimulate and interact with T cells. Typically, the disease presents with skin lesions e. In consequence, the disease has a poor overall prognosis and newer chemotherapeutic and novel non-chemotherapeutic drug regimens to improve the situation are under study. As mentioned earlier, maturation also induces the expression of both MHC Class I and Class II molecules in pDCs as well, which allows the cell to optimize its antigen-presenting abilities. Type 1 interferon production is strongly correlated with the progression of lupus, and is thought to drive excessive maturation of pDCs and activation of B cells, among many other effects. In patients with lupus, pDC levels in the circulating blood are decreased most of the pDCs have migrated toward the inflamed and affected tissues. Like in lupus and psoriasis, the pDCs leave peripheral circulation to the affected areas. However, it seems that in HIV, pDCs not only lose their interferon secreting properties but also die, expediting the progression of the disease. Thus, maintaining balance and regulation of pDC activity is crucial for a more positive prognosis in HIV patients. Annual Review of Immunology. Postepy Dermatologii I Alergologii. Recent Progress and Open Questions". Linking Innate and Adaptive Immunity". Key players in viral infections and autoimmune diseases". Seminars in Arthritis and Rheumatism. A Systematic Literature Review". Journal of Lipid Research. Journal of Leukocyte Biology.

Chapter 3 : Publications Authored by Eric Gehrie | PubFacts

Chapter 9 Plasmacytoid Dendritic Cells in Tolerance Eric Gehrie, William Van der Touw, Jonathan S. Bromberg, and Jordi C. Ochando Abstract Dendritic cells (DC) are professional antigen-presenting cells (APCs) that modulate the outcome of the.

Chapter 4 : The Role of Dendritic Cells in Central Tolerance

Dendritic cells (DC) are professional antigen-presenting cells (APCs) that modulate the outcome of the immune response toward immunity or tolerance. There are a large variety of DC subsets.

Chapter 5 : Eric Gehrie â€“ Research Output â€” Johns Hopkins University

Dr. Eric Gehrie is a pathologist in Baltimore, Maryland and is affiliated with multiple hospitals in the area, including Bridgeport Hospital and Johns Hopkins Bayview Medical Center.

Chapter 6 : Dr. Eric Gehrie, MD â€“ Baltimore, MD | Pathology

Plasmacytoid dendritic cells in tolerance / Eric Gehrie [et al.] In vitro-generated DC with tolerogenic functions: perspectives for in vivo cellular therapy / Cees van Kooten and Kyra A. Gelderman.

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Chapter 7 : Dendritic cell-based cancer vaccine - Wikipedia

Dendritic cells (DCs) play a significant role in establishing self-tolerance through their ability to present self-antigens to developing T cells in the thymus. DCs are predominantly localized in the medullary region of thymus and present a broad range of self-antigens, which include tissue.

Chapter 8 : Plasmacytoid dendritic cells in tolerance. â€" Johns Hopkins University

Plasmacytoid dendritic cells (pDCs) are a rare type of immune cell that are known to secrete large quantities of type 1 interferon (IFNs) in response to a viral infection. They circulate in the blood and are found in peripheral lymphoid organs.

Chapter 9 : Publications Authored by William van der Touw | PubFacts

Dendritic cells (DCs) are the principal cell type responsible for bridging innate and adaptive immunity and are central for the initiation of antigen-specii¬•c immunity and tolerance (Steinman.