

# Role of the Thymus in Transplantation Tolerance in Miniature Swine. I. Requirement of the Thymus for Rapid and Stable Induction of Tolerance to Class I-mismatched Renal Allografts

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## Summary

The almost uniform failure in transplant patients of tolerance-inducing regimens that have been found to be effective in rodents, has made it necessary to examine large animal models before testing of new approaches clinically. Miniature swine have been shown to share many relevant immunologic parameters with humans, and because of their reproducible genetics, have proved extremely useful in providing such a large animal model. We have previously shown that indefinite systemic tolerance to renal allografts in miniature swine is induced in 100% of cases across a two-haplotype class I plus minor histocompatibility antigen disparity by a 12-d course of Cyclosporine A (CyA), in contrast to irreversible rejection observed uniformly without CyA treatment. In the present study, we have examined the role of the thymus during the induction of tolerance by performing a complete thymectomy 21 d before renal transplantation. This analysis demonstrated a striking difference between thymectomized and nonthymectomized animals. Thymectomized swine developed acute cellular rejection characterized by a T cell (CD25<sup>+</sup>) infiltrate, tubulitis, endothelialitis and glomerulitis, and anti-donor CTL reactivity in vitro. Nonthymectomized and sham thymectomized animals had a mild T cell infiltrate with few CD25<sup>+</sup> cells and no anti-donor CTL response in vitro. These results indicate that the thymus is required for rapid and stable induction of tolerance.

Many methods by which transplantation tolerance can be induced in rodents have failed when applied to large animals or to patients (1–4), making testing in large animals a necessary step before applying new techniques clinically. Miniature swine provide the only large animal model in which one can reproducibly study the effects of selective matching within the MHC on parameters of transplantation (5–7). We have therefore used MHC inbred and recombinant lines of miniature swine extensively for preclinical studies of transplantation tolerance (8–12). Previous studies from this laboratory have demonstrated that tolerance to renal allografts in miniature swine occurs spontaneously in about one-third of animals selectively matched for class II antigens and mismatched for a single class I MHC locus plus minor antigens (8, 13). The induction of spontaneous long-term tolerance was associated with a transient antidonor class I humoral response which has been shown to be almost entirely of the IgM class. Rejection animals developed antidonor class I IgG and promptly rejected their allografts. The failure to switch from IgM to

IgG in spontaneous acceptors, suggested that the pathway to tolerance involved a deficiency of T cell help. Studies in miniature swine mismatched for two class I haplotypes were consistent with this hypothesis. Such animals reject renal allografts in 100% of cases without immunosuppression, but when T cell help was limited by the administration of a 12-d course of Cyclosporine A (CyA), 100% of animals developed long-term tolerance (9). Subsequent studies demonstrated that transplants of second renal allografts, MHC-matched to the original donors, were accepted without further immunosuppression if grafted at the time of the transplant nephrectomy (14). These results indicate that long-term graft acceptance is associated with the induction of systemic tolerance.

The role of the thymus has been shown to be critical for systemic central tolerance to self antigens in which poten-

\*Abbreviations used in this paper: CD, cluster of differentiation; CML, cell-mediated lysis; CyA, Cyclosporine A; GIC, graft-infiltrating cell; PAS, periodic acid-Schiff; POD, postoperative day; PSL, percent specific lysis; SLA, swine lymphocyte antigen.

# Role Of Thymus In Tolerance Induction

**Geraldo A. Passos, Daniella Arêas  
Mendes-da-Cruz, Wilson Savino**



## **Role Of Thymus In Tolerance Induction:**

### **Immunological Aspects of Neoplasia — The Role of the Thymus** Bela Bodey, Stuart E. Siegel, Hans E.

Kaiser, 2006-04-11 Our work began where the greatest classical morphologists left off their best work was the start of ours As our work progressed the rigidity of basic previous embryological principles was broken down as scientific knowledge advanced At the same time the molecular biological characterization of the cell surface receptor systems progressed enormously with the invention of NUMEROUS monoclonal antibodies Thus thymology became once again very important because the thymus is the first and central organ of the human immunological system Then the question of immuno neuroendocrine regulation arose and has only been partially answered Our book seeks to explore what has not been explored The topic of thymic epithelial cells is a unique one and has never been explored in any previous book as it is explored in this one Only a handful of great thymologists remain in the world today especially after the great loss the medical community suffered with the passing of Dr Good the list includes but is not limited to Dr Ritter and Dr Kendall in England Dr Savino in Brazil Dr Dardenne in France Dr von Gaudecker in Germany a few others in Belgium and Holland and it is our hope that Dr Bodey is among them Nonetheless a book on the thymus has not been written in the last five years and a book such as this one has never been This book is based on a 30 year period of research and includes references from a broad range of sources spanning the globe and all sources even those that were the beginning of thymic research The book thus is uniquely well rounded more so that previous works

*Thymus Function and Aging: A Focus on Thymic Epithelial Cells* Mariastefania Antica, Valentin Shichkin, Isabella Screpanti, Maria Pia Felli, 2022-09-23  
*Specificity and Function of Clonally Developing T Cells* Bernhard Fleischer, Jörg Reimann, Hermann Wagner, 2012-12-06

**Mechanisms of Lymphocyte Activation and Immune Regulation III** Sudhir Gupta, William E. Paul, Max D. Cooper, Ellen V. Rothenberg, 2012-12-06 Recent advances in the understanding of the major events that shape the immune recognition system have been remarkable The analysis of immunoglobulin Ig gene organization and Ig repertoire diversification in lower vertebrates has provided new insight into this process in mammals Similarly the understanding of the early development of lymphocytes and of the acquisition of immunological tolerance has been aided by elegant studies in quail chicken chimeras using the power of the distinctive markers of the constitutive cells of these birds Great strides have been made in understanding the role played by major histocompatibility complex MHC molecules in antigen presentation and in repertoire selection within the thymus The use of transgenic mice expressing specific T cell receptor TCR genes has elucidated the process of both positive and negative selection In parallel there has been considerable progress in our understanding of tolerance based in part on the use of markers for the V $\beta$  genes of T cell receptors and in part on the analysis of the behavior of long term T cell lines This has led to the realization that both clonal deletion and clonal anergy may play critical roles in the maintenance of unresponsiveness to self antigen Molecular analysis of the requirements for expression of membrane immunoglobulin molecules has revealed

the existence of a complex that appears to be of critical importance in mediating signalling through Ig receptors In addition major insights have been obtained into the regulation of expression of genes of immunologic interest **Thymic**

**Development and Selection of T Lymphocytes** Thomas Boehm,Yousuke Takahama,2013-11-06 The thymus is an evolutionarily ancient primary lymphoid organ common to all vertebrates in which T cell development takes place Failing thymus function is associated with immunodeficiency and or autoimmunity In this volume leading experts provide a comprehensive overview of recent advances in thymopoiesis research The chapters cover the development of the thymic epithelial microenvironment address the formation of a diverse and self tolerant repertoire of T cell receptors as the basis for cellular immunity discuss the mechanisms by which progenitor cells colonize the thymus and detail the molecular basis for T lineage decisions The reviews illustrate the important role of the multifaceted process of thymopoiesis for adaptive immunity

*The Role of Aire, microRNAs and Cell-Cell Interactions on Thymic Architecture and Induction of Tolerance* Geraldo Aleixo Passos,Daniella Areas Mendes-da-Cruz,Ernna Hérída Oliveira,2016-02-03 The focus of this eBook is to bring new insights into central immune tolerance To fulfill that much has been discussed about the master in the regulation of tolerance the autoimmune regulator Aire gene the main thymus cell type that expresses this gene the medullary thymic epithelial cells mTECs It includes one Editorial and 12 other excellent contributions in the format of mini reviews or original research papers covering one or more of these aspects promiscuous gene expression PGE epigenetics miRNAs association of the Aire gene and miRNAs thymocyte TEC interaction coxsackievirus and type 1 diabetes exosomes in the thymus thymic crosstalk thymic B cells T cell development chemokines and migration of T cells miRNAs and the thymic atrophy cell cell interactions and thymus ontogeny Authors raised hypothesis discuss concepts and show open questions The remaining important issues to resolve questions within the central tolerance research are briefly discussed below The first mini review is authored by Olga Ucar and Kristin Rattay They focused on the posttranscriptional control of PGE by miRNAs as well as epigenetic control involving DNA methylation histone modifications and topology of chromosomes These processes represent additional factors to be explored and that might regulate the expression of Aire independent tissue restricted antigens TRAs which are implicated in the central tolerance Are the Eph ephrins important for thymocyte TEC interaction This issue was reviewed by Javier Garcia Ceca and cols The maturation of thymocytes is depending on their interaction with TECs within the thymus Authors argue the importance of Ephs and ephrins on the intrathymic maturation of both thymic epithelial microenvironment and thymocyte maturation and on the recruitment of lymphoid progenitors into the thymus Another stimulating mini review is authored by H l ne Michaux and cols in which they discuss the hypothesis that infection by coxsackievirus B4 CV B4 could be associated with etiopathogenesis of type 1 diabetes mellitus T1D Authors consider that besides their tropism to the pancreatic beta cells CV B4 could also involve the thymus Once within this organ the virus might somehow perturbs central tolerance to the insulin family triggering thus autoimmune T1D Our group contributed with a mini review focusing on cell

cell interactions within the thymus involving TECs and thymocytes and the role of the Aire gene on the induction of central tolerance throughout the modulation of TRA expression in mTECs. In addition, we discuss the recent evidence that Aire also regulates the expression of miRNAs in these cells. On its turn, the Aire-dependent miRNAs might exert control over TRAs. We raise issues that besides the transcriptional control exerted by Aire, PGE could also be being controlled through a posttranscriptional mechanism involving miRNAs. A very pertinent question raised by Gabriel Skogberg and cols is on the role of exosomes on TRA presentation by TECs to thymocytes and its implication in the thymocyte selection. Exosomes may be liberated by TECs to the extracellular milieu and transport TRAs as well as MHC molecules establishing intercellular communication to enhance antigen presentation to developing thymocytes. Authors discuss how intercellular communication via exosomes within the thymus could have consequences on TRA presentation and finally on central tolerance. The thymic crosstalk, i.e. the reciprocal control by the close contact between TECs and thymocytes which influences the differentiation of both types of cells, was elegantly reviewed by Nolla Lopes and cols. Authors discuss the role of dendritic cells (DCs) subsets in the process of deletion of autoreactive T cells and the generation of natural Tregs and raise questions how hematopoietic cells may control the organization of the thymic medulla. Thymus is an organ composed of different cell types including TECs, DCs, macrophages among other cell types and of course thymocytes. Recently, researchers have identified an unexpected cell type formed by B cells which may be originated from intrathymic B lymphopoiesis or immigration from the periphery. Tomoyoshi Yamano and cols contributed with a mini review discussing the role of thymic B cells expressing MHC II, CD80 and Aire in the crosstalk with CD4 single positive cells. Authors raise questions how these cells might play a role as antigen presenting cells in an unpredicted way within the thymus. The regulation of T cell development is apparently well resolved; however, several unsolved questions remain. This important aspect is represented in this Research Topic through the mini review by Iris Caramalho and cols. Authors show new questions on the beginning of Treg lineage commitment, their spatial localization within the human thymus and their molecular components. Cell migration within the thymus is crucial for the central tolerance. Developing thymocytes migrate throughout the thymus, being exposed initially to the cortex and then to the thymic medulla where they respectively undergo positive and negative selection. Chemokines represent key regulators for thymocyte migration. Zicheng Hu and cols argue the role of chemokines in the thymic cell migration and induction of central tolerance. Thymic atrophy during senescence is widely recognized, however, poorly understood. In addition to the atrophy due to senescence, thymus involutes in response to a variety of stimuli including microbial infections. The mouse model of *Trypanosoma cruzi* infection corresponds to an adequate mouse model to address this question. Leandra Linhares Lacerda and cols show results on the role of miRNAs on regulation of chemotaxis which contribute to a better understanding while incites new issues of thymic involution. Cellularity of mTECs is pivotal for cell-cell interactions within the thymus which is required for central tolerance. Taishin Akiyama and cols argue the role of cytokines on cellularity of mTECs focusing into the molecular

basis of cell cell interactions opening perspective on the use of mathematical models for understanding these processes

Thymus morphogenesis is a central point with many open questions The mini review authored by Arnon Dias Jurberg and cols addresses the role of the large superfamily of TGF beta bone morphogenetic protein ligands in the thymus morphogenesis and in T cell differentiation This eBook provides an international and updated insight into the latest developments and open questions on the cellular and molecular bases of central tolerance induction

**Thymic Epithelial Cells: New Insights into the Essential Driving Force of T-Cell Differentiation** Marita Bosticardo,Izumi Ohigashi,Jennifer Elizabeth Cowan,Nuno L. Alves,2021-09-30

**Tolerogenic Antigen-Presenting Cells - Modulating Unwanted Immune Response at Their Core** John Isaacs,Catharien Hilkens,2019-12-27

Fundamental Immunology William E. Paul,2012-12-03 This standard setting textbook has defined the field of immunology since 1984 and is now in its Seventh Edition continuing to deliver the detailed authoritative and timely coverage readers expect This comprehensive up to date text is ideal for graduate students post doctoral fellows basic and clinical immunologists microbiologists and infectious disease physicians and any physician treating diseases in which immunologic mechanisms play a role Now full color throughout the book s fully revised and updated content reflects the latest advances in the field Current insights enhance readers understanding of immune system function The text s unique approach bridges the gap between basic immunology and the disease process Extensive coverage of molecular biology explains the molecular dynamics underlying immune disorders and their treatment Abundant illustrations and tables deliver essential information at a glance Plus a convenient companion website features the fully searchable text and image bank This is the tablet version of Fundamental Immunology which does not include access to the supplemental content mentioned in the text

**Mechanisms of Immune Regulation** R. D. Granstein,1994 Immunologists molecular and cell biologists oncologists pharmacologists and those working in the pharmaceutical field will find this book of particular interest

*Thymic Stromal Alterations and Genetic Disorders of Immune System* Claudio Pignata,Ana E. Sousa,2015-12-07 The pathogenic mechanisms underlying primary T cell disorders are mainly related to molecular alterations of genes whose expression is intrinsic to hematopoietic cells However since the differentiation process requires a crosstalk among thymocytes and the thymic microenvironment molecular alterations of genes involved in the differentiation and functionality of the stromal component of the thymus may lead to a severe T cell defect or failure of central tolerance as well The first example of severe combined immunodeficiency SCID not related to an intrinsic alteration of the hematopoietic cell but rather of the thymic epithelial component is the Nude SCID phenotype inherited as an autosomal recessive disorder whose hallmarks are the T cell defect and the absence of the thymus The clinical and immunological phenotype is the human equivalent of the murine Nude SCID syndrome which represents the first spontaneous SCID identified in nude mice in 1966 For over 3 decades studies of immune system in these mice enormously contributed to the overall knowledge of cell mediated immunity in the assumption that the athymia of these mice was solely

responsible for the T cell immunological defect This syndrome is due to mutations of the transcription factor FOXP1 belonging to the forkhead box gene family which is mainly expressed in the thymus and skin epithelial cells where it plays a critical role in differentiation and survival An alteration of the thymic structure is also a feature of the DiGeorge syndrome DGS which has been long considered the human counterpart of the nude mice phenotype This syndrome is frequently associated to a deletion of the 22q11 region which contains approximately 30 genes including the TBX1 gene which is responsible for most of the clinical features of DGS in humans and mice In this syndrome common manifestations are cardiac malformations speech delay hypoparathyroidism and immunodeficiency even though the immunological hallmarks of the T cell defect in DiGeorge syndrome are profoundly different from those reported in human Nude SCID The divergence of the phenotype among these 2 entities raised the possibility that the FOXP1 transcription factor represents the real key stromal molecule implicated in directing the hematopoietic stem cell toward a proper T cell fate Thymic stromal component of the primary lymphoid organ is also required to negatively select the autoreactive clones a process driven by the expression of tissue specific antigens TSA by medullary thymic epithelial cells mTECs The expression of genes encoding TSA antigens is mediated by autoimmune regulator AIRE gene encoding a transcription factor expressed in mTECs Molecular alterations of this gene are associated to autoimmune polyendocrinopathy candidiasis ectodermal dystrophy APECED a rare autosomal disorder which may be considered the prototype of an autoimmune disease due to the failure of central tolerance homeostasis All these experiments of nature led to unravel novel pathogenic mechanisms underlying inherited disorders of immune system and of note to clarify the pivotal role of epithelial cells in the maturation and education process of T cell precursors

*The Physiology of Immunity* James A. Marsh, Marion D. Kendall, 1996-07-24 The study of neuroendocrine immune interactions has become a highly visible and fast growing segment of mainstream immunology This book provides an overview of the immune system and in depth coverage of the many different areas that make up neuroendocrine immune research The main emphasis is on the physiology of the processes involved stressing an integrated approach to immunology The text is organized in seven sections beginning with an introduction to the immune system Section II outlines how the central nervous system CNS communicates with central and peripheral lymphoid organs Section III provides information on factors from the immune system that act as messengers to the CNS The metabolic regulation of growth and development is discussed in Section IV Section V examines the interactions occurring between the reproductive and immune systems The effects of other physiologic stressors on immunity are reviewed in Section VI Section VII considers cyclic and periodic influences on the immune system Finally there is a consideration of a new unifying theory for immunology Students researchers clinicians and veterinary scientists can discover new areas of interest in specific diseases and immune interactions in this novel presentation

**Paul's Fundamental Immunology** Martin Flajnik, 2022-07-19 Selected as a Doody's Core Title for 2022 Defining the field of immunology for 40 years Paul's Fundamental Immunology continues to

provide detailed authoritative up to date information that uniquely bridges the gap between basic immunology and the disease process The fully revised 8th edition maintains the excellence established by Dr William E Paul who passed away in 2015 and is now under new editorial leadership of Drs Martin F Flajnik Nevil J Singh and Steven M Holland It s an ideal reference and gold standard text for graduate students post doctoral fellows basic and clinical immunologists microbiologists and infectious disease physicians and any physician treating diseases in which immunologic mechanisms play a role

Crossroads between Innate and Adaptive Immunity II Stephen P. Schoenberger, Peter D. Katsikis, Bali

Pulendran, 2008-12-10 Aegean Conferences is an independent nonprofit educational organization directed and managed by the scientific community The board is made up of nine researchers scientists in various disciplines from Harvard Brown University of Pennsylvania UCSD Princeton Biovista and the Foundation for Biomedical Research Academy of Athens The board both invites and approves unsolicited proposals for Conferences in all fields of Science Engineering Arts and Humanities The purpose of the Conferences is to bring together individuals with common interests to examine the emerging and most advanced aspects of their particular field This volume will include mini reviews derived from work to be presented at the Aegean Conference Second Crossroads between Innate and Adaptive Immunity in Crete Greece June 17-22 2007 This meeting is designed to serve as a forum to discuss the most recent progress in complement research as it pertains to human disease pathogenesis and therapeutics The rapid pace of development in complement basic research and the advent and application of new experimental approaches in this field have now allowed us to take an integrated view of the in vivo biology of the complement system The availability of new reagents e g synthetic and recombinant inhibitors and animal models e g transgenic and knockout mice has enabled us to address in an in vivo setting its involvement in various pathophysiological conditions Such studies are shedding new light on the pathogenetic mechanism of complement related diseases such as autoimmune diseases and inflammatory tissue damage as well as defining new areas of high interest such as the developmental biology of complement They also provide the basis for developing new therapeutic strategies for these diseases through manipulation of in vivo complement activity This volume will serve as a resource where the latest development in these specific areas will be discussed in a more focused and detailed manner **Clinical**

**Immunology, Principles and Practice (Expert Consult - Online and Print), 4** Thomas A. Fleisher, William T.

Shearer, Anthony J. Frew, Harry W. Schroeder, Jr., Cornelia M. Weyand, 2013-01-01 Written and edited by international leaders in the field this book has through two best selling editions been the place to turn for authoritative answers to your toughest challenges in clinical immunology Now in full color and one single volume the 3rd Edition brings you the very latest immunology knowledge so you can offer your patients the best possible care The user friendly book and the fully searchable companion web site give you two ways to find the answers you need quickly and regular online updates keep you absolutely current Leading international experts equip you with peerless advice and global best practices to enhance your diagnosis and



management of a full range of immunologic problems A highly clinical focus and an extremely practical organization expedite access to the answers you need in your daily practice Cutting edge coverage of the human genome project immune modifier drugs and many other vital updates keeps you at the forefront of your field A new organization places scientific and clinical material side by side to simplify your research and highlight the clinical relevance of the topics covered A multimedia format allows you to find information conveniently both inside the exceptionally user friendly book and at the fully searchable companion web site Regular updates online ensure that you ll always have the latest knowledge at your fingertips Includes many new and improved illustrations and four color design Your purchase entitles you to access the web site until the next edition is published or until the current edition is no longer offered for sale by Elsevier whichever occurs first If the next edition is published less than one year after your purchase you will be entitled to online access for one year from your date of purchase Elsevier reserves the right to offer a suitable replacement product such as a downloadable or CD ROM based electronic version should access to the web site be discontinued

*Thymus Transcriptome and Cell Biology* Geraldo A. Passos, Daniella Arêas Mendes-da-Cruz, Wilson Savino, 2025-03-11 This volume focuses on a challenging field in biomedicine the genetic control of central immune tolerance The thymus gland is a lymphoid organ implicated in T cells maturation differentiation and selection Its function is associated with the control of immune homeostasis in the body establishing central immune tolerance and preventing the onset of autoimmune diseases This book focuses on thymus development their cellular components and their respective function and the peculiar gene expression profiling transcriptome found in the medullary thymic epithelial cells mTECs that are implicated in the self representation in the thymus and the Autoimmune regulator Aire gene Chapters also explore the mutations in the Aire gene manifestation of autoimmune diseases and the role of cell cell interactions within the thymus with implications in the negative selection elimination of nascent autoreactive T cells in preventing aggressive autoimmunity This new edition includes two new chapters devoted to the genome editing of the Aire gene through Crispr Cas9 system and thymic involution All chapters have been updated to reflect the latest research in the field

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Questions Answer with Explanation Design by Professor JRF Qualified Faculties      Clinical Immunology E-Book Robert R. Rich, Thomas A. Fleisher, William T. Shearer, Harry Schroeder, Anthony J. Frew, Cornelia M. Weyand, 2018-01-13 Keep abreast of the latest advances in this complex field with the 5th Edition of Clinical Immunology Principles and Practice This substantially revised edition by Drs Robert R Rich Thomas A Fleisher William T Shearer Harry W Schroeder Jr Anthony J Frew and Cornelia M Weyand offers authoritative guidance from some of the most respected global leaders in immunology helping you navigate today's latest knowledge and evidence based practices that result in improved patient care This trusted resource features sweeping content updates rewritten chapters a highly clinical perspective and an easy to use organization designed to enhance your diagnosis and management skills in daily practice User friendly format features color coded boxes highlighting critical information on Key Concepts Clinical Pearls Clinical Relevance and Therapeutic Principles Includes new chapters on the Microbiota in Immunity and Inflammation Immune Responses to Fungi and Genetics and Genomics of Immune Response Features extensive revisions to many chapters including the Major Histocompatibility Complex Multiple Sclerosis Diabetes and Related Autoimmune Diseases Biologic Modifiers of Inflammation and Tumor Immunotherapy Covers hot topics such as the role of genetics and genomics in immune response and immunologic disease atherosclerosis recurrent fever syndromes aging and deficiencies of innate immunity the role of microbiota in normal immune system development and the pathogenesis of immunologic and inflammatory diseases and novel therapeutics Addresses notable advances in key areas such as the importance of the microbiota to normal immune system development and to the pathogenesis of immunologic and inflammatory diseases relationships between the innate and adaptive immune systems progress in rapid and cost effective genomics cell signaling pathways and the structure of cell surface molecules and many more Summarizes promising research and development anticipated over the next 5 10 years with On the Horizon boxes and discussion of translational research Includes new multiple choice questions in every chapter online ideal for allergists and rheumatologists seeking certification or recertification in these subspecialties Expert Consult™ eBook version included with purchase This enhanced eBook experience allows you to search all of the text figures and references from the book on a variety of devices      New Insights into Thymic Functions during Stress, Aging, and in Disease Settings Nicolai Stanislas van Oers, Dong-Ming Su, Ann Chidgey, Jarrod Dudakov, 2020-12-23 This eBook is a collection of articles from a Frontiers Research Topic Frontiers Research Topics are very popular trademarks of the Frontiers Journals Series they are collections of at least ten articles all centered on a particular subject With their unique mix of varied contributions from Original Research to Review Articles Frontiers Research Topics unify the most influential researchers the latest key findings and historical advances in a hot research area Find out more on how to host your own Frontiers Research Topic or contribute to one as an author by contacting the Frontiers Editorial Office frontiersin.org about contact      *Application of Antigen Cross-Presentation Research into Patient Care* Marianne Boes, 2017-05-16 The activation of adaptive immune responses requires the processing and presentation of

protein antigens to lymphocytes Especially dendritic cells are effective at display of antigen derived peptides in the form of immunogenic peptide MHC complexes to CD4 and CD8 positive T cells and can stimulate even naive T cells to clonally expand During the last 40 years mechanisms that facilitate antigen processing and presentation were clarified mostly from work in cell lines and mouse models From mouse based work it is now clear that dendritic cells represent a collection of specialized cell subsets that are particularly well endowed to stimulate antigen transport to distinct tissue locations to transfer antigens between cellular subsets or to trigger T cell responses Dendritic cell subsets hold great promise for therapeutic application for example as dendritic cell based vaccines to bolster immune responses against viruses or malignant growths Hurdles remain that preclude the efficient application of high quality pre clinical research into standardized patient care In this research topic efforts in dendritic cell research and dendritic cell based vaccines are discussed from both pre clinical and application points of view

## Decoding **Role Of Thymus In Tolerance Induction**: Revealing the Captivating Potential of Verbal Expression

In a time characterized by interconnectedness and an insatiable thirst for knowledge, the captivating potential of verbal expression has emerged as a formidable force. Its power to evoke sentiments, stimulate introspection, and incite profound transformations is genuinely awe-inspiring. Within the pages of "**Role Of Thymus In Tolerance Induction**," a mesmerizing literary creation penned by way of a celebrated wordsmith, readers embark on an enlightening odyssey, unraveling the intricate significance of language and its enduring effect on our lives. In this appraisal, we shall explore the book's central themes, evaluate its distinctive writing style, and gauge its pervasive influence on the hearts and minds of its readership.

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