MAJOR ARTICLE

Role of Mannose-Binding Lectin in the Innate Defense against *Candida albicans*: Enhancement of Complement Activation, but Lack of Opsonic Function, in Phagocytosis by Human Dendritic Cells

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Mannose-binding lectin (MBL) is a serum collectin believed to be of importance in innate immunity. We have investigated the role of MBL in the first-line defense against *Candida albicans*, an opportunistic fungal pathogen. MBL bound *C. albicans* via its lectin domain, resulting in agglutination of the organisms upon their outgrowth of hyphae. In a human in vitro MBL system, deposition of C4 fragments on *C. albicans* was increased when exogenous MBL was added to serum samples from MBL-deficient individuals. Similar enhancement of deposition of iC3b also was observed. MBL and enhanced opsonic C3 fragments mediated by MBL did not facilitate opsonophagocytosis of the organisms by monocyte-derived dendritic cells (DCs). However, MBL was found to inhibit the growth of *C. albicans* independently of complement activation, although, with complement activation, further inhibition was observed. We concluded that MBL plays an important role in the first-line defense against *C. albicans* without the need for opsonophagocytosis by DCs, in which a direct interaction of MBL with *C. albicans* results in agglutination and accelerated complement activation via the lectin pathway, leading to inhibition of growth.

Mannose-binding lectin (MBL) is a serum protein of hepatic origin that belongs to the collectin family [1] and plays an important role in innate immunity [2, 3]. MBL binds, through multiple lectin domains, to carbohydrate structures on microbial surfaces and is believed to mediate direct killing via complement activation [4] or via enhancing phagocytosis by acting as an opsonin [5–7]. On binding to a sugar-rich microbial surface, MBL activates the complement system via MBL-associated serine protease (MASP)–2 [8]. The activated serine protease is then able to cleave, sequentially, C4 and C2, resulting in the generation of covalently bound C4b2a complexes, C3 convertases, which allows conversion of C3 into C3a and C3b/iC3b, the key reaction leading to initiation of the terminal pathway. Accumulating evidence has shown that MBL can modulate the host inflammatory response to infections in both ex vivo and in vivo models [6, 9–12].

In humans, a single MBL gene on chromosome 10 encodes the protein [13, 14]. MBL deficiency and low levels of serum MBL are strongly associated with the gene polymorphisms in the exon 1 [15–18] and promoter regions [19]. At present, 7 different haplotypes have been described, and 4 of these (LYPB, LYQC, HYPD, and LXPA) are associated with low levels of the protein [20]. In many populations, MBL deficiency is the most common immunodeficiency described at present, and several clinical studies have established an association between MBL deficiency and susceptibility to disease [21, 22].

Candida albicans is a component of the normal mi-

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Role Of The Mannose Binding Lectin In Innate Immunity

Kathleen Armour

Role Of The Mannose Binding Lectin In Innate Immunity:

Mannose-Binding Lectin in the Innate Immune System Iara De Messias-Reason,Angelica B. W. Boldt,2009 Mannose binding lectin MBL is a plasma protein with an important role in the innate immune system MBL recognises pathogens through carbohydrate structures present on the surface of a range of pathogenic organisms including viruses bacteria fungi and protozoans These structures may be referred to as pathogen associated molecular patterns PAMPs After binding to PAMPs MBL promotes C1 and antibody independent activation of complement leading to complement mediated killing and or phagocytosis MBL is also known to modulate the secretion of cytokines from macrophages and to mediate the clearance of apoptotic cells as such playing a role in the inflammatory response This book summarises the actual understanding of human MBL biology and introduces the general aspects of the structure function and genetics of MBL as well as an analysis of the role of MBL in the predisposition to clinically relevant diseases **Lectins and Their Ligands in Shaping Immune Responses** Bernd Lepenies,Roland Lang,2019-12-23 The Collectin Protein Family and Its Multiple Biological Activities Uday Kishore,Taruna Madan,Robert B. Sim,2021-03-12 The topic of this book Collectins is a family of proteins whose major function is in innate immunity where Collectins act as pattern recognition receptors PRRs In general they recognize targets such as microbial surfaces and apoptotic cells and once bound to a target Collectins promote the clearance of microorganisms and damaged host tissue New cell surface proteins and glycoproteins which act as Collectin receptors are currently being identified Some Collectins particularly MBL activate the complement system which enhances the ability of antibodies to fight pathogens via three MBL associated proteases the MASPs Additionally recent research has begun to show wider ranging activities of Collectins such as Their role in metabolism and therefore their involvement in lifestyle diseases such as obesity and cardiovascular disease Their ability to modulate the adaptive immune response as well as to recognize and trigger apoptosis of cancer cells which makes them effective in the annihilation of cancer cells with multiple mutations The regulation of their expression by gonadal steroid hormones implicates them with critical roles in both male and female fertility Altered levels of Collectins have been associated with various autoimmune diseases This book brings together current knowledge of the structure functions and biological activities of Collectins to describe their integral role in human health **Negative Regulators of Innate Immunity and their Role in Host Responses to Injury and Infection, 2nd edition** Maciej Lech ,Shrikant R. Mulay,2024-07-22 Every organism must recognize damage associated and pathogen associated molecular patterns DAMPs and PAMPs to react rapidly The immune system requires potent negative regulators to control unnecessary or overshooting responses and balance the homeostasis in all tissues A significant number of negative regulators of pattern recognition receptors PRR consist of modified innate sensors and downstream molecules that regulate inflammatory signals initiated by sterile damage associated inflammation as well as responses to pathogens These conserved mechanisms contribute to immune homeostasis maintain a constant number of immune cells and limit the activation of the

cells during frequent stimulations by antigens The same mechanisms enable maintaining the symbiotic relationship between host and tissue microbiota Moreover negative regulators of PRRs play a fundamental role in the training of the host immune system and the development of immune tolerance They ensure that the response of immune cells is precise and potent enough to eliminate the source of inflammation but do not develop into fatal inflammatory disease The complex cellular environment in which cells are organized allows interactions between different cell types Various environmental signals determine their phenotype the degree of maturation and responses Regulatory mechanisms and molecules determine the necessity and efficiency of host defense disease progression and restoring of the homeostasis Various studies have revealed the crucial role of homeostasis and mechanisms of immune control under physiological and pathological conditions as well as their substantial potential as a target in clinical applications However the molecular instruments that reshape the tissue responses remain poorly understood In this Research Topic we welcome contributions as Original Research Reports Case Reports Reviews Mini Reviews and Perspective articles focusing on immunomodulatory molecules in the context of the host response to pathogen and tissue injury Manuscripts on the following subtopics are welcome 1 Regulation of inflammatory responses by negative regulators of diverse PRRs TLRs NLRs RLRs CLRs etc 2 Maintaining of tissue homeostasis and disorders caused by an imbalance between triggers and negative regulators 3 Strategies used by pathogens targeting modifications of negative regulators Innate Immunity: Pattern Recognition and Effector Mechanisms Uday Kishore,Andrew J. T George,2025-08-08 This contributed volume follows up and expands upon Target Pattern Recognition in Innate Immunity 2009 providing a much needed update on an area that has surged to the forefront of medical research in recent years From the initial idea of pattern recognition on microbial surfaces innate immunity is now recognized as a key player in human health and disease by virtue of its ability to regulate adaptive immune responses with important physiological and pathological consequences This book presents cutting edge research and future perspectives on nearly all aspects of innate immunity Coverage includes cells of the innate immune system pattern recognition receptors and effector mechanisms soluble PRRs and humoral factors immune response to viral bacterial fungal and parasitic pathogens disease mechanisms and comparative studies in non mammalian innate immunity It is an excellent introduction to the field for students and state of the art reference for researchers and professionals *Target Pattern Recognition in Innate Immunity* Uday Kishore,2010-01-01 Target pattern recognition in innate immunity is responsible for the immediate usually protective responses shown against invading microorganisms and it is the principal feature of self and non self recognition by virtue of the recognition of structures on the microbial pathogens which are not found on host cells This is an area that has been very actively researched over approximately the past 12 years and therefore this volume provides a timely comprehensive and up to date summary of the types and range of cell surface intracellular and secreted host proteins involved in the recognition of microbial products and of the protective mechanisms triggered as a result of the recognition events The Toll like receptors

first described in Drosophila and now well characterised on human cells provide an excellent demonstration of the wide range of different microbial products recognised by this family of receptors and of the signalling pathways which are triggered thus leading to induction of inflammatory cytokines and the activation of genes producing antimicrobial products In addition several cell surface proteins involved in target pattern recognition have been described on the surfaces of macrophages macrophage mannose receptor and macrophage scavenger receptors and on dendritic cells DEC205 and to be involved with the uptake and clearance of whole microorganisms and polyanioic ligands Pattern recognition is also utilised by intracellular receptors with NOD like receptors in the cytosol recognizing microbial molecules and activating the production of inflammatory cytokines or pathways that induce the production of inflammatory molecules Secreted proteins such as the pentraxins which includes the acute phase reacting C reactive protein CRP and serum amyloid protein SAP and the collectins mannan binding lectin lung surfactant protein A and D and ficolins can also readily recruit killing and clearance systems Indeed the serum complement system which is one of the major defence systems in the bloodstream is efficiently activated by CR P on its binding to the phosphocholine groups of microbial phospholipids and the subsequent interaction of the bound CR P with C1q to give classical pathway activation or MBL or ficolin binding to arrays of mannose or N acetyl glucosamine residues respectively on the surfaces of microorganisms to give lectin pathway activation Also in addition to the activation and clearance events associated with complement activation by some of the secreted pattern recognition receptors it is accepted that all these pattern recognition receptors can generally accelerate the uptake and clearance of microbes via phagocytic cells In view of the growing interest in the cross talk between innate and adaptive immunity a thorough understanding of the initial recognition and triggering events mediated via innate immune receptors as addressed in this volume is clearly very useful in helping to also fully understand the mechanisms of activation and control of the adaptive immune system and to allow a full assessment of the relative roles played by innate immunity and adaptive immunity against a particular infection in higher organisms *Lectin in Host Defense Against Microbial Infections* Shie-Liang Hsieh,2020-03-09 This book systemically presents the latest research on lectins covering all the major topics in the field including the heterocomplex of lectins and Toll like receptors protective versus pathogenic functions in connection with microbial infections and novel strategies for enhancing host immunity against infectious diseases caused by viruses bacteria and fungi Lectins are a large group of glycan binding proteins that recognize diverse glycan and non glycan structures expressed on prokaryotic and eukaryotic cells and are vital to cell cell interactions the attachment of microbes to host cells and the recognition and activation of immune responses to exogenous and endogenous danger signals The composition and structure of microbes are complex and include numerous pathogen associated molecular patterns or damage associated molecular patterns As such microbes interactions with immune cells activate multiple innate immunity receptors and produce distinct inflammatory reactions which can be protective to contain microbial invasion or pathogenic to cause tissue damage

and shock syndrome in the host The book shares lessons learned from state of the art research in this field highlights the latest discoveries and provides insightful discussions on lectin mediated inflammatory reactions while also outlining future research directions *The Role of Myeloid-Derived Cells in the Progression of Liver Disease* Hannelie Korf,Reiner Wiest,Rajiv Jalan,Schalk Van Der Merwe,2020-01-22 **Animal Lectins: Form, Function and Clinical Applications** G. S. Gupta,2012-11-13 Animal Lectins Form Function and Clinical Applications presents up to date knowledge of animal lectins Detailed descriptions on biological activities tissue and or subcellular distribution molecular structure gene organization possible functions clinical applications lectin ligand interactions and their intervention for therapeutic purposes are provided The recently discovered C type lectins as well as further novel super families of this group of molecules are described in detail Furthermore the clinical significance of animal lectins in inflammatory diseases defects of immune defense and autoimmunity are described and their application as drugs and therapeutic targets is discussed With the increasing interest in lectins in biomedical research and their therapeutic applications this book on animal lectins and associated proteins is a must have for researchers in the area *Innate Immunity* R. Alan B. Ezekowitz,Jules A. Hoffmann,2002-12-06 The concept of innate immunity refers to the first line host defense that serves to limit infection in the early hours after exposure to microorganisms Recent data have highlighted similarities between pathogen recognition signaling pathways and effector mechanisms of innate immunity in Drosophila and mammals pointing to a common ancestry of these defenses In addition to its role in the early phase of defense innate immunity in mammals appears to playa key role in stimulating the subsequent clonal response of adaptive immunity Recent exciting information has determined that the templates that are laid down in primitive life forms like flowering plants and insects form the basic principles of first line host defense that are conserved in mammalian systems The next frontier in the field is to understand the dynamic adaptive changes that occur as a result of the inter play between host defenses and infectious agents One emerging theme is that microorganisms are constantly seeking ways to co opt host defenses On the other hand host defense to infection is mediated by the coordinate action of pattern recognition molecules and receptors that in mammals are important and probably necessary antecedents to the development of an adaptive immune response Innate Immunity aims to explore the intersection between host pathogen interactions across an evolutionary spectrum that will inform our understanding of the dynamic interplay between infectious agents and host defense in man Skin and Connective Tissue Diseases: New Insights for the Healthcare Professional: 2012 Edition ,2012-12-10 Skin and Connective Tissue Diseases New Insights for the Healthcare Professional 2012 Edition is a ScholarlyEditions eBook that delivers timely authoritative and comprehensive information about Skin and Connective Tissue Diseases The editors have built Skin and Connective Tissue Diseases New Insights for the Healthcare Professional 2012 Edition on the vast information databases of ScholarlyNews You can expect the information about Skin and Connective Tissue Diseases in this eBook to be deeper than what you can access anywhere else as well as consistently reliable

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Immunology and Infectious Disease Lesley A. Doughty,Peter Linden,2003 This unique volume provides a mechanistic look at key aspects of the inflammatory response seen in critical illness Key cells and mediators involved in the innate inflammatory response and the pathways employed to combat infection or respond to injury are emphasized It has become clear that a delicate balance exists to allow eradication of infection with minimal immune mediated tissue injury in the process For this reason an up to date discussion of how the inflammatory response down regulates itself has been included The inflammatory response in the critically ill is vastly different than in healthy hosts For this reason discussions about the mechanisms of pharmacologic immune suppression and other less commonly considered immunomodulated states seen frequently in critical care medicine have been included Given the differences in immune function seen in critical illness the importance of considering the immune system an organ whose function must be monitored and optimized for the best possible outcome has been highlighted In addition we have included up to date discussions of prevention and diagnostic approaches to extremely common infectious entities which must be monitored for and treated appropriately in the setting of critical illness induced immune dysfunction The Hypothalamus-Pituitary-Adrenal Axis ,2008-09-12 The hypothalamic pituitary adrenal axis controls reactions to stress and regulates various body processes such as digestion the immune system mood and sexuality and energy usage This volume focuses on the role it plays in the immune system and provides substantive experimental and clinical data to support current understanding in the field and potential applications of this knowledge in the treatment of disease Evidence presented in this book suggests that the nervous endocrine and immune systems form the

Neuroendoimmune Supersystem which integrates all the biological functions of higher organisms both in health and disease for their entire life cycle Contributors include both the scientists who initiated the work on the HPA axis and on the autonomic nervous system and those who joined the field later *Encyclopedia of Cell Biology* ,2015-08-07 The Encyclopedia of Cell Biology Four Volume Set offers a broad overview of cell biology offering reputable foundational content for researchers and students across the biological and medical sciences This important work includes 285 articles from domain experts covering every aspect of cell biology with fully annotated figures abundant illustrations videos and references for further reading Each entry is built with a layered approach to the content providing basic information for those new to the area and more detailed material for the more experienced researcher With authored contributions by experts in the field the Encyclopedia of Cell Biology provides a fully cross referenced one stop resource for students researchers and teaching faculty across the biological and medical sciences Fully annotated color images and videos for full comprehension of concepts with layered content for readers from different levels of experience Includes information on cytokinesis cell biology cell mechanics cytoskeleton dynamics stem cells prokaryotic cell biology RNA biology aging cell growth cell Injury and more In depth linking to Academic Press Elsevier content and additional links to outside websites and resources for further reading A one stop resource for students researchers and teaching faculty across the biological and medical sciences Diagnostic Pathology: Transplant Pathology - E-BOOK Anthony Chang,2024-05-31 This volume in the Diagnostic Pathology series is an ideal point of care resource for practitioners at all levels of experience and training Covering the full range of solid organ transplantation SOT of the kidney liver heart lung pancreas intestine and more it provides a current understanding of transplant immunology and pathology to help ensure accurate diagnosis for optimal clinical management Richly illustrated and easy to use Diagnostic Pathology Transplant Pathology third edition is a visually stunning one stop reference for practicing pathologists transplant practitioners and students of organ transplantation Covers all areas of transplant pathology incorporating the collective knowledge and experience from a team of transplant pathology experts with the latest updates from the 2022 Banff classification Groups content by specific organ transplant including kidney liver heart lung intestine pancreas and vascularized composite allotransplantation Features sweeping updates throughout including new chapters on transplant immunology that cover chronic viral infections and the immune response immune manipulation and accommodation and graft vs host disease Contains a new chapter on islet cell transplantation and new detailed information on xenotransplantation specifically kidney xenograft Covers advances in vascularized composite allografts hands face uterus phallus transplantation Features more than 1 500 superb images including histology gross pathology full color illustrations and radiologic images Employs consistently templated chapters bulleted content key facts annotated images and an extensive index for quick expert reference at the point of care Any additional digital ancillary content may publish up to 6 weeks following the publication date *Carbohydrates: the yet to be tasted sweet spot of immunity* Deirdre R Coombe,Christopher

R Parish,2015-07-10 Carbohydrates are extremely abundant bio molecules they are on all mammalian cell surfaces as well as on bacterial cell surfaces In mammals most secreted proteins are glycosylated with the glycan component comprising a significant amount by mass of the glycoprotein Although many years ago carbohydrate protein recognition events were demonstrated as involved in invertebrate self non self recognition the contribution of carbohydrate protein binding events to the mechanisms of the mammalian immune response was not embraced with the same enthusiasm Adaptive immunity and the contribution of antibodies T cells and T lymphocyte sub sets and protein antigen presentation dominated immunological theory Unlike protein structures carbohydrate structures are not template driven yet the numerous enzymes involved in carbohydrate biosynthesis and modification are encoded by a major component of the genome and the expression of these enzymes is tightly regulated As a consequence carbohydrate structures are also regulated with different structures appearing according to the stage of cell differentiation and according to the age or health of the individual The advent of technologies that have allowed carbohydrate structures and carbohydrate protein binding events to be more easily interrogated has resulted in these types of interactions taking their place in modern immunology We now know that glycans and their ligands or lectins are involved in numerous immunological pathways of both the innate and adaptive systems However it is clear that our understanding is still in its infancy as more and more examples where carbohydrate structures contribute to aspects of the immune response are being recognised The goal of this research topic is to explore the variety of roles undertaken by glycans and lectins in all aspects of the immune response The particular focus is how the interactions of glycans with their ligands contribute to the mechanism of immune responses **Henry's Clinical Diagnosis and Management by Laboratory Methods E-Book** Richard A. McPherson,Matthew R. Pincus,2017-04-05 Recognized as the definitive reference in laboratory medicine since 1908 Henry s Clinical Diagnosis continues to offer state of the art guidance on the scientific foundation and clinical application of today s complete range of laboratory tests Employing a multidisciplinary approach it presents the newest information available in the field including new developments in technologies and the automation platforms on which measurements are performed Provides guidance on error detection correction and prevention as well as cost effective test selection Features a full color layout illustrations and visual aids and an organization based on organ system Features the latest knowledge on cutting edge technologies of molecular diagnostics and proteomics Includes a wealth of information on the exciting subject of omics these extraordinarily complex measurements reflect important changes in the body and have the potential to predict the onset of diseases such as diabetes mellitus Coverage of today s hottest topics includes advances in transfusion medicine and organ transplantation molecular diagnostics in microbiology and infectious diseases point of care testing pharmacogenomics and the microbiome Toxicology and Therapeutic Drug Monitoring chapter discusses the necessity of testing for therapeutic drugs that are more frequently being abused by users **Avian Immunology** Bernd Kaspers,Karel A. Schat,2012-12-02 The second edition of Avian

Immunology provides an up to date overview of the current knowledge of avian immunology From the ontogeny of the avian immune system to practical application in vaccinology the book encompasses all aspects of innate and adaptive immunity in chickens In addition chapters are devoted to the immunology of other commercially important species such as turkeys and ducks and to ecoimmunology summarizing the knowledge of immune responses in free living birds often in relation to reproductive success The book contains a detailed description of the avian innate immune system encompassing the mucosal enteric respiratory and reproductive systems The diseases and disorders it covers include immunodepressive diseases and immune evasion autoimmune diseases and tumors of the immune system Practical aspects of vaccination are examined as well Extensive appendices summarize resources for scientists including cell lines inbred chicken lines cytokines chemokines and monoclonal antibodies The world wide importance of poultry protein for the human diet as well as the threat of avian influenza pandemics like H5N1 and heavy reliance on vaccination to protect commercial flocks makes this book a vital resource This book provides crucial information not only for poultry health professionals and avian biologists but also for comparative and veterinary immunologists graduate students and veterinary students with an interest in avian immunology With contributions from 33 of the foremost international experts in the field this book provides the most up to date review of avian immunology so far Contains a detailed description of the avian innate immune system reviewing constitutive barriers chemical and cellular responses it includes a comprehensive review of avian Toll like receptors Contains a wide ranging review of the ecoimmunology of free living avian species as applied to studies of population dynamics and reviews methods and resources available for carrying out such research

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