

# 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 ac-

tivated 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

**Anthony L. DeFranco, Richard M.  
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## **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

**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 **Immunity**

Anthony L. DeFranco, Richard M. Locksley, Miranda Robertson, 2007 An understanding of the immune system is central to the understanding of how the body interacts with its surroundings Presenting an insight into this biological system this book leads students through both innate and adaptive immunity how infection is detected and how the cells of the immune system interact to generate a response **Complement Therapeutics** John D. Lambris, V. Michael Holers, Daniel

Ricklin, 2012-09-19 This book highlights progress and trends in the rapidly evolving field of complement related drug discovery and spotlights examples of clinical applications As an integral part of innate immunity and critical mediator in homeostatic and inflammatory processes the human complement system has been identified as contributor to a large number of disorders including ocular cardiovascular metabolic autoimmune and inflammatory diseases as well as in ischemia reperfusion injury cancer and sepsis In addition complement is often involved in adverse immune reactions to biomaterials cell and organ transplants or drug delivery systems Although the complement cascade with its close to 50 extracellular protein targets has long been recognized as an attractive system for therapeutic modulation the past few years have seen a particularly strong boost in interest Fueled by novel research insight and the marketing of the first complement targeted drugs a plethora of highly creative treatment approaches and potent drug candidates have recently emerged and are currently evaluated in disease models and clinical trials The chapters in this book cover a wide range of topics related to the development of complement therapeutics ranging from the molecular and functional description of complement targets to the presentation of novel inhibitors improved treatment strategies as well as examples of disease models and clinical applications The broad and up to date overview on a highly versatile and dynamic field renders this book an indispensable source of information for researchers and clinicians dealing with therapeutic and disease related aspects of the human complement system **Primitive Immune Systems** Jules Hoffmann, 2004 Options for the Control of Influenza III Lorena E.

Brown, 1996 Hardbound This is one of the most comprehensive publications dealing with influenza and opportunities for control The volume comprises papers from scientists involved in all aspects of influenza from basic research through development and licensing of new vaccines and therapeutics to epidemiology and control programs **The Journal of**

**Immunology**, 2006 **Chemical Abstracts**, 2002 Principles of Orthopedic Infection Management Stephen L.

Kates, Olivier Borens, 2016-12-14 Principles of Orthopedic Infection Management The medical world continues to make extraordinary advances in both scientific knowledge and surgical skill yet despite these achievements surgeons continue to struggle with the challenge of postoperative infection Without proper prevention or treatment orthopedic infection can become just as life threatening as the initial trauma This highly informative clinical go to text provides the core principles treatment options and the latest information and research specifically for the purpose of helping physicians manage orthopedic infections and related issues The book s key features include Contributions from 63 world renowned specialists

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