Short communication

Lectin pathway components and its transfer from blood to cerebrospinal fluid

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RESUMEN

Introduction: Defining mechanisms governing the diffusion from blood to cerebrospinal fluid is central to understanding immune function in the central nervous system. **Objective:** To describe the dynamics of diffusion of the lectin pathway components from blood to cerebrospinal fluid.

Methods: It was organized the information available in PubMed database and of papers from journals, and abstract books from international congresses belongs mainly to Cuban authors all about the lectin pathway of complement including manan-binding lectin (MBL) and ficolins complexed with the MBL-associated serine proteases (MASP2), and of other components like MASP3, Map44 as regulatory components and the different starters like MBL, ficolins and CLLK.

Results: All the lectin pathways component are blood derived proteins but at the same time it could be synthesized intrathecally. Most of the protein can be transferred from blood to cerebrospinal fluid in different aggregation forms and some of them can be described as a consuming curve. The control mechanism of regulation the lectin pathway can be followed by molecules as MASP3 and Map44.

Conclusions: The under- constructed lectin pathway of the complement system required not only the available information in different journals. It had to be completed by reviewing the congress abstract book and congress website of the last years

Keywords: lectin pathway, blood-cerebrospinal fluid barrier, MBL, MASP2, MASP3. Map44, ficolins.

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INTRODUCTION

Mannose-binding lectin (MBL), collectin-10, collectin-11, and the ficolins (ficolin-1, ficolin-2, and ficolin-3) are soluble pattern recognition molecules in the lectin complement pathway. These proteins act as mediators of host defense and participate in maintenance of tissue homeostasis.[(1)]

All molecules exhibit distinct expression in different tissue compartments, but all are found to a varying degree in the circulation. A common feature of these molecules is their ability to interact with a set of serine proteases named MASPs (MASP-1,MASP-2,and MASP-3).MASP-1and -2 trigger the activation of the lectin pathway and MASP-3 may be involved in the activation of the alternative pathway of complement and acts as a control molecule.[(2)]

Defining mechanisms governing the diffusion from blood to cerebrospinal fluid is central to understanding immune function in the central nervous system.

The aim of this review is to summarize the dynamics of diffusion of the lectin pathway components from blood to cerebrospinal fluid.

METHODS

This review was based on the information available in PubMed database and of papers from journals, and abstract books from international congresses belongs mainly to Cuban authors from the last five years about the lectin pathway of complement including manan-binding lectin (MBL) and ficolins complexed with the MBL-associated serine proteases (MASP)-2, and of other components like MASP3, Map44 as regulatory components and the different starters like MBL, ficolins and CLLK.

The following sections provide an overview of the key molecules of the lectin pathway of complement including their cross-talk with other molecules and/or pathways. Some of our most important findings obtained during the past five years about the participation of the lectin pathway as well as the other ones related to the immune response in Angiostrongylus cantonensis meningoencephalitis will be highlighted.

Due of the length of this review, it is not possible to scan all the papers related to the lectin pathway also if it was reduced to the last 5 year. Taking into account it can be observed in Table 1 some of the papers presented in different congress and published in abstracts book from Cuban authors.

MBL

The first molecule of the lectin pathway to be discovered was MBL. MBL in serum is characterized by a mixture of different forms, and it is now generally accepted that the main portion of MBL in serum consists of trimers and tetramers of MBL subunits, but that both higher (pentamers and hexamers) and lower forms containing only a monomer and dimers may be formed.

The dynamics of MBL from blood to cerebrospinal fluid (CSF) demonstrated that this protein originates in the periphery and raisin the CSF in small quantities taking into account its high molecular weight. It is in located in the leptomeninges although it can be synthesized in the SNC. It is possible to quantify the MBL intrathecal portion by the corresponding reibergram.[3] The discovery that MBL deficiency leads to a phagocytic defect initiated an effort to resolve the molecular mechanism behind this deficiency and later it was found MBL deficiency in patients with Angiostrongylus cantonensis meningoencephalitis

The collectins CL-L1, CL-K1 and CL-P1

The collectins play important roles in our innate immune system. The collectins are pattern recognition molecules and act as starters of the lectin pathway as the well characterized proteins mannan-binding lectin (MBL). Collectin liver 1 (CL-L1), collectin kidney 1 (CL-K1) and collectin placenta 1 (CL-P1) are the most recently discovered collectins. CL-L1, CL-K1 and CL-P1 play important roles in host defense by recognizing a variety of microorganisms and interacting with effector proteins.

The collectins as the same as the rest of the initiators of the lectin pathway has its origin in organs of the periphery like the liver and the kidney. However the difficulty of finding some of these components of the lectin pathway in soluble state and not associated to any structure it was a question marc until it was found that the soluble form is a hybrid CL-LK (4) that passes from the blood to the CSF and that it can also be synthesized in the central nervous system. Collectins can pass in a non-aggregated state and forming aggregated forms from CSF to blood.

Ficolins

There are three ficolins classes: M ficolin, H ficolin and L ficolin. All of them are synthesized in the periphery but ficolins are able to be synthesized in the SNC besides passing the barrier blood-CSF for simple diffusion in trimmers and tetramers structures besides diverse aggregation forms that can cross the blood-brain barrier. [5]

MASP2

The MASP2 is a serine protease found in the periphery but it can pass to CSF throughout the blood-CSF barrier. This protein transfers him the enzymatic characteristics to the initiators of the lectins pathway when they joint to the starters. It has a characteristic distribution according to the variation of Q albumin as a saturation curve. It can be also synthesized in CNS.[6]

MASP3

Until very recently their function was not known. Today it is known that it is a regulatory protein from the lectin pathway. It seems has the same distribution as MASP2 similar than a leptomeningeal protein. The distribution between blood and CSF is according to its molecular weight and it is possible to be synthesized in CNS too.[7]

MAp44

This protein has the same regulatory function as MASP3 because it a truncated protein without enzymatic activity that occupied the same locus to MASP2 and stop the enzymatic chain. It has a similar structure to a serine protease but it is truncated molecule without enzymatic activity. It has an important role controlling the lectin pathway. It is possible to be synthetize in CNS too.[8]

Final remark

Due to the length limitation of a short communication it was convenient to add a table with all the references of Cuban LABCEL authors as you may see at Table. It is important to gather all these information together in order to have a general idea about the blood-CSF diffusion of the lectin pathway components.

Table 1- Papers about lectin pathway published by Cuban LABCEL authors

Molecule	Title	Reference	Journal or Abstract book	Year
MBL	Mannose-binding lectin deficiency with eosinophilic meningoencephalitis due to Angiostrongylus cantonensis in children: a case series	J Med Case Reports 2011, 5:330	J Med Case Reports	2011
	Mannan-binding lectin in cerebrospinal fluid: a leptomeningeal protein.	Fluids Barriers CNS. 2012;9(1):17	PubMed	2012
MBL/MASP2	MASP2 and MBL: Dynamics and Intrathecal synthesis.	Front. Immunol 2013. Conference Abstract: 15th International Congress of Immunology (ICI). doi: 10.3389/conf.fimmu.2013.02.00929 Disponible en: http://www.frontiersin.org/10.3389/conf.fimmu.2013.02.00929/event_abstract	Conference Abstract: 15th International Congress of Immunology	2013
MBL	Reibergrama para evaluar la síntesis intratecal de Lectina de unión a Manosa.	Rev Cubana de Invest Biomed 2014;33(2):168-176	Rev Cubana de Invest Biomed	2014
MAp44	MAp44: diffusion from blood to cerebrospinal fluid and intrathecal synthesis.	The FASEB Journal 2016;30(1) Supplement 970.1 DOI: 10.1096/fj.1530-6860.Disponible en: http://www.fasebj.org/content/30/1_Supplement/970.1.short	The FASEB Journal	2016
MAp44	MAp44 passage from blood to cerebrospinal fluid and the theory of the molecular flow/ cerebrospinal flux.	Immuno Mexico 2018, XII Congress of the Latin American Association of Immunology and XXIII Congress of the Mexican Society of Immunology. Frontiers Abstract Book. Pelayo R. (ed) ISBN: 978-2-88945-511-9, DOI: 10.3389/978-2-88945-511-9 pp. 178-182.	XII Congress of the Latin American Association of Immunology and XXIII Congress of the Mexican Society of Immunology	2018
CL-K1	CL-K1, a Novel Lectin Pathway Component is a Leptomeningeal Protein	FASEB J 2017;321: 882.3 Disponible en: http://www.fasebj.org/content/31/1_Supplement/882.3.abstract?sid=bf1491af-e5d3-4336-900f-5037ec95f49f	The FASEB Journal	2017
H Ficolin	H Ficolin: Polymerization and Aggregation from Blood to Cerebrospinal Fluid.	FASEB J 2017; 31: 882.4 Disponible en http://www.fasebj.org/content/31/1_Supplement/882.4.abstract?sid=622e9756-4b1a-429e-85d9-f1fcd037d9d0	The FASEB Journal	2017
MASP-3	MASP-3. Aggregation and Its Blood to Cerebrospinal Fluid Diffusion.	FASEB J 2018; 32, 1_supplement: 741.1. Disponible en: https://www.fasebj.org/toc/fasebj/32/1_supplement, Abstract 741.1; Consultado Abril 22, 2018.	The FASEB Journal	2018
MASP-3	MASP-3: A New Leptomeningeal Protein in the Lectin Pathway.	FASEB J 2018; 32, 1_supplement: 741.5. Disponible en: https://www.fasebj.org/toc/fasebj/32/1_supplement , Abstract 741.5 ; Consultado Abril 22, 2018.	The FASEB Journal	2018
C1q	C1q Intrathecal Synthesis in Patients Without Inflammatory Diseases with Blood-Brain Dysfunction	FASEB J 2018; 32, 1_supplement: 741.3. Disponible en: https://www.fasebj.org/toc/fasebj/32/1_supplement , Abstract 741.3; Consultado Abril 22, 2018	The FASEB Journal	2018
M Ficolin	M Ficolin: Diffusion Dynamics from Blood to Cerebrospinal Fluid.	FASEB J 2018; 32, 1_supplement: 741.4. Disponible en: https://www.fasebj.org/toc/fasebj/32/1_supplement , Abstract 741.4 ; Consultado Abril 22, 2018.	The FASEB Journal	2018

CONCLUSIONS

According to the state of the art the lectin pathway that is not completely discovered it not possible to find easily in the actual literature. It should be completed with the different sources where the new knowledge is appearing as abstract or short communication from abstract book and congress websites.

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