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Commentary

Role of ficolin-3 in acute kidney graft rejection: A new diagnostic tool

Fateme Shamekhi Amiri

Nephrologist, Imam Khomeini Hospital, Faculty of Medicine (Poursina), Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

The complement system has been implicated in a variety of conditions: autoimmune diseases, sepsis, transplantation, ischemia-reperfusion injuries, traumatic brain injury, infections, and bone biology. Complement activation in kidney transplantation may also induce allograft injury and contribute to delayed graft function. Activation of the complement system leads to the formation of molecules with proinflammatory properties. This may result in the killing of microorganisms, or it may lead to attack of altered self-tissue. The complement system may be activated through either of the three ways; that is, classic, alternative, and lectin pathways. The lectin pathway is initiated by binding of the pattern recognition molecules mannose-binding lectin or the three ficolins (ficolins 1, 2, 3) to the surfaces of pathogens or altered self-cells. It appears that a dual role of ficolin 3 may be present; while one being beneficial, the other be unfavorable effect, which does not result in bacterial or cellular clearance, but may lead to uncontrolled complement activation, resulting in adverse effects on the host. Research group demonstrated that decreased serum ficolin-3 was independently correlated with insulin resistance, and low serum ficolin-3 predicted the development of type 2 diabetes mellitus. Contrastingly, several studies showed that ficolin-3 might be one of the initiating factors involved in kidney rejection.

1. Introduction

There is no doubt that cells of the adaptive immune system, both T and B-cells, are the central players of the graft rejection. However, elements of the innate immune system also play an important role in the initiation of early inflammatory responses and in the modulation of the graft rejection. Complement is a key component of innate immune system, presented in the plasma that participates in graft rejection. The complement system is an integral part of the immune response and acts as a bridge between innate and acquired immunity.[1]

2. Biologic activities of ficolin-3

The complement system has an essential role in antibody-mediated kidney rejection via the classical C1q-dependent pathway. Deposition of downstream complement component

E-mail address: fa.shamekhi@gmail.com.
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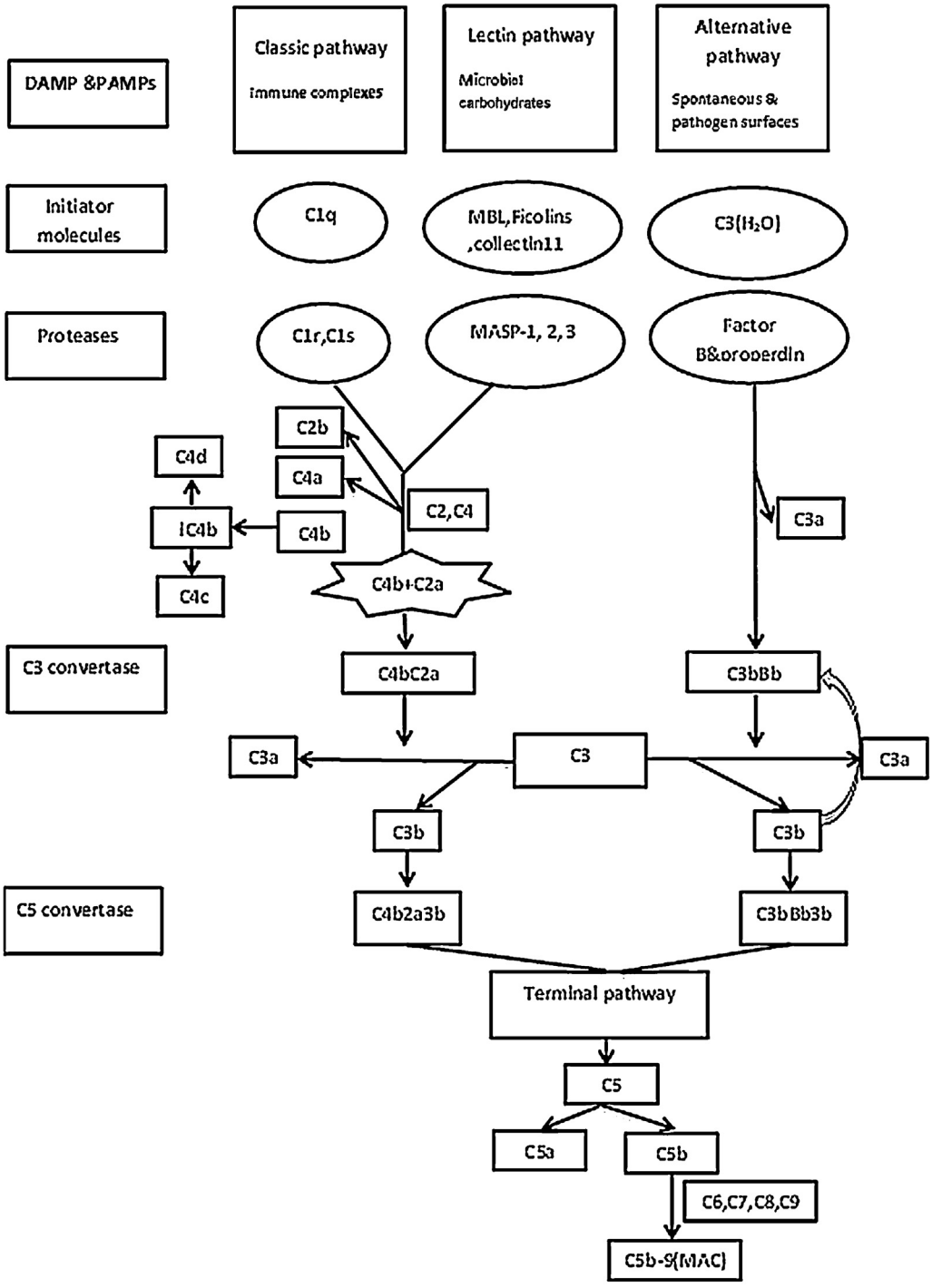

Fig. 1 – Pathways of compliment activation. The third pathway is known as MBL (mannose binding lectin)/MASP (MBL-associated serine protease) pathway. The initiating molecules (MBL, ficolins) for the MBL pathway are multimeric lectin complexes that bind to specific carbohydrate patterns uncommon in the host, leading to activation of the pathway through enzymatic activity of MASP. DAMPs, damage-associated molecular patterns; iC4b, inactive C4b; MAC, membrane attack complex; PAMPs, pathogen associated membrane patterns.

factor C4 is a prognostic marker of reduced long-term graft survival.[2,3] There are three known pathways for complement activation: classical, alternative and lectin pathways (Fig. 1). Forty years after the proposal of the alternative pathway, the MBL (mannose-binding lectin)/MASP (MBL-associated serine protease) pathway was discovered. This pathway was characterized by using proteins isolated from rabbit liver and serum, but its function remained unclear initially. The initiating molecules for this pathway are collectins (MBL and ficolin), which are ultimeric lectin complexes. These bind to specific