

Dietary sugars inhibit biologic functions of the pattern recognition molecule, mannose-binding lectin

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ABSTRACT

Mannose-binding lectin (MBL), a mammalian lectin, is a pattern recognition molecule of the innate immune system and recognizes carbohydrates that are exposed on pathogens. In this study, we observed that fructose down regulates MBL-mediated innate immune mechanisms against both influenza A virus (IAV) and *Staphylococcus aureus*. These mechanisms include the lectin complement pathway and coagulation enzyme-like activities on both pathogens. Furthermore, fructose also reduces MBL-mediated phagocytosis of *S. aureus* and IAV and MBL-mediated IAV infection to epithelial cells. In contrast, sucrose inhibits MBL-mediated immune mechanisms against *S. aureus* but not IAV. Together, our studies show that dietary sugars, in particular fructose, negatively regulate the innate immunity against viral and bacterial pathogens.

Keywords: Mannose-Binding Lectin; Fructose; Influenza A Virus; *Staphylococcus Aureus*; Complement; Coagulation

1. INTRODUCTION

The innate immune system represents the first line of host defense against pathogens. It is widely accepted that in the lumen of our intestines, the innate immune system is constantly interacting with the microbiota [1,2]. This interaction is tightly regulated and is essential for both immune tolerance and immunity against pathogens [3,4]. How our nutrition affects host-microbiome interactions

remains unknown but an increase risk of infection is observed in patients with diabetes and obesity. These diseases have been linked to excess consumption of fructose and fatty foods [5,6]. Fructose, in the form of high fructose corn syrup, along with sucrose is the main dietary sugars in our diet [7]. How dietary sugars affect human disease is an important question that remains unanswered. A human study in 1973 showed that dietary sugar intake, but not starch intake, dramatically reduced bacterial phagocytosis [8]. Although the precise mechanisms of this observation have not been understood, these observations support the idea that dietary sugars influence immune functions.

The innate immune system like the adaptive immune system utilizes both cellular and humoral pathways. Cellular defense includes epithelial cells and phagocytes, such as macrophages and neutrophils [9]. Cell surface receptors on innate immune cells together with soluble lectins recognize pathogens by specific pathogen-associated molecular patterns (PAMPs) and therefore termed pattern recognition molecules [10]. MBL, a serum pattern recognition molecule, is primarily synthesized in the liver and in small quantity by the small intestinal epithelial cells [11-14]. MBL was also identified as an opsonin critical for bacterial (and yeast) phagocytosis [15,16]. In addition, it is critical for defense against viruses as MBL is identical to -inhibitor found in serum and caused calcium-dependent viral neutralization [17,18]. Thus, molecular patterns from virus, bacteria and yeast are recognized by MBL.

Pattern recognition by MBL results in activation of innate immune cascades. For example, MBL activates complement via the lectin pathway, which is mediated by MBL-associated serine protease (MASP) 1 - 3