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Galectins participate in virus infection, friend or foe?

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Galectins, previously called as S-type lectins, have high affinity to β-galactose-containing glycoconjugates. Galectins contain carbohydrate-recognition domains (CRDs) that share structural homology. Galectins are known to widely express in all organisms and participate in regulation of various biological, physiological and immunological functions. In recent years, galectins have been reported to play certain roles in viral infections. Some viruses take advantage of galectins to enhance their propagation. However, some viral infections are reported to be ameliorated by galectins. Some galectins are known to address dual roles (promotion or inhibition) mainly determined on their intracellular or extracellular functions. Here, we briefly address the roles of galectins in virus infection.

Galectins were firstly found in vertebrates in 1976, the first found of galectins is named as Galectin-1. After that, a number of galectins have been identified. Currently, there are 15 galectins found in mammals and 12 of them were identified in humans (Figure 1). The primary structure of galectins shares the carbohydrate recognition domains (CRDs) that interact to β-galactosides and some of them connect to a tandem repeat domain. Galectins are classified into three main groups including prototype, chimera and tandem repeat type (Figure 1). Presently, limited information is available regarding the role of galectins in virus infection, replication and dissemination. Several reports indicate that galectins regulate virus infections through their intracellular and extracellular interactions with factors that reside in the nucleus and cytoplasm and glycans on cell surface, respectively. Galectin-1 has been reported to act as a host soluble factor to promote HIV-1 infection via a mechanism that interacts with gp120 envelope protein of HIV-1 as well as CD4 receptors on the cell surface, contributing to enhancement of virions attaching to CD4. Similar phenomenon was found in monocytes and macrophages receiving HIV-1 infection in presence of Galectin-1. In addition, Galectin-1 is reported to bind to influenza virus and ameliorates influenza induced pathogenesis [1], also Galectin-1 was found to facilitate suppression of Epstein-Barr virus (EBV)–specific T-cell replication [2]. Galectin-1 is also reported to inhibit cell fusion by envelope glycoproteins of Nipah virus and triggered the secretion of proinflammatory cytokines [3] and exerts inhibitory effects against dengue virus serotype 1(DV-1) infection [4]. Further, herpes simplex virus(HSV) infection is known to induce Galectin-1 expression and secretion, leading to cause of apoptosis of activated T cells [5]. These observations are mainly relied on the extracellular functions of Galectin-1 to virus infection using *in vitro* models.

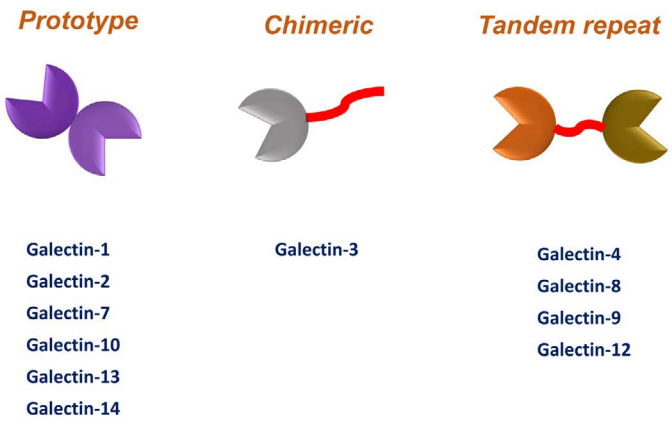

Figure 1. Different types of galectins in humans

Human galectins have been classified into three groups according to their structure: prototypical, chimeric, and tandem repeat.

Regarding to Galectin-3, it has a unique chimeric structure composed by one CRD linking and a tandem repeat domain. An earlier report indicates that herpes simplex virus type 1(HSV-1) infection rose Galectin-3 secretion and contributed to pro-inflammatory immune response against HSV-1 infection [6]. The other report indicates that Aloe-emodin treatment up-regulated Galectin-3 to against Influenza A virus infection, since Galectin-3 presented cytokine-like regulatory function to activate JAK/STAT pathway and further to augment expression of antiviral genes, such as IFN-β, IFN-α and PKR [7]. More recently, Galectin-3 was reported to express and correlate with HIV-1 expression in latent infected cells through interacting with Tat and activating NF-κB pathway. In addition, the endogenous function of Galectin-3 in virus infection has been recently addressed. A report indicates that endogenous Galectin-3 was up-regulated in HIV-1 infected CD4 T cells and further promoted HIV-1 budding through stabilizing Alix and $p6^{Gag}$ interaction [8]. Recently, another study indicated that endogenous gaectin-3 triggered NLRP3 inflammasome activation to increase severity of H5N1-avian influenza virus-induced pulmonary inflammation [9].

Regarding the regulatory capabilities of Galectin-9 in virus infection, several researches indicated that Galectin-9 displayed inhibitory effects on virus replication and propagation. Previous reports indicate that Galectin-9 interacted with T cell immunoglobulin and mucin protein-3 (Tim-3) which induced apoptosis of virus infected T cells such as HTLV-1 [10]. Galectin-9/Tim-3 interaction also known to constrain

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CD8 T cell immunity to HSV infection and ameliorates HSV-induced inflammation [11,12]. Similar results were also found in influenza A virus and respiratory syncytial virus when Galectin-9 bound to virus infected T cells [13,14]. Furthermore, Tim-3/Galectin-9 pathway up-regulation resulted in exhaustion of T cells in chronic hepatitis B virus infection [15]. In addition, the increase of Galectin-9 expression in sera or plasma was correlated with influenza A virus, HIV-1 and dengue virus infections in the early phase, suggesting Galectin-9 as a biomarker to monitor some virus infection and disease severity [16-18].

Here, we briefly introduced the current research status of galectins in virus infection. Although significant positive or negative viral regulation by galectins were reported using recombinant galectin pretreated in *in vitro* assays, we need to consider the possibility of these galectins' regulation in *in vivo* models, because the concentrations of most galectins are in nanomolar (nM) range in human body. We suggest that endogenous function of galectins is worthy to study, the mechanism may be through protein-protein interaction inside the cells.

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