SPHINGOSINE ANALOG AAL-R ENHANCES DENDRITIC CELL RESPONSES UPON TLR7 LIGATION

Young-Jin Seo (Postdoctoral Fellow)
Celeste Blake
(Bumsuk Hahm, PhD)
Departments of Surgery and Molecular Microbiology & Immunology

Sphingosine analogs display immune suppressive activities and thus have therapeutic potential in the treatment of autoimmune diseases. In this study, we investigated the effect of a sphingosine analog, AAL-R, on the host immunity of dendritic cell (DC) response upon the stimulation of toll-like receptors (TLRs) or a viral infection. AAL-R impaired DC maturation in response to TLR3 or TLR4 activation, representing its immunosuppressive activity. In contrast, AAL-R increased TLR7-mediated DC responses by elevating the level of MHC-I molecule and type I interferon (IFN), and enhancing DC capacity to induce CD8+ T cell proliferation. Further, AAL-R increased the phenotypic maturation and functionality of DCs infected with lymphocytic choriomeningitis virus. Since AAL-R failed to change the response of type I IFN receptor-deficient DCs to the viral infection, the underlying molecular mechanism involves type I IFN signaling. Thus, our results indicate that AAL-R’s regulatory action is strongly affected by the form of pathogenic molecular patterns and is stimulatory when TLR7 is activated on DCs. These findings could provide a basis for the development of novel DC-mediated therapeutic vaccines.