Immunology Summit-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference on
Clinical & Cellular Immunology
October 15-17, 2013 Hampton Inn Tropicana, Las Vegas, USA

A unique role for phagocytosis in herpes simplex virus infection

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Abstract

Phagocytosis is a common mechanism by which the mediators of innate immunity can fight off microbial infections. Our ongoing research demonstrates that human herpesviruses may have evolved a common mechanism to avoid phagocytic degradation by exploiting a phagocytosislike entrapment to gain entry into the cells of the eye. The three representative herpesviruses included in our study are herpes simplex virus-1 (HSV-1) that causes corneal keratitis, cytomegalovirus (CMV), which is associated with retinitis in immunocompromised individuals and the third herpesvirus, human herpesvirus-8 (HHV-8), is related to the pathogenesis of Kaposi's sarcoma, a common AIDS-related tumor of eyelid and conjunctiva. Using laser scanning confocal microscopy imaging, we have found that successful infection of ocular cell types by all the three viruses, belonging to three divergent subfamilies of herpesviruses, is facilitated by induction of F-actin rich membrane pseudopods. Inhibitors of F-actin polymerization and pseudopod formation, cytochalasin D and latrunculin B, show strong efficacy in stopping the infection by all three viruses. We also found that an identical inhibition was seen by preventing phosphoinositide 3 kinase signaling, which is required for the phagocytosis of microbes. Transmission electron microscopy data using human corneal fibroblasts for HSV-1, human retinal pigment epithelial cells for CMV, and human conjunctival epithelial cells for HHV-8 provide further support to our argument that pseudopod-like membrane protrusions facilitate virus uptake by the ocular cells. Our findings suggest a novel mechanism by which the nonprofessional mediators of phagocytosis can be infected by human herpesviruses.

Biography

Deepak Shukla completed his Ph.D in Microbiology and Immunology in 1996 from the University of Illinois at Chicago and finished his postdoctoral studies from Northwestern University School of Medicine in 2001. Currently, he is Marion Schenk Esq. Professor of Ophthalmology and an Associate Professor of Microbiology and Immunology at the University of Illinois at Chicago. He also serves as the Director of the Ocular Virology Laboratory. He has published more than 80 papers in reputed journals and serves as an editorial board member of a number of scientific journals