Marcela Kudelova, Virol-mycol 2016, 5:1 (Suppl)
http://dx.doi.org/10.4172/2161-0517.C1.009

OMICS International
conferenceseries.com

6th Euro Virology Congress and Expo

March 10-12, 2016 Madrid, Spain

Modulation of binding of immunomodulatory M3 protein encoded by Murine gammaherpesvirus 68 to chemokines by site-directed mutagenesis

Marcela Kudelova and **Radka Matuskova**
Department of Molecular Pathogenesis of Viruses, Institute of Virology, Biomedical Research Center, Slovak Academy of Sciences, Dúbravská cesta 9, Bratislava. Slovak Republic

The major function of the immune system is to protect the host from various infectious agents, including viruses thereby preserving the integrity of the body. Key components of inflammatory signalization are small soluble proteins - chemokines that attract immunocompetent cells into the site of inflammation. After all, chemokines and their receptors represent potential therapeutic targets for anticancer drugs. However, large DNA viruses, particularly poxviruses and herpesviruses, have evolved several mechanisms to modulate host immune system. One strategy includes the production of chemokine-binding proteins involved in negative regulation of the host chemokine signalization. Murine gammaherpesvirus 68 (MHV-68), firstly discovered in Slovakia by prof. Dionýz Blaškovič, is known naturally infect rodents. MHV-68 still actually provides a unique model for dissecting important topics of human immunity to large DNA viruses that persist in B lymphocytes. MHV-68 encodes M3 protein (44 kDa) which possess immunomodulatoy properties by binding to a broad spectrum of host chemokines and their receptors. In E. coli bacterial expression system, we prepared several native recombinant M3 proteins, confirmed their identity by Western blotting and quantified their binding to human chemokines CCL5(RANTES), CXCL8(IL-8), and CCL3(MIP-1α) by ELISA tests. By site-directed mutagenesis we prepared mutated M3 proteins displaying modulated in the strength and specificity binding to chemokines. We confirmed that even one mutation localized near predicted chemokine binding site alters the binding of M3 protein to some chemokines.

Biography

Marcela Kudelova has completed her postdoctoral studies from Comenius University in Bratislava and ScD thesis from Slovak Academy of Sciences. She is a head of Department of Molecular Pathogenesis of Virology, Institute of Virology, Biomedical Research Center, Slovak Academy of Sciences, Slovak Republic. She has published more than 60 papers in reputed journals and has been serving as an editorial board member of repute.

virukude@savba.sk

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