Abstract

Vaccinia virus (VACV) is an enveloped DNA virus, member of the *Orthopoxviridae* genus. VACV genome size is about 200 kbp. This huge genome capacity allows VACV to encode a set of factors that are non-essential for virus replication and spread *in vitro*. While these factors are needed for interfering with host immune responses, VACV remains strongly immunogenic. Cell-mediated and humoral immune responses in atopic disorders are deregulated to a certain extent, leading to complications in case of infection or vaccination with vaccines based on replicating viruses, such as *eczema vaccinatum* caused by VACV. VACV effects on immune responses consist among others in the inhibition of expression of type I interferon (IFN) at various levels – for example in a specific inhibition of phosphorylation of the interferon regulatory factor-3 (IRF-3) via inhibition of the activity of TANK-binding kinase 1 (TBK 1) that normally phosphorylates IRF-3. Phosphorylation allows IRF-3 to translocate into the nucleus where it initiates transcription of IFNβ followed by induction of expression of IFNα and interferon stimulated genes. Expression of these genes is shut down when IRF-3 activity is inhibited. To overcome this block, a recombinant VACV expressing murine IRF-3 under VACV p7.5 promotor (WR-IRF3) was generated. Previously, it was confirmed that the expression of recombinant IRF-3 leads to expression of IFNβ. The aim of this thesis is to characterize the effects of WR-IRF3 and control VACV expressing luciferase (WR-Luc) in a spontaneously atopic organism, Nc/Nga mice, and in a normal one, Balb/c mice. The presented results indicate that expression of the recombinant IRF-3 increases expression of IFNβ and IL-1β in tissue cultures and modulates expression of various cytokines in the skin of both mouse strains used. Further, immunization with WR-IRF3 induces higher protective immunity against a lethal poxviral infection.

Key words: vaccinia virus, atopic dermatitis, interferon regulatory factor-3, interferon β, interleukin-1β, Nc/Nga mice, Balb/c mice