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