

P050 The vaccinia virus protein K7 modulates innate immune signalling pathways

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Viral recognition is mediated at least partially by two classes of pattern-recognition receptors: Toll-like receptors (TLR) and RIG-like helicases (RLH). Many viruses encode highly evolved mechanisms to evade this anti-viral response. Studying them provides novel insights into the biology of the virus and the resulting host response. For example, the discovery of the *vaccinia virus* (VACV)-encoded TLR-signalling inhibitors A46 and A52 provided early evidence for a role of TLRs anti-viral immunity. Here we describe a VACV protein, K7 that has significant sequence similarity to A52, yet is more highly conserved amongst poxviruses. Like A52, K7 inhibits TLR-induced NF- κ B activation and interacts with TRAF6 and IRAK2. However, K7 also interferes with TLR-dependent and -independent IRF activation and IFN- β promoter induction. This effect cannot be mediated by TRAF6 or IRAK2, therefore we sought to identify additional host targets of K7. We demonstrate here that K7, but not A52, interacts with a cellular DEAD-box protein and that this mediates the inhibitory effect of K7 on IRF activation. In murine infection models K7 makes a greater contribution to virulence than A52, therefore it seems to be physiologically relevant for VACV to interfere with TLR-independent IRF activation.