

P007 Identification of residues within Vaccinia virus protein A52 that are critical for MAP kinase activation via TRAF6
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The Vaccinia virus (VV) genome encodes numerous proteins that modulate innate immune responses, including proteins that disrupt Toll-like receptor (TLR) and cytokine function. One of these proteins, A52, inhibits IL-1 and TLR-induced NF- κ B activation and contributes to virulence. A52 activates p38 MAP kinase, enhancing TLR-dependent IL-10 induction. A52-induced MAP kinase activation is primarily mediated by an interaction with TRAF6, and here we investigated the molecular mechanism of A52-TRAF6 binding and subsequent MAP kinase activation. We identified a putative TRAF6 interaction motif in A52 at residues 149-154(RNEKLF), which is located in the C-terminal region of A52 required for TRAF6 binding. Compellingly, a F154A mutation abrogated the A52-induced activation of p38 MAP kinases but did not affect the ability of A52 to inhibit NF- κ B. Surprisingly, the F154A mutant still bound to TRAF6. Since TRAF6 is an E3 ubiquitin ligase, we investigated whether A52 was a substrate for TRAF6-mediated ubiquitination. We have found that A52 is ubiquitinated, but have not yet determined a role for TRAF6 in A52 ubiquitination. Therefore we have identified a single residue in A52 critical for MAP kinase activation, which may be more important for TRAF6-dependent activation of MAP kinases than for TRAF6 interaction.