DISTINCT ROLES PLAYED BY C-JUN IN THE ORTHOPOXVIRUSES *VACCINIA* AND *COWPOX* BIOLOGY

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We have been studying the activation of MAPKs by the Orthopoxviruses *Vaccinia* (VACV) and *Cowpox* (CPVX), and previously we demonstrated that both viruses activate the MAPKs ERK1/2 and JNK1/2. Since the transcription factor c-Jun is a common signal transducer of both pathways, we decided to investigate whether it plays a role in the Orthopoxviruses´ biology. Here we demonstrated that c-Jun is activated from early until late times during the infection by both viruses. The utilization of pharmacological inhibitor or knockout cells demonstrated that both pathways contribute to the activation of c-Jun during the infection with VACV and that just JNK1/2 does it on CPVX. After that, cell lines stably-expressing c-Jun-dominant-negative mutation were generated and used for infectivity assays. In the DN cells, the expression of viral proteins weren't affected and we observed a significant reduction in the induction of Egr-1 and virus yield during the infection with VACV, but not with CPVX. In contrast, there was a reduction in plaque size with both viruses. These data suggest that the pathway MEK/ERK1/2/c-Jun/Egr-1 is necessary only for an efficient VACV production. It also seems that the JNK1/2/c-Jun pathway plays a role in the dissemination of both viruses as verified by the altered viral plaque phenotype.