ACTIVATION OF PI3K/AKT PATHWAY BY VACCINIA AND COWPOX VIRUSES IS REQUIRED TO THEIR EFFICIENT MULTIPLICATION

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Vaccinia virus (VACV) and *Cowpox virus* (CPXV) are double-stranded DNA viruses belonging to the *Poxviridae* family. In the last years we have been studying the activation of the pathways MEK1/2/ERK1/2/Egr-1 and MKK4/MKK7/JNK1/2/c-Jun during VACV and CPXV infection. Since the PI3K pathway is vitally important for cell survival and activated by many viruses, we analyzed whether VACV and CPXV were also able to activate this pathway. A31 cells were infected with VACV or CPXV at multiplicity of infection 10 in the presence or in the absence of the pharmacological inhibitor of PI3K (LY294002). Western blot analysis demonstrated that both viruses stimulated Akt phosphorylation from 15 minutes post-infection up to 7 hpi. Akt stimulation was independent on early steps of virus multiplication, because viruses inactivated upon UV irradiation were able to phosphorylate Akt. Furthermore, VACV and CPXV stimulated Akt through PI3K, because Akt phosphorylation was blocked when the infection was carried out in the presence of LY294002. The PI3K/Akt pathway is biologically relevant, since LY294002 caused a profound effect on viruses multiplication. Moreover, TUNEL assay demonstrated that the viruses induce PI3K/Akt pathway to keep the cells alive, because its blockade resulted in an increase in apoptotic cells.