ROLE PLAYED BY RAC1 IN *VACCINIA VIRUS* AND *COWPOX VIRUS* BIOLOGY

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Vaccinia virus (VACV) and *Cowpox virus* (CPXV) are members of the *Poxviridae* family of viruses. We showed previously that infection with VACV and CPXV, promoted a sustained activation of the mitogen-activated proteins kinases (MAPKs) MEK/ERK, although this pathway only affected VACV multiplication. In this study our aim was to investigate the upstream signals to MAPK generated after VACV and CPXV infection. To this end, we generated cell lines expressing dominant-negative mutation to the small GTPase Rac1 (DN Rac1). A significant reduction in phosphorylation of JNK, c-JUN and altered Akt phosphorylation was verified when these cells were infected only with VACV. Furthermore, Rac1 was required for efficient VACV multiplication, since a significant decrease in the virus yield was observed under the same conditions. Our data also showed that the pharmacological inhibitor of PI3K (LY294002) caused about one log reduction in the VACV yield. Since PI3K is an upstream molecule that may deliver the signals to Rac1 and the latter to JNK, it is currently under investigation whether or not the signals are transmitted via PI3K/Rac1/JNK. While Rac1 seems to play an important role in VACV biology, another GTPase can be involved in CPXV multiplication.