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General Research » Intracellular sensing of nucleic acids and interferon signaling

DNA FROM BK POLYOMAVIRUS IS SENSED DURING INFECTION OF RESERVOIR CELLS VIA CGAS-STING PATHWAY

Sandra Huerfano, Katerina Brustikova, Boris Ryabchenko, Vojtech Sroller, Jitka Forstova
Department of Genetics and Microbiology, Faculty of Science, BIOCEV, Charles University, Vestec, 25250, Czech Republic.

OBJECTIVES:Human polyomaviruses (HPyVs) include 14 species that cause primary asymptomatic infections after which the virus persists in the host by a mechanism that is not well understood. Reactivation of the infection in immunosuppressed patients leads to severe disease. Recently, it has been suggested that moderate innate immune responses in reservoir cells contribute to viral persistence. For BK polyomavirus (BKPyV), cells from the urinary tract are thought to act as viral reservoirs.
Here, we investigated the potential role of the cGAS-STING signalling pathway in the interferon (IFN) responses launched by primary microvascular endothelial cells from bladder (HMVECs bd) in response to BKPyV infection.

METHODS:We followed the kinetics of viral proteins and virion production using confocal and infectivity assays. IFN responses were analysed by measuring IFN β, ISG 56, CXCL10 and CCL20 by RT-qPCR. The role of the cGAS sensor was evaluated by examining its binding to viral DNA by fluorescent in situ hybridization and by measuring 2-3 cGAMP levels by ELISA. Then, the role of STING was investigated by detecting its phosphorylation at serine 366 by Western blotting.

RESULTS:First massive production of viral LT and VP1 proteins was detected after 36hpi and 48hpi, respectively. Virions were detected in the medium from 48hpi. Next, we showed that HMVECs bd elicit a moderate IFN response at a late time point after infection (around 72hpi). In the cytosol, we observed colocalization of cGAS with both incoming viral DNA (24hpi) and viral DNA leaked to the cytosol (62hpi). However, cGAMP production and activation of STING were detected only after 62hpi.

CONCLUSIONS:Our data show that BKPyV infection in reservoir cells leads to cGAS-STING activation at late time post-infection. Interestingly, the observed non-productive binding of cGAS to incoming virus could indicate a non-IFN-related function of cGAS during infection.

Keywords: BKPyV, cGAS, STING, INTERFERON