STING regulation in polyomavirus infections

Lenka Horníková, Jitka Lišková, Aneta Šnejdarová and Sandra Huerfano

Department of Genetics and Microbiology, BIOCEV, Charles University, Prague, Czech Republic

Stimulator of interferon genes (STING) is an indispensable component of cGAS-STING signalization pathway that plays a key role in the innate immune response to polyomavirus infection. Infection of cells by polyomaviruses resulted in cGAS-STING pathway activation but only moderate interferon beta production was detected indicating possible regulation of the pathway during the infection. STING is a transmembrane protein that predominantly resides in the endoplasmic reticulum (ER). After binding to cGAMP di-nucleotide, STING oligomerizes. Oligomers translocate from ER to trans Golgi reticulum which leads to TBK1 and IRF3 phosphorylation and subsequent interferon-beta production. Later, STING is degraded in proteasomes or autophagosomes.

In this study, we focused on studying possible regulatory events that could lead to the down regulation of the cGAS-STING pathway during polyomavirus infection. For this, we followed the trafficking of STING and possible interactions of STING with viral proteins. We used mouse fibroblast infected by mouse polyomavirus (MPyV) and microvascular endothelial cells infected by BK polyomavirus (BKV). In BKV-infected cells significant reorganizations of ER and trans-Golgi network were detected. ER signal was detected in huge clusters in the cytoplasm of BKV-infected cells and these clusters were also STING positive. Similarly, signal of trans-Golgi network formed several small clusters in infected cells and these clusters were positive for STING. Whether these morphological changes play a role in the regulation of STING activity during BKV infection requires further studies. Contrary to BKV-infected cells, no significant difference in localization of STING between MPyV-infected and non-infected cells was detected. However, we observed abundant co-localization of STING and viral regulatory protein, middle T antigen (MT) signals in cells infected as well as individually expressing MT suggesting the possible participation of MT in STING function regulation.

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