P 009

Role of TRAF6 adaptor in the immune responses to murine polyomavirus

Sandra Huerfano Meneses[1], Boris Rjabchenko[1], Vaclav Janovec[1,2], Jitka Forstova[1]

[1]Charles University, Genetics and Microbiology, Prague, Czech Republic

[2]Institute of Organic Chemistry and Biochemistry of the CAS, Prague, Czech Republic

Polyomaviruses are associated with many diseases due to their ability to persistently infect the host. Since 2008, twelve new human polyomaviruses have been discovered. Among the new species, Merkel cell polyomavirus (MCPyV) was identified as the etiological agent of skin Merkel cell carcinoma. Unfortunately, the cell type productively infected by MCPyV is unknown and therefore in vitro studies of the MCPyV are still a challenge. Nevertheless, its closest related member, Murine polyomavirus (MPyV) has been used per decades as in vitro model to understand fundamental questions about the biology of polyomaviruses. We demonstrated that MPyV activates innate immunite responses via GAS-STING and TLR4. It is known that the transcription factors, NF-Kβ and IRF3 are activated during launching of the above pathways. However, NF-Kβ is mainly activated by TLR4 for pro-inflammatory cytokines production and IRF3 by cGAS-STING for interferon (IFN) production.

Here, we focus on TRAF6, because, apart from its well-known role as one of the possible adaptors in the TRL4 pathway, recently it was suggested to play some role in the cGAS-STING pathway. We used TRAF6 knockout mouse embryo fibroblast and inhibitor of TLR4 to follow activation of NF-Kβ, the levels of IFN β and levels of pro-inflammatory cytokines (CXCL10, IL6) in response to MPyV infections. We found that the knockout of TRAF6 or the inhibition of TLR4 lead to almost complete inhibition of the translocation of NF-Kβ to the nucleus and downregulation of the production of pro-inflammatory cytokines in response to the infection. Truly suggesting a major role of TRAF6 as the adaptor for TLR4. Finally, the interferon responses to the virus were decreased in absence of TRAF6. Since the promoter of IFN-β gene has binding sites for both NF-Kβ and IRF3, our results so far indicate a cross talk between TLR4-TRAF6 and cGAS STING via NF-Kβ.