P-8

IFI16 is a Restriction Factor of AAV2 Infection

Sereina O. Sutter, Kurt Tobler, Michael Seyffert, Elisabeth M. Schraner, Bernd Vogt, and Cornel Fraefel

Institute of Virology, University of Zurich, Zurich, Switzerland

We recently assessed the global gene expression profile (RNAseq) of AAV2 infected normal human fibroblasts (NHFs). The screening revealed 1`929 genes as differentially expressed (DE; $p < 0.01$, number of reads ≥ 40) in AAV2- and mock-infected cells. Gene Ontology (GO) term biological process analysis was performed using DAVID and graphically visualized as enrichment map using Cytoscape. IFI16, a cytosolic and nuclear sensor of ds- and ssDNA, was among the top 50 DEs of the GOterm "innate immune response". IFI16 has been shown to be a restriction factor of many different viruses through various mechanisms, including interferon response and epigenetic modifications. In this study we addressed the question whether IFI16 is a restriction factor for AAV2 infection. Indeed, the post-transcriptional knockdown of IFI16 resulted in a significant increase in transduction efficiency of both single-stranded and self-complementary AAV2 vectors. However, the exogenous complementation of IFI16 in U2OS IFI16$^{-/-}$ cells led to a significant decrease in transduction efficiency. Furthermore, interferon signaling does not appear to be required for the inhibition, as the post-transcriptional knockdown of IFI16 resulted in an increased transduction efficiency also in 2fTGH Jak1$^{-/-}$ cells. Moreover, in NHF cells the AAV2 transduction efficiency was enhanced also upon knockdown of both IFI16 and STING. Multicolor immunofluorescence analysis of AAV2 infected NHF cells showed that IFI16 accumulates in nucleoli together with AAV2 capsids, indicating that the inhibitory effect of IFI16 on AAV2 infection is linked to its sub-nucleolar localization.