Abstract

Viruses have a simple structure and are well described in scientific literature. Based on studies conducted on viruses, many discoveries regarding RNA modifications have been made.

HIV-1 infection reduces the amount of cellular nicotinamide adenine dinucleotide (NAD). Recent studies have shown that NAD can serve as a 5' non-canonical cap for some RNAs in bacteria, yeast, plants, and mammals. NAD capping affects RNA stability and the efficiency of RNA translation. However, surprisingly little is known about the function of NAD cap. This work focuses on NAD capping in the context of HIV-1 infection, while in another study, we also investigated the m^1A modification in HIV-1.

We found that HIV-1 infection affects not only cellular levels of NAD but also the amount of NAD caps on sRNA. Using NAD captureSeq, we identified four snRNAs (U1, U4ATAC, U5E, and U7) and four snoRNAs (SNORD3G, SNORD102, SNORA50A, and SNORD3B) that lose their NAD caps after HIV-1 infection. Particularly interesting is U1 snRNA, which has a sequence complementary to HIV-1 pre-mRNA and binds to it during splicing. We discovered that the NAD cap destabilizes the complex between HIV-1 pre-mRNA and U1 snRNA.

DXO is an NAD decapping enzyme. We prepared cells with DXO overexpression and examined the amount of NAD-RNA in connection with HIV-1 infectivity. DXO overexpression causes reduced amounts of NAD-RNA and increased HIV-1 infectivity. In contrast, repletion of cellular NAD leads to decreased HIV-1 infectivity.

This work identifies new sRNAs with NAD caps in human cells and proposes that NAD-RNA decreases HIV-1 infectivity and may play a role in antiviral defense.

Key words: RNA modifications, NAD, U1 snRNA, RNA-seq, LC-MS, DXO, HIV-1