Control of HIV replication in astrocytes by a family of highly conserved host proteins with a common Rev-interacting domain (Risp).

In human astrocytes, restriction of HIV replication involves inhibition of HIV Rev activity. We previously identified a Rev-interacting human protein fragment (16.4.1) that can reduce Rev activity. The 16.4.1 sequence is contained in a group of highly similar host cell proteins, which we call the Risp family. Here we investigate whether the Risp family is connected to HIV replication in astrocytes. Cell/tissue lysates were analyzed for Risp expression by western blot with various anti-Risp antibodies. The interaction of astrocytic Risp members with Rev was investigated by affinity chromatography. Astrocytes were transfected with expression plasmids containing cDNAs encoding full-length Risp or the isolated 16.4.1 region for Risp overexpression or with siRNAs designed for Risp knock-down. Rev activity was investigated with a Rev-reporter assay. RNA levels were quantified by real-time RT-PCR, HIV Gag levels by p24ELISA. Expression of the Risp family was demonstrated in human brain tissues and astrocytes. Astrocytes were shown to produce Risp family members that interact with Rev. Production of HIV Gag proteins and Rev-dependent RNAs in persistently infected astrocytes increased upon Risp knock-down and decreased upon Risp overexpression. Risp knock-down increased Rev activity.
activity and raised proportions of Rev proteins in the nucleus of astrocytes. Our results link the Risp family to restriction of HIV production and inhibition of Rev activity in astrocytes. We conclude that the Risp family represents a novel family of host factors that can control HIV replication and may be important for the containment of HIV infection in brain reservoirs.