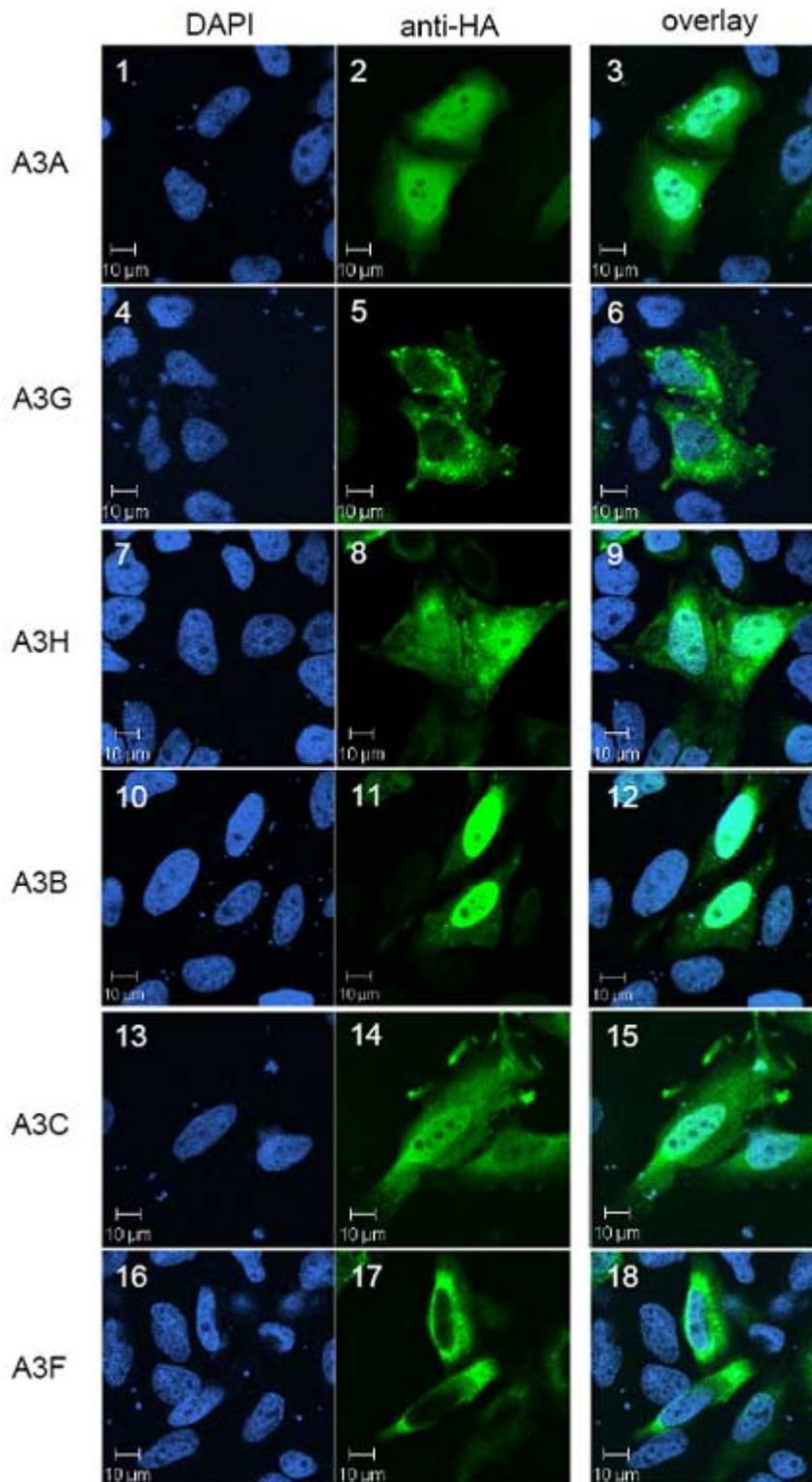


## Mechanisms of intracellular defence against LINE-1 retrotransposition mediated by APOBEC3 proteins

### Research project summary



To limit the negative effects of retrotransposition, mammalian cells have adopted several strategies to restrict mobility and potentially deleterious consequences of uncontrolled retrotransposition. Such host-encoded strategies include DNA methylation, RNA interference (RNAi) and inhibition of retrotransposition by the activity of members of the APOBEC3 (apolipoprotein B mRNA-editing enzyme catalytic polypeptide 3) protein family of Zn<sup>2+</sup>-dependent DNA cytidine deaminases which comprises seven closely related proteins. The APOBEC3 protein family represents a novel group of proteins in the field of innate defense mechanisms that has been shown to be active against a variety of retroviruses and an incredible range of mobile genetic elements. Applying the [L1 retrotransposition reporter assay](#), we demonstrated that APOBEC3A, 3B, 3C, and 3F are inhibitors of L1 retrotransposition in cell culture and major players in intracellular defence against human L1-mediated retrotransposition. Expression of each of these deaminases reduced L1 retrotransposition rates by 75-90 %. However, sequence analysis of L1 retrotransposition events that occurred in the presence of overexpressed APOBEC3 proteins did not reveal an enhanced rate of G-to-A transitions, pointing to an APOBEC3-mediated mechanism of L1 inhibition which is DNA deamination-independent. L1 inhibiting APOBEC3 proteins are expressed in every human cell type or tissue tested so far except the brain. This is consistent with the observation that endogenous L1 retrotransposition can occur during neuronal differentiation. We set out to uncover the different mechanisms by which the seven members of the APOBEC3 protein family restrict L1 retrotransposition in humans.

Figure: Differences in the subcellular localization of six diverse human APOBEC3 proteins (A3A, A3B, A3C, A3F, A3G, and A3H).

Human HA-tagged APOBEC3 proteins were expressed in HeLa cells. To detect APOBEC3 proteins, immunofluorescence staining was performed with anti-HA antibodies. Nuclei were visualized by 4,6-diamidino-2-phenylindole (DAPI) staining.

Source: PEI