Abstract:
APOBEC1 is a cytidine deaminase involved in cholesterol metabolism that has been linked to retrovirus restriction, analogous to the evolutionarily-related APOBEC3 proteins. In particular, murine APOBEC1 was shown to inhibit Friend retrovirus (FV) in vitro, generating high levels of C-to-T and G-to-A mutations. These observations raised the possibility that FV infection might be altered in APOBEC1-null mice. To examine this question directly, we infected wild-type and APOBEC1-null mice with FV complex and evaluated acute infection levels. Surprisingly, APOBEC1-null mice exhibited similar cellular infection levels and plasma viremia relative to wild-type mice. Moreover, next-generation sequencing analyses revealed that APOBEC1 did not enhance retroviral C-to-T and G-to-A mutational frequencies in genomic DNA. Thus, in contrast to APOBEC3, APOBEC1 neither inhibited nor drove the molecular evolution of FV in vivo. Our findings reinforce that not all retrovirus restriction factors characterized as potent in vitro may be functionally relevant in vivo.

Research Category: Basic Science