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Mouse APOBEC3 affects the production of virus-neutralizing antibodies by restricting early retroviral replication, not by altering the B-cell repertoire

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Recent genetic analyses have indicated that polymorphisms in the mouse *APOBEC3* locus constitute the *Rfv3* gene that influences the production of virus-neutralizing antibodies in mice infected with Friend leukemia retrovirus [1,2]. Mice of the resistant genotype preferentially express the exon 5-lacking transcript in higher levels, while susceptible mice express the full-length transcript in lower levels [2,3]. Mouse APOBEC3 expressed in the resistant strains restricts the replication of mouse retroviruses *in vitro* through a mechanism independent of its deaminase activity [2]. However, the mechanisms through which mouse APOBEC3 affects the production of virus-neutralizing antibodies remain unclear. To address this question, we analyzed retroviral replication and the production of virus-neutralizing antibodies in mice of different *APOBEC3* genotypes and those lacking its expression.

Strain A mice with the susceptible *APOBEC3* genotype nevertheless produced high levels of virus-neutralizing antibodies when they possessed the H-2^b haplotype, and class-switching to IgG was observed in the presence of virus-specific T helper cells. Further, APOBEC3-deficient mice produced virus-neutralizing antibodies when their T helper cells had been primed with the viral antigen. Friend virus-induced derangements in the hematopoiesis and resultant splenomegaly are not directly responsible for the delayed antibody responses, because higher levels of viremia and lower antibody responses were observed upon infection with nonpathogenic Friend murine leukemia helper virus in the absence of APOBEC3. In mice of the resistance-associated *APOBEC3* genotype lower levels of viremia were observed even before the detection of virus-neutalizing antibodies in the blood, indicating that the polymorphisms in the *APOBEC3* locus affect the production of neutralizing antibodies as a result of restricted retroviral replication.

Conclusion

B cells from the mice of susceptible *APOBEC3* genotypes produce neutralizing antibodies in the presence of virus-specific T helper cells. Polymorphisms in the *APOBEC3* affect the levels of viremia prior to the production of neutralizing antibodies, indicating that APOBEC3 may indirectly influence B cell functions by restricting viral replication.

References

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