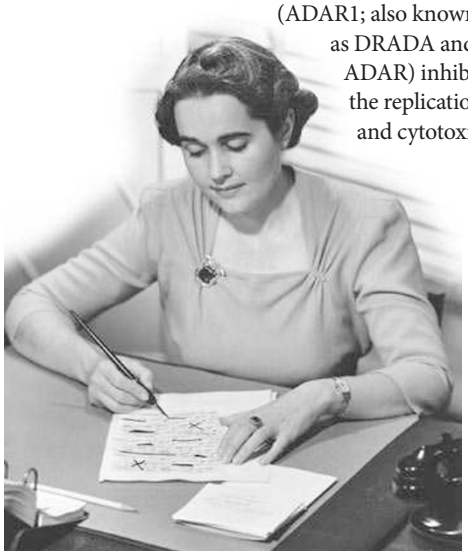
VIROLOGY

Host RNA editor restricts measles

> ADAR1… inhibits the replication and cytotoxicity of MV and other respiratory RNA viruses

Infection by measles virus (MV) can, with very low frequency, lead to a fatal neurodegenerative disease called subacute sclerosing panencephalitis (SSPE). The genomes of MV isolates from these patients show a very high rate of A-to-G mutations, which suggests that MV might be under selective pressure from a host defence mechanism that targets the viral RNA genome. Now, Michael Oldstone and colleagues show that the host protein adenosine deaminase acting on RNA (ADAR1; also known as DRADA and ADAR) inhibits the replication and cytotoxicity of MV and other respiratory RNA viruses.



Mouse *Adar1* (and the human homologue) encodes two protein isoforms: p150, the production of which is induced by interferons, and p110, which is constitutively expressed. It was previously shown that an *Adar1* deletion, which abolished the synthesis of both isoforms in mice, resulted in embryo death. Oldstone *et al.* generated a targeted gene disruption that specifically eliminated the expression of p150 in mice while maintaining p110 expression, but this also resulted in embryo death. To study the role of ADAR1 in MV replication, the authors then prepared immortalized cell lines (mouse embryo fibroblasts; MEFs) from the p150-deficient embryos and from normal embryos. Given that MV cannot infect mouse cells because of the lack of an adequate receptor, the researchers expressed a human MV receptor, CD150 (also known as SLAMF1), in both types of MEF. Infection of these cell lines with MV produced faster and more extensive cytotoxicity, as well as higher MV titres, in p150-deficient MEFs than in wild-type MEFs, indicating that p150 expression restricts MV replication. Remarkably, similar experiments revealed that p150 also inhibited the replication of related paramyxoviruses (Newcastle disease virus, Sendai virus and canine distemper virus) and of a mouse-adapted influenza A virus.

Although p150 clearly has a role in restricting MV infection under normal circumstances, the high mutation rate observed in MV genomes suggests that MV can adapt to overcome this restriction, facilitating persistent infection in SSPE patients. The authors speculate that the role of p150 as a restriction factor of RNA respiratory viruses may be analogous to that of the cytidine deaminase APOBEC3G, which exerts its antiviral function by generating numerous mutations in the DNA of retroviruses, including HIV.

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ORIGINAL RESEARCH PAPER Ward, S. V. *et al.* RNA editing enzyme adenosine deaminase is a restriction factor for controlling measles virus replication that also is required for embryogenesis. *Proc. Natl Acad. Sci. USA* **108**, 331–336 (2010)

FURTHER READING Moss, W. J. & Griffin, D. E. Global measles elimination. *Nature Rev. Microbiol.* **4**, 900–908 (2006)

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