Insights: Publications

A single polymorphic residue in humans underlies species-specific restriction of HSV-1 by the antiviral protein MxB

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Myxovirus resistance proteins A and B (MxA and MxB) are interferon-induced proteins that exert antiviral activity against a diverse range of RNA and DNA viruses. In primates, MxA has been shown to inhibit myxoviruses, bunyaviruses, and the hepatitis B virus, whereas MxB restricts retroviruses and herpesviruses. As a result of their conflicts with viruses, both genes have been undergoing diversifying selection during primate evolution. Here, we investigate how MxB evolution in primates has affected its restriction of herpesviruses. In contrast to human MxB, we find that most primate orthologs, including the closely related chimpanzee MxB, do not inhibit herpes simplex virus (HSV-1) replication. However, all primate MxB orthologs tested restricted human cytomegalovirus. Through the generation of human and chimpanzee MxB chimeras, we show that a single residue, M83, is the key determinant of restriction of HSV-1 replication. Humans are the only primate species known to encode a methionine at this position, whereas most other primate species encode a lysine. Residue 83 is also the most polymorphic residue in MxB in human populations, with M83 being the most common variant. However, ~2.5% of human MxB alleles encode a threonine at this position, which does not restrict HSV-1. Thus, a single amino acid variant in MxB, which has recently risen to high frequency in humans, has endowed human MxB with HSV-1 antiviral activity.

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