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IN BRIEF

VIRAL PATHOGENESIS

Macaque model for AIDS

HIV-1 replicates well in humans but not in atypical host species, which has limited the development of animal models for AIDS. This study now shows that HIV-1 adapts to replicate efficiently and cause AIDS in pig-tailed macaques. The animals were inoculated with HIV-1 and treated with a CD8-specific antibody to cause transient $CD8^+$ T cell depletion. Serial animal-to-animal infection resulted in persistently high viraemia and decreased $CD4^+$ T cell counts in the blood and gut-associated lymphoid tissue, as well as immune activation and *Pneumocystis* pneumonia, which is indicative of HIV-1-induced pathogenesis and progression to AIDS. Host adaptation of the virus was conferred by four amino acid deletions in the envelope gene, which is associated with co-receptor switching, and mutations in Vpu, which contribute to the ability of the virus to antagonize the host restriction factor tetherin. Further development of this animal model will facilitate the study of HIV-1 therapies and vaccines.

ORIGINAL RESEARCH PAPER Hatziioannou, T. *et al.* HIV-1-induced AIDS in monkeys. *Science* **6190**, 1401–1405 (2014)

ANTIMICROBIALS

A fungal compound restores antibiotic activity

β-lactams are the most frequently used class of antibiotics for the treatment of Gram-negative infections, but the acquisition of metallo-β-lactamases (MBLs) results in the emergence of antibiotic-resistant pathogens. King *et al.* used a cell-based screen for inhibitors of the MBL NDM1 and found that an extract from *Aspergillus versicolor* restored the antibiotic activity of meropenem against a genetically engineered NDM1-containing *Escherichia coli* strain. They identified the fungal peptide aspergillomarasmine A (AMA), which is an inhibitor of metalloproteinases, as the active compound. *In vitro* assays showed that AMA is a selective inhibitor of the MBLs NDM1 and VIM2 and that it restored meropenem activity against clinically relevant isolates. NDM1-positive *Klebsiella pneumoniae* were resistant to treatment with meropenem alone, whereas the addition of AMA prevented lethal infection *in vivo*. Thus, a combination of AMA and β-lactams has therapeutic potential for the treatment of carbapenem-resistant pathogens.

ORIGINAL RESEARCH PAPER King, A. M. *et al.* Aspergillomarasmine A overcomes metallo-β-lactamase antibiotic resistance. *Nature* **510**, 503–506 (2014)

VIRAL INFECTION

Manipulation of DNA repair pathways

Herpes simplex virus 1 (HSV-1) replicates in the nucleus and induces chromosomal DNA damage, including DNA double-strand breaks (DSBs). Host cells repair DSBs by non-homologous end joining (NHEJ) or homologous recombination, but how the cell chooses between these pathways and the impact of this decision on viral replication has been unclear. Karttunen *et al.* now show that HSV-1 inhibits NHEJ by triggering the Fanconi anaemia pathway. HSV-1 infection induced mono-ubiquitination of the two Fanconi anaemia pathway effectors, FANCI and FANCI-D2, which resulted in their redistribution from sites of DNA damage to viral replication compartments. Furthermore, HSV-1 replication was severely reduced in cells lacking components of the Fanconi anaemia pathway, and inhibition of NHEJ in these cells was sufficient to restore viral growth. These data suggest that HSV-1 manipulates the Fanconi anaemia pathway to suppress NHEJ and promote viral replication.

ORIGINAL RESEARCH PAPER Karttunen, H. *et al.* Co-opting the Fanconi anemia genomic stability pathway enables herpesvirus DNA synthesis and productive growth. *Mol. Cell* **55**, 111–122 (2014)