Human antimicrobial peptide inactivates enveloped viruses

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Enveloped viruses are responsible for numerous diseases, including influenza and Covid. Wide range antiviral therapies that inactivate viruses through non-specific interactions are mostly non-existent. The cathelicidin LL-37 is an antimicrobial peptide part of the human innate immune system and a promising antiviral therapeutic.[1] LL-37 interacts with lipid structures and modify the lipid colloidal structures. Its antibacterial activity has been linked to the reorganisation of the bacterial membrane’s lipid structure.[2] However, the mechanism of interaction that inactivates viruses needs to be better understood.

Here, LL-37’s antiviral mechanism is studied by investigating the enveloped virus’ function-structure modifications upon interaction with LL-37. The bacteriophage Phi6 is used as surrogate for pathogenic enveloped virus. The particle’s size and morphology are investigated with multi-angle dynamic light scattering. Whereas the particle’s nanostructure is studied by the combination of small angle X-ray scattering and model independent data fitting. Infectivity assays allowed to correlate the resolved structures with the viral biological function. LL-37 is found to actively integrate into the lipid envelope, leading to lipid packing modifications. Eventually, the lipid envelopes peels off the nucleocapsid, inactivating the virus by separating the genomic material from the host cell recognition function, as depicted in Figure 1. Understanding the structural effect antimicrobial peptides on viral self-assembled lipid structures will allow to guide the design of peptide-based antiviral drugs and therapies.

Figure 1. Antiviral mechanism of human antimicrobial peptide LL-37. The peptide integrates the lipid envelope modifying the packing and curvature which leads to inactivation.