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Molecular interference with SARS-CoV-2 replication by the antiviral peptide TAT-I24

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The recent SARS-CoV-2 pandemic highlights the urgent medical need for antiviral therapeutics in addition to an immunisation with vaccines. At the moment, only a few safe and effective antivirals are available for the treatment of virus infections. Experimental peptides might be a future treatment option, as these peptides can act as entry-inhibitors that block or alter virus entry into the cell. The peptide TAT-I24, composed of I24, a 9-mer which inhibits gene expression from "foreign"- nucleic acids, might be such a candidate. This 9-mer sequence is linked to a TAT-peptide, which facilitates cell penetration and supports the transport of I24 into the cytosol in parallel with virus capsids. In previous studies, TAT-I24 has shown a broad range antiviral activity against DNA viruses, but also an inhibitory effect against the RNA virus SARS-CoV-2 could be observed in recent in-vitro neutralization experiments (unpublished data). We observed a reduction of virus particles in the presence of TAT-I24 in various cell lines when infected with SARS-CoV-2, although differences in the sensitivity to the peptide was observed for individual virus variants (Wuhan, Delta, Omicron). Considering differences on viral gene expression levels, preliminary data suggest a delayed assembly of virus particles and a reduced release, when cells are infected in the presence of TAT-I24. Further evaluation of the effects on host gene expression as well as intracellular localization and virus uptake studies (virus and peptide specific antibody staining) are currently ongoing. In addition, air-liquid interface cultures with human alveolar cells are planned as in-vitro models to mimic a possible future therapeutic target region.