Novel compound protects against infection by virus that causes COVID-19, preliminary studies show

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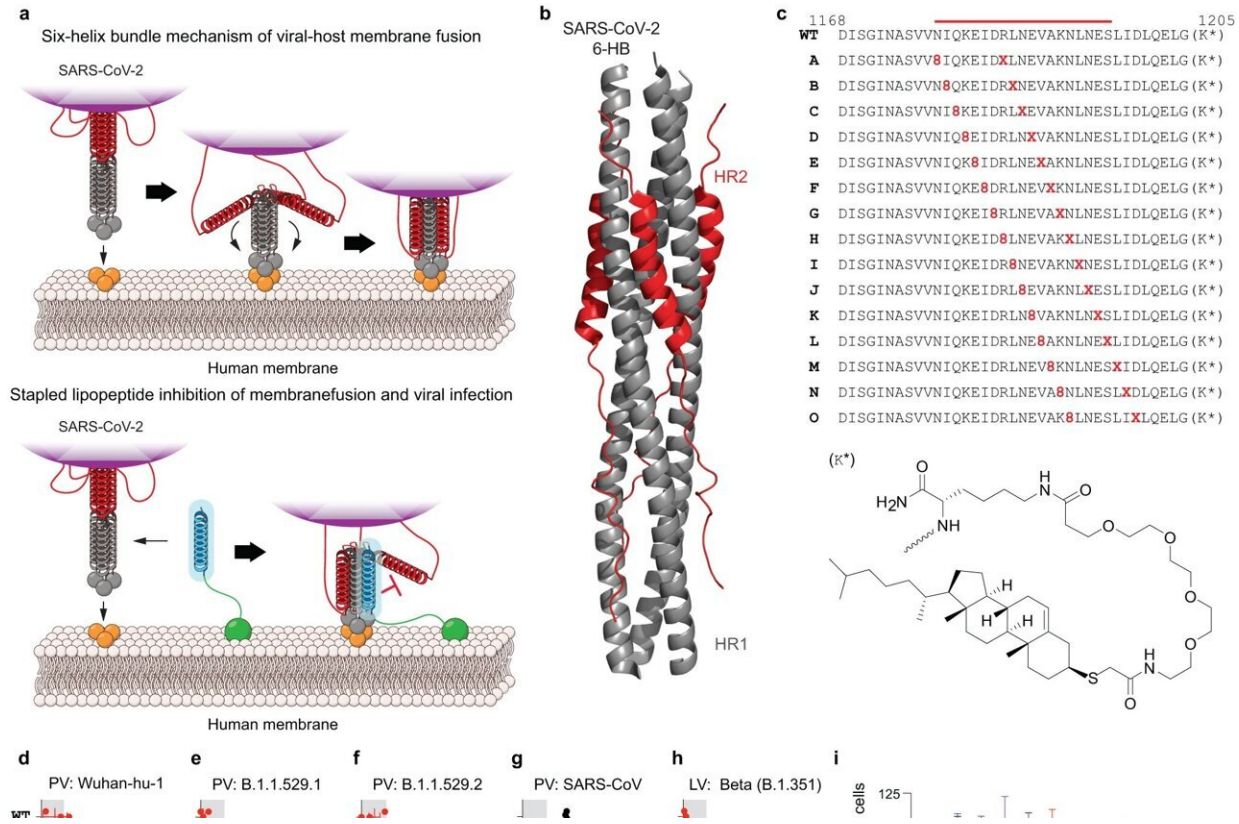

Design and screening of stapled lipopeptide inhibitors of SARS-CoV-2. **a** Schematic of the six-helix bundle (6-HB) fusion mechanism of SARS-CoV-2 and the mechanism by which a stapled lipopeptide decoy of the HR2 domain disrupts 6-HB assembly and thus blocks viral entry. **b** Structure of the SARS-CoV-2 6-HB assembly (PDB ID 7TIK), with the HR2 domain that formed the basis for stapled lipopeptide designs colored in red. **c** Compositions of the *i, i + 7*

staple scanning library of HR2 amino acid sequences 1168-1205 with the structure of the PEG_4-thiocholesterol moiety appended to the C-terminal lysine. WT, unstapled lipopeptide bearing the indicated wild-type HR2 domain sequence. **d–h** The stapled lipopeptide library was tested in infectivity assays using a series of pseudoviruses (PV), including the initial Wuhan-Hu-1 strain (**d**), Omicron variants B.1.1.529.1 (**e**) and B.1.1.529.2 (**f**), and SARS-CoV Urbani (**g**) in ACE2-expressing HEK293T cells, and SARS-CoV-2 Beta strain live virus (**h**) in ACE2-A549 cells at screening doses of 250 nM (**e**, **f**), 500 nM, (**d**, **g**) or 4 μM (**h**). The data are normalized to the percent infected cells treated with vehicle control. Data are mean ± SEM for assays performed in technical quadruplicate (PV) or triplicate (LV) and then repeated with similar results. The gray shading highlights those lipopeptides that inhibited infectivity to