

lipopeptides with a target, increase a binding constant, and improve the activity. The relatively stable secondary structure is also conducive to the polypeptide to resist hydrolysis by a protease *in vivo*, improves the stability *in vivo*, and is also beneficial to the antiviral activity.

- 5 The CD results of the complexes were shown in FIG. 2. Each lipopeptide can interact with the polypeptide simulating a target sequence to form a complex with a typical α -helix structure, wherein the IPB20-N52 complex, IPB24-N52 complex, and IPB28-N52 complex had the α -helix content of 66%, 48%, and 37%, respectively, and the IPB29-N52 complex and IPB30-N52 complex had the α -helix content of 68% and 53%, respectively (left of FIG. 2). *T_m* values of the IPB20-N52 complex, IPB24-N52 complex, and IPB28-N52 complex were 90°C, 90°C, and 89°C, respectively. *T_m* values of the IPB29-N52 complex and IPB30-N52 complex were 86°C and 78°C, respectively (right of FIG. 2). This indicates that the lipopeptides with an EAAAK linker can maintain a specific and stable binding with a target, and increase the binding capability with a cell membrane and a virus membrane.

- 15 Example 3. Inhibitory effect of lipopeptides on novel coronavirus SARS-CoV-2 and mutant strains

293T cell is a product in the American Type Culture Collection (ATCC, Cat. No. CRL-3216). Huh-7 cell is a product of a national experimental cell resource sharing platform. 293T/ACE2 cells are described in reference 2.

- 20 Test cells: 293T/ACE2 cells or Huh-7 cells.

I. Inhibitory effect of lipopeptides on novel coronavirus SARS-CoV-2

The to-be-tested lipopeptides: lipopeptide IPB29, lipopeptide IPB30, lipopeptide IPB20, lipopeptide IPB24 or lipopeptide IPB28 prepared in example 1.

1. Preparation of SARS-CoV-2 pseudovirus

- 25 The plasmid expressing an S protein of SARS-CoV-2 (defined as pCoV2-S) is described in “a plasmid expressing the S protein of SARS-CoV-2” in “Single-cycle infection assay” of the section of materials and methods of reference 5. The HIV backbone plasmid pNL4-3.luc.RE was provided by the project of acquired immunodeficiency syndrome reagents and reference substances of National Institutes of Health (Cat. No. 3418).
- 30 pCoV2-S and pNL4-3.luc.RE were co-transfected into 293T cells at a ratio of 1:1, the cells were cultured in a 5% CO₂ cell incubator at 37°C for 48 hours, and the supernatant containing SARS-CoV-2 pseudovirus was collected, filtered, and stored at -80°C for later