

Supplementary data (SD1)

Inhibitor synthesis and stability tests

Peptides and lipopeptides were obtained by solid phase synthesis using classical Fmoc/tBu methodology (25). The commercial sources of C16-OMe and AC16 were Sigma and Fluka, respectively. The Fmoc-amino acid-Wang resins, Fmoc-amino acids, 1-hydroxybenzotriazole (HOBt), *O*-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyl-uronium tetrafluoroborate (TBTU), diisopropylethylamine (DIEA) were purchased from Senn Chemicals or Novabiochem. The peptide chains were assembled using the *in situ* neutralization protocol described previously (25). The side chains of tyrosine, lysine, threonine, serine, aspartic and glutamic acids were protected by tBu (*tert*-butyl) or Boc groups (Boc, *tert*-butoxycarbonyl) as appropriate. Asparagine was protected by a trityl group. Each coupling step employed 3 equivalents of Fmoc-amino acid in the presence of 3 equivalents of HOBt and TBTU, and 9 equivalents of DIEA in DMF, at room temperature. Coupling was usually complete within 1 h, as determined by the 2,4,6-trinitrobenzenesulfonic acid (TNBSA) test. The Fmoc group was deprotected with 25 % (v/v) piperidine in DMF. The peptide sequences were capped with the acyl chloride $\text{CH}_3\text{-(CH}_2\text{)}_n\text{-CO-Cl}$ ($n = 4$ to 16) to obtain the lipopeptides. The peptides or lipopeptides were cleaved from the resin, and the side-chains deprotected, by treating with a mixture of 0.75 g crystalline phenol, 0.25 mL 1,2-ethanedithiol, 0.5 mL thioanisole, 0.5 mL deionized H_2O , and 10 mL trifluoroacetic acid (TFA) for 1.5 h. Crude peptides, which were generally >85% pure by analytical reverse phase HPLC, were purified by preparative RP-HPLC to final purities of >97%. The purification conditions were : (1) for peptides: linear gradient of acetonitrile (Carlo-Erba) in Ultra-High Quality water containing 0.1 % (v/v) trifluoroacetic acid (TFA, sequencing grade, Sigma) for 30 min at 4 mL/min with UV detection at 214 nm on an Interchrom UP5ODB.25M 5- μm column (250 x 10 mm); (2) for lipopeptides: linear gradient of acetonitrile (Carlo-Erba) in Ultra-High Quality water containing 0.1 % (v/v) TFA (sequencing grade, Sigma) for 40 min at 4 mL/min with UV detection at 214 nm on an Macherey-Nagel Nucleosil 300-7C4 column (250 x 10 mm). ^1H NMR spectra for peptides and lipopeptides were fully consistent with the assigned structures. Chemical structure of C16-YEL, C16-LEY and A16-T(0) and A16-T(4) are described in the Fig. SD2.