Combinatorial optimization of a CD4-mimetic miniprotein and co-crystal structures with HIV-1 gp120 envelope glycoprotein

Supplementary material

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Table S1. Surface complementarity of CD4 and CD4-mimetics with gp120

Complex (CD4 mimetic:gp120)*	Shape correlation, Sc
sCD4:core HXB2 gp120	0.716
sCD4:core YU2 gp120	0.674
sCD4M33(1):core YU2 gp120	0.769
sCD4M33(2):core YU2 gp120	0.769
[Phe^{23}]M33(1):core YU2 gp120	0.801
[Phe^{23}]M33(2):core YU2 gp120	0.798
CD4M47(1):core YU2 gp120	0.793
CD4M47(2):core YU2 gp120	0.769
[Phe^{23}]M47(1):core YU2 gp120	0.791
[Phe^{23}]M47(2):core YU2 gp120	0.773

* 'sCD4' in these complexes represents the N-terminal 2-domains of CD4, and the numbers in parentheses indicate molecule 1 or molecule 2 of the two molecules in the CD4-mimetic crystal lattice.

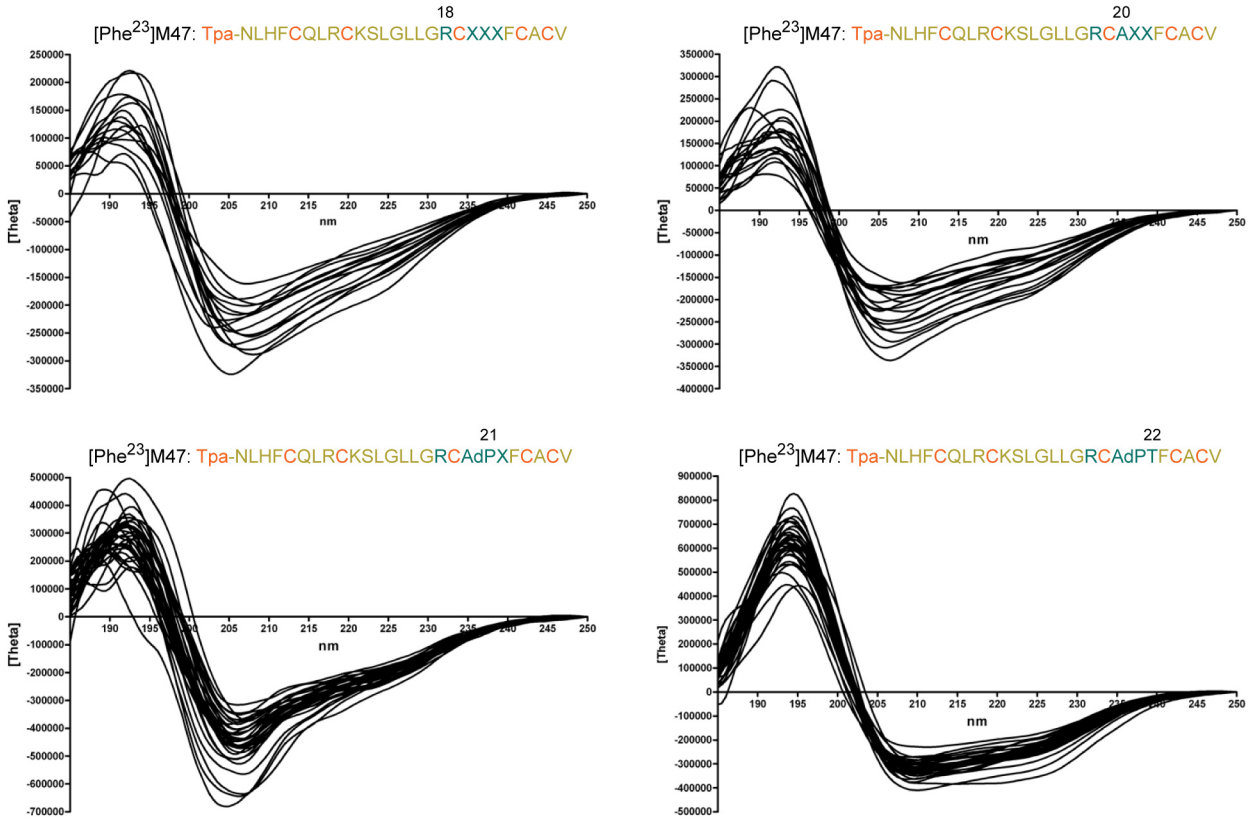

Figure S1. Circular dichroism (CD) spectra of libraries B1, B2, B3 and B4, for position 18, 20, 21 and 22, respectively, of CD4M33. CD spectra were recorded using a Jobin-Yvon CD6 dichrograph at 25°C in 2 mM sodium phosphate, pH 7.0, which were collected in a 0.1 cm quartz cuvette. Spectra of the far UV region (180-250 nm) were obtained with 0.5 nm steps using 200 µl of each sub-library sample at 50 µM in 2 mM phosphate buffer, pH 7.4, by accumulating 4 spectra with 0.5 seconds integration at every step.

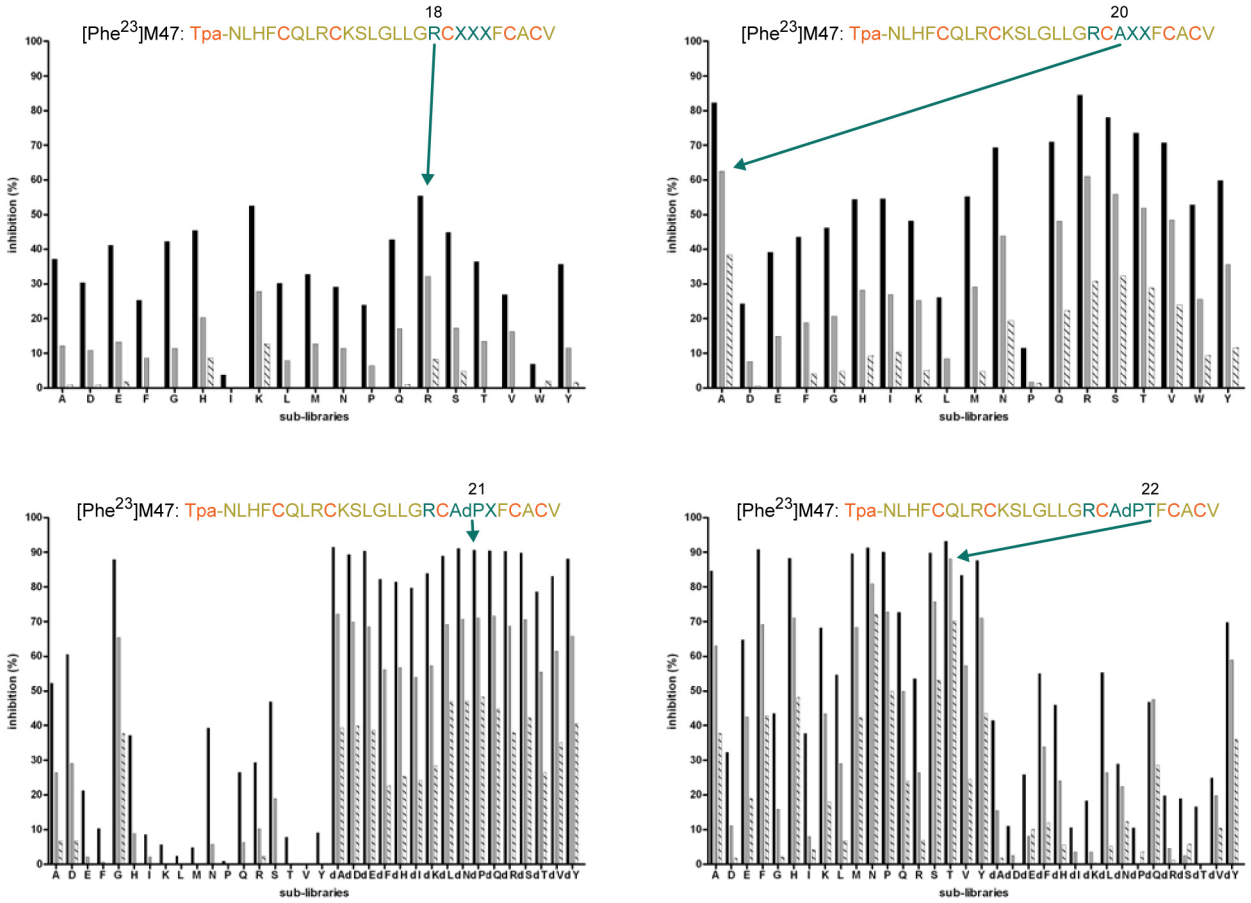

Figure S2. Combinatorial optimization of CD4M33: screening of the peptide libraries by means of competitive ELISA. Inhibition of soluble CD4 binding to $gp120_{HxB2}$ was measured by ELISA for combinatorial libraries B1, B2, B3 and B4, at positions 18, 20, 21 and 22, respectively, of CD4M33. All results are given as the percentage of inhibition of soluble CD4 binding (the mean of duplicate measurements is shown). Each sub-library was tested at three concentrations: 10^{-6} (black), 10^{-7} (grey) and 10^{-8} M (stripes). An arrow highlights the selected residue at each position (X represents an equimolar mixture of (L) amino acids at position 20 and of (L/D)-amino acids at position 21 and 22).