SUPPORTING INFORMATION

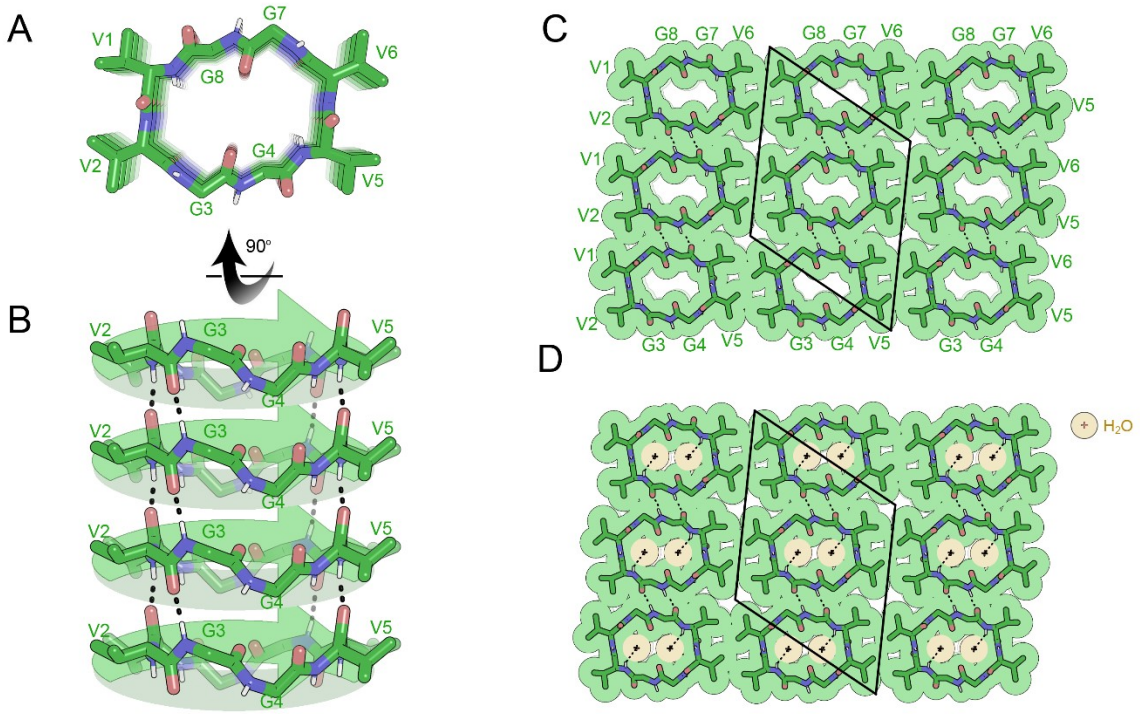

Figure S1. Figure 5. X-ray crystal structure of the self-sorted pleated β-sheet formed by the cyclic peptide VVGGVVGG and its enantiomer vvggvvgg in a mixture of hexafluoroisopropanol (HFIP) and water. (A) A view down the sheet hydrogen-bonding direction reveals pleating of the sheet. L-peptides are shown in green. (B) A view of the sheet face revealing in-register parallel stacking of valine residues. Backbone amides V1, V6, G3 and G7 are involved in stabilizing the pleated sheet. (C) Crystal packing viewed along the H-bonding direction shows that the pleated sheets mate face-to-face and are connected by hydrogen-bonding between glycine residues. The unit cell is outlined. (D) Gaps in the packing are filled by water molecules (yellow color).

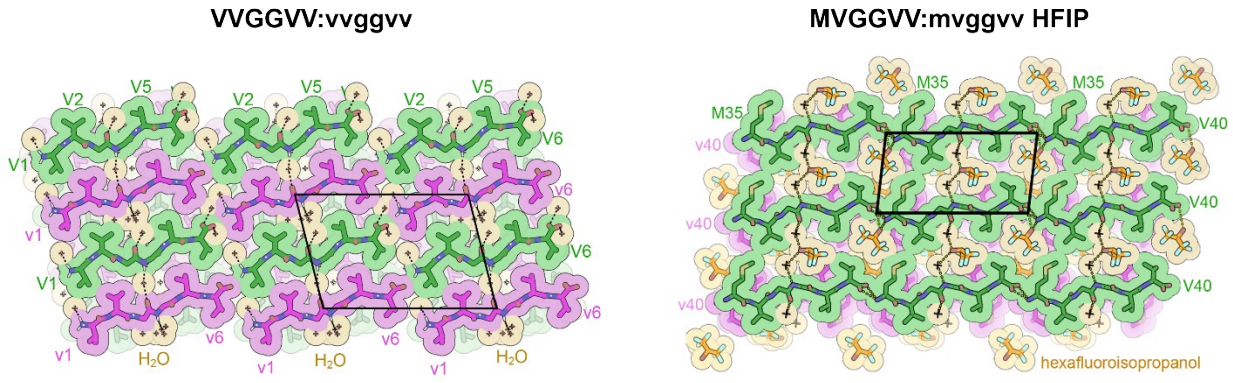

Figure S2. A comparison of the three-dimensional lattices of VVGGVV:vvggvv and MVGGVV:mvggvv HFIP.

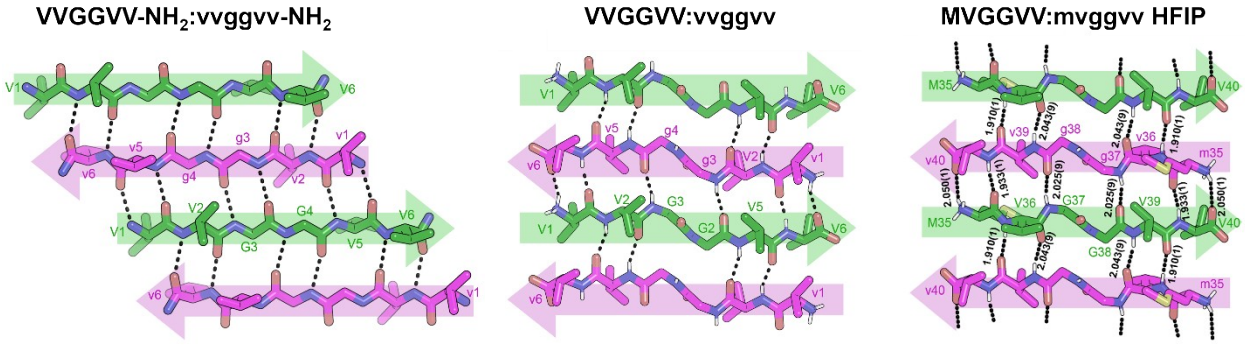

Figure S3. A comparison of the hydrogen bonding between individual strands of the rippled dimers of VVGGVV-NH_2:vvggvv-NH_2, VVGGVV:vvggvv and MVGGVV:mvggvv HFIP.

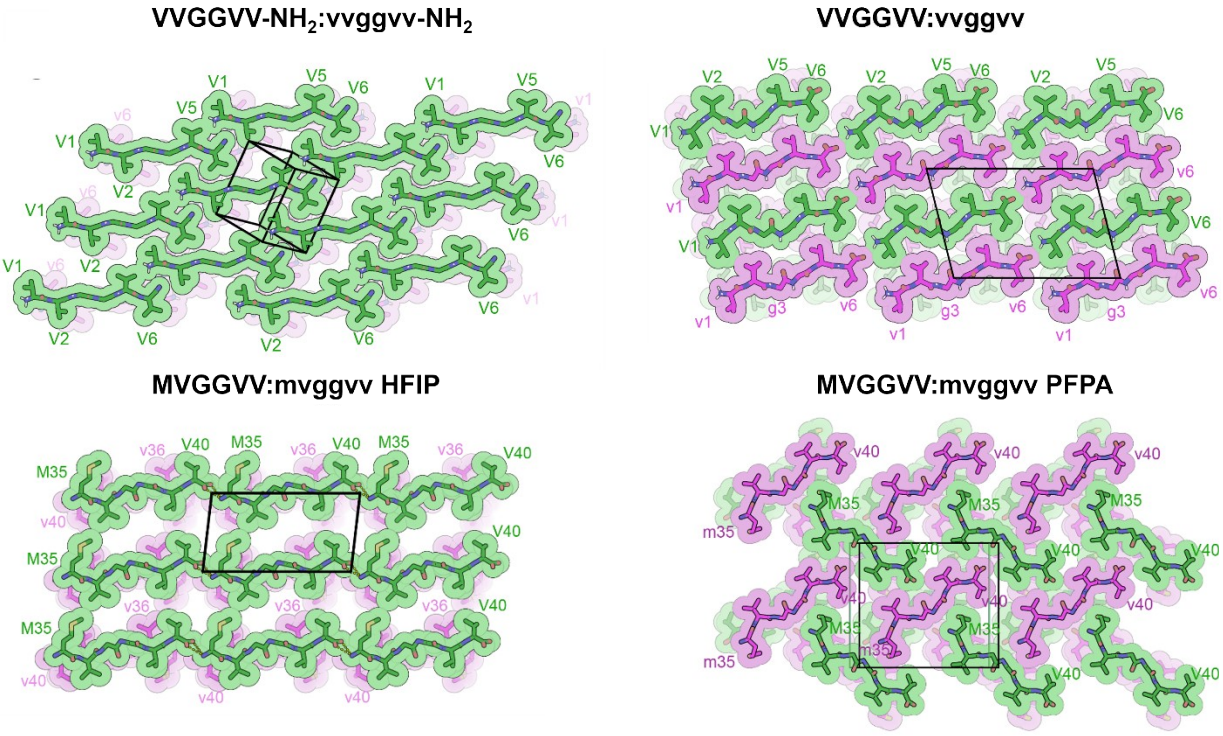

Figure S4. A comparison of the three-dimensional lattices of XVGGVV:xvggvv type structures.

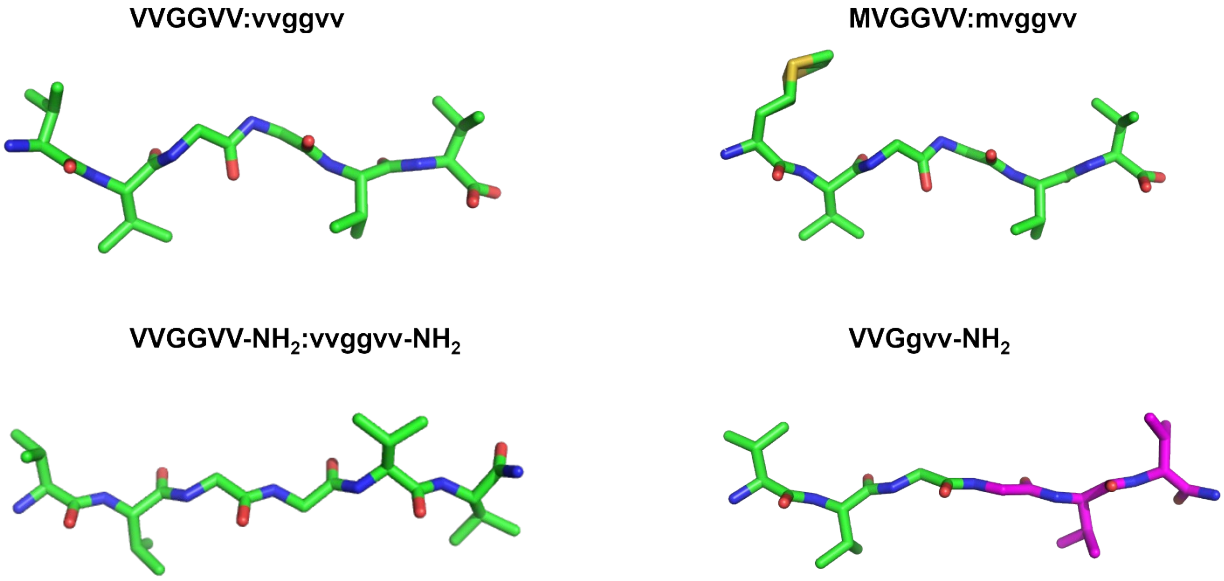

Figure S5. A comparison of the backbone configurations of XVGGVV:xvggvv type structures and VVGgvv-NH_2.

Material and Methods

Peptide Synthesis and Crystallization

Peptides were purchased from Anaspec or synthesized on Rink Amide or pre-loaded Wang resins by standard Fmoc based, solid-phase peptide chemistry. Syntheses were performed manually at 0.2 mM scale relative to resin loading. The peptides were cleaved and deprotected with a mixture consisting of trifluoroacetic acid (10 mL), tri-isopropylsilane (1 mL), and liquefied phenol (0.5 mL). The cleavage solution was added to the resins and agitated for 2 h. The solution was then evaporated to 2 mL under nitrogen gas, and the peptides precipitated with cold diethyl ether and centrifuged at 6000 rpm. The peptide pellet was washed with cold diethyl ether, dried, dissolved in 1:1 acetonitrile:water, flash frozen in liquid nitrogen, and lyophilized. No further purification was performed prior to crystallization.

VVGGVV:vvggvv

Stock solutions of the L-VVGGVV and D-vvggvv peptides in Nanopure water were prepared separately at concentrations of 2 mg/mL. Aliquots (100 ul) of each solution were combined and trifluoroethanol (20 uL) was subsequently added. Colorless needles grew over the course of several weeks.

QVGGVV:qvggvv

Stock solutions of the L-QVGGVV and D-qvggvv peptides in Nanopure water were prepared separately at concentrations of 2 mg/mL. Aliquots (100 ul) of each solution were combined and isopropanol (20 uL) was subsequently added. Colorless needles grew over the course of several weeks.

FVGGVV:mvggvv

Stock solutions of the L-FVGGVV and D-mvggvv peptides in Nanopure water were prepared separately at concentrations of 2 mg/mL. Aliquots (100 ul) of each solution were combined and hexafluoroisopropanol (20 uL) was subsequently added. Colorless needles grew over the course of several weeks.

VVGGVV-NH_2:vvggvv-NH_2

Stock solutions of the L-VVGGVV-NH_2 and D-vvggvv-NH_2 peptides in Nanopure water were prepared separately at concentrations of 7 mg/mL. Aliquots (100 ul) of each solution were combined and pentafluoropropionic acid (20 uL) was subsequently added. Colorless needles grew over the course of several weeks.

VVGgvv-NH_2

A solution of cyclic VVGGvvgg was prepared by dissolving 1 mg of the peptide in 1 mL of Nanopure water. 100 ul of HFIP was subsequently added. Colorless needles grew over the course of several weeks.

Cyclic VVGGVVGG/vvggvvgg

Solutions of cyclic L-VVGGVVGG and D-vvggvvgg were prepared separately by dissolving of 1 mg of each individual peptide in 100 ul of DMSO. The solutions were combined and 1 mL of Nanopure water was then added. Colorless needles grew over the course of several hours.

Cyclic VVGGvvgg

A solution of cyclic VVGGvvgg was prepared by dissolving 1 mg of the peptide in 100 ul of DMSO. 900 ul of Nanopure water was subsequently added. Colorless needles grew over the course of several hours.

Cyclic FKFGGfefgg

A solution of cyclic FKFGGfefgg was prepared by dissolving 1 mg of the peptide in 100 ul of DMSO. 900 ul of Nanopure water was subsequently added. Colorless needles grew over the course of several hours.

Crystallographic Structure Determination:

We used microfocus X-ray beam optics to measure crystal diffraction intensities from our crystals since they were needle-shaped, and less than 5 microns thick. Specifically, we used microfocus beamline 17-ID-2 of the National Synchrotron Light Source-II and beamline 24-ID-E of the Advanced Photon Source located at Argonne National Laboratory (Table S1). Crystals were cooled to a temperature of 100 K. Diffraction data were indexed, integrated, scaled, and merged using the programs XDS and XSCALE[1]. Data collection statistics are reported in Supplemental Table 1. Phases were obtained by direct methods using the program ShelxD (VVGGVV:vvggvv, VVGGVV-NH_2:vvggvv-NH_2, VVGgvv-NH_2, and FKFGGfefgg-cyclic)[2] and ShelxT (for VVGGvvgg-cyclic and VVGGVVGG-cyclic:vvggvvgg-cyclic)[3]. Model building was performed using the graphics program Coot[4]. Atomic refinement was performed using the program Phenix[5]. Subsequent rounds of refinement were performed using the program Refmac[6] in all cases except VVGGVV-NH_2:vvggvv-NH_2. Structures were illustrated using PyMOL[7].

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7. The PyMOL Molecular Graphics System, Version 1.2r3pre, Schrödinger, LLC.

Table S1. Data Collection and Refinement Statistics

Peptide(s)	**VVGGVV:vvggvv**	**VVGGVV-NH_2: vvggvv-NH_2**	**VVGgvv-NH_2**	**VVGGvvgg-cyclic**	**FKFGGfefgg-cyclic**	**VVGGVVGG-cyclic: vvggvvgg-cyclic**
Co-solvent	TFE	PFPA	HFIP	HFIP	DMSO	HFIP
Data Collection						
Beamline	NSLS-II FMX	NSLS-II FMX	NSLS-II FMX	NSLS-II FMX	NSLS-II FMX	APS 24-ID-E
Space group	P-1	P-1	$P2_12_12_1$	P-1	$P2_1$	C2
Resolution (Å)	1.10 (1.13-1.10) *	1.10 (1.13-1.10)	1.30 (1.37-1.30)	1.10 (1.15-1.10)	1.10 (1.13-1.10)	1.10 (1.19-1.10)
Unit cell dimensions: a,b,c (Å)	22.95, 15.49, 9.52	12.29, 12.46, 11.78	33.12, 44.27, 9.34	17.59, 10.36, 4.83	14.13, 29.32, 9.52	21.10, 4.81,18.87
Unit cell angles: α,β,γ (°)	88.67, 92.76, 103.95	76.00, 89.29, 88.49	90, 90, 90	98.28, 95.07, 100.37	90, 103.77, 90	90, 118.44, 90
Measured reflections	12396 (485)	3708 (139)	18712 (2641)	6235 (324)	26554 (973)	3361 (346)
Unique reflections	4615 (211)	2331(102)	3738 (531)	1113 (69)	2926 (156)	656 (73)
Overall completeness (%)	89.4 (56.4)	84.7 (47.4)	99.5 (99.8)	82.7 (32.1)	94.3 (72.2)	83.7 (43.7)
Overall redundancy	2.7 (2.8)	1.6 (1.4)	5.0 (5.0)	5.6 (4.7)	9.1 (6.2)	5.6 (4.7)
Overall R_{merge}	0.155 (0.280)	0.080 (0.427)	0.241 (1.986)	0.144 (0.469)	0.113 (0.350)	0.079 (0.280)
$CC_{1/2}$	98.1 (85.3)	99.2 (76.4)	99.5 (34.3)	99.1 (88.5)	99.6 (97.2)	99.6 (96.0)
Overall I/δ	4.0 (2.2)	3.8 (1.3)	3.7 (0.9)	7.1 (3.1)	10.7 (3.9)	12.1 (4.7)
Refinement						
R_{work} / R_{free}	0.151/ 0.167	0.179 / 0.178	0.181 / 0.188	0.093/ 0.112	0.129/0.136	0.133/0.150
RMSD bond length (Å)	0.013	0.012	0.019	0.012	0.017	0.008
RMSD angle (°)	2.0	1.9	1.8	1.5	2.0	0.9
Number of peptide atoms**	78	37	178	44	78	44
Number of water atoms	12	0	0	2	13	2
Number of other solvent atoms	0	10	10	0	4	0
Average B-factor of peptide ($Å^2$)	6.5	11.0	13.1	5.4	8.1	6.8
Average B-factor of water ($Å^2$)	10.1	N/A	N/A	8.7	23.7	18.3
Average B-factor other solvent ($Å^2$)	N/A	15.9	20.4	N/A	38.0	N/A
PDB ID code	9DYW	9DYX	9DYY	9DYZ	9DZ0	9DZ1

Peptide(s)	**QVGGVV:qvggvv**	**FVGGVV:mvggvv**
Co-solvent	iPrOH	HFIP
Data Collection		
Beamline	NSLS-II FMX	NSLS-II FMX
Space group	P-1	P1
Resolution (Å)	1.10 (1.13-1.10) *	1.10 (1.13-1.10)
Unit cell dimensions: a,b,c (Å)	23.72, 7.36, 9.24	20.92, 11.50, 9.39
Unit cell angles: α,β,γ (°)	91.19, 90.62, 98.09	97.22, 90.77, 94.60
Measured reflections	7911 (239)	13845 (587)
Unique reflections	2243 (94)	3263 (182)
Overall completeness (%)	89.4 (52.2)	92.7 (67.4)
Overall redundancy	3.5 (2.5)	4.2 (3.2)
Overall R_{merge}	0.169 (0.390)	0.130 (0.618)
$CC_{1/2}$	98.0 (84.3)	98.6 (62.9)
Overall I/δ	4.8 (2.5)	6.5 (2.1)
Refinement		
R_{work} / R_{free}	0.157/ 0.184	0.163 / 0.188
RMSD bond length (Å)	0.011	0.016
RMSD angle (°)	1.4	2.0
Number of peptide atoms**	53	79
Number of water atoms	4	3
Number of other solvent atoms	0	40
Average B-factor of peptide ($Å^2$)	7.7	7.1
Average B-factor of water ($Å^2$)	10.0	8.0
Average B-factor other solvent ($Å^2$)	N/A	12.4
PDB ID code	9N31	9N35

*Numbers in parentheses report statistics in highest resolution shell.

**Count excludes hydrogen atoms.

Computational details:

We conducted density functional theory (DFT) calculations using Vienna Ab-initio Software Package (VASP)[1] program with the projector-augmented wave (PAW) method.[2] The exchange-correlation interactions were described using the Perdew-Burke-Ernzerhof (PBE)[3] functional, with D3 correction[4] applied to account for dispersion forces. A kinetic energy cut-off 800 eV was used, and the reciprocal space was sampled using (3×3×5) Monkhorst-Pack mesh.[5] The convergence criterion of the self-consistent field iteration was set as 10^{-6} eV. Both the cell parameters and atomic positions were fully optimized until the force became less than 10^{-2} eV/Å each atom.

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