1	Supporting Informat	ion
2		
3	Prediction for 3D conformation of small pep	otide vaccine targeting Aβ
4	oligomers	
5		
6 7	Yvning Guan, Jinfei Mei, Xvzhi Gao, Chuanbo Wang, Mengke Jia, Saj and Hongqi Ai*	ijad Ahmad, Fahad Nouman Muhammad
8	School of Chemistry and Chemical Engineering, University of Jin	an, Jinan 250022, P.R. China
9	*To whom correspondence should be addressed, E-m	ail:
10		
11		
12	<u>Contents</u>	
13	MM/PBSA Calculational details	S2
14	Figures S1-S21	S3-S13
15	Tables S1-S29	S14-S19
16	References	S20
17		
18		
19		
20		
21		
22		
23		
24		
25		
26		
27		
28		
29		

MM/PBSA Calculational details 1

2 Molecular Mechanics/Poisson-Boltz Area (MM mann Surface /PBSA) is a widely used approach to estimate binding free energies by combining molecular mechanics and continuum 3 solvation models ¹⁻³. The binding free energy (ΔG_{bind}) between pentamer and vaccine in the present 4 study is calculated by the following equations ⁴. 5

$$6 \qquad \Delta G_{\rm bind} = \Delta G_{\rm complex} - \Delta G_{\rm rec} - \Delta G_{\rm lig}$$

7
$$\Delta G_{\text{bind}} = \Delta E_{\text{MM}} + \Delta G_{\text{solv}} - T\Delta S$$

8
$$\Delta E_{\rm MM} = \Delta E_{\rm VDW} + \Delta E_{\rm COU}$$

9
$$\Delta G_{\text{solv}} = \Delta G_{\text{PB}} + \Delta G_{\text{SA}} = \gamma \text{ SASA} + \beta$$

10
$$\Delta G_{\text{SA}} = \gamma \text{ SASA} + \beta$$

10

Where $\Delta G_{\text{complex}}$, ΔG_{rec} , ΔG_{lig} represent the free energy values of A β pentamer-vaccine complex, 11 receptor A β pentamer and ligand vaccine. ΔE_{MM} includes two terms, ΔE_{COU} for electrostatic 12 interaction and ΔE_{VDW} for van der Waals interaction. ΔG_{solv} refers to the total solvation free energy, 13 which includes polar solvation energy ΔG_{PB} and nonpolar solvation energy ΔG_{SA} . SASA refers to 14 the solvent accessible surface area with values of constants γ and β as 2.2 kJ/mol.nm² and 3.84 15 16 kJ/mol, respectively.

The ΔG_{bind} calculated above often overestimates the screening effect to some extent when 17 studying binding ability ⁵. Therefore, Huang et al. proposed a new correction method ⁶ to modify 18 19 the electrostatic and polar solvent terms, resulting in a highly applicable fitted equation, as shown below. The entropy contribution in the original method is usually obtained by normal mode analysis. 20 21 Drastically different from the widely employed but extremely expensive normal mode method for 22 calculating entropy change in protein-ligand binding, the calculation of the interaction entropy simply involves the natural log of an ensemble average, which can be readily extracted along with 23 24 MD simulation without extra computational cost. That is, the fitting method is based on the 25 interaction energy between ligand and receptor, termed interaction entropy⁷.

 $\Delta G_{\rm fittd} = 0.0542 \ (\Delta E_{\rm COU} + \Delta G_{\rm PB}) + 0.14852 \ \Delta E_{\rm VDW} + 0.05584 \ \Delta G_{\rm SA} + 0.11351 \ (-T\Delta S) - 4.77148 \ \Delta G_{\rm Fittd} = 0.0542 \ (\Delta E_{\rm COU} + \Delta G_{\rm PB}) + 0.14852 \ \Delta E_{\rm VDW} + 0.05584 \ \Delta G_{\rm SA} + 0.11351 \ (-T\Delta S) - 4.77148 \ \Delta G_{\rm Fittd} = 0.0542 \ (\Delta E_{\rm COU} + \Delta G_{\rm PB}) + 0.14852 \ \Delta E_{\rm VDW} + 0.05584 \ \Delta G_{\rm SA} + 0.11351 \ (-T\Delta S) - 4.77148 \ \Delta G_{\rm Fittd} = 0.0542 \ (\Delta E_{\rm COU} + \Delta G_{\rm PB}) + 0.14852 \ \Delta E_{\rm VDW} + 0.05584 \ \Delta G_{\rm SA} + 0.11351 \ (-T\Delta S) - 4.77148 \ \Delta G_{\rm Fittd} = 0.0542 \ (\Delta E_{\rm COU} + \Delta G_{\rm Fittd} + 0.05584 \ \Delta G_{\rm SA} + 0.01351 \ (-T\Delta S) - 4.77148 \ \Delta G_{\rm SA} + 0.01351 \ (-T\Delta S) + 0.01351 \ (-T\Delta S)$ 26

 ΔG_{fittd} stands for the binding free energy value after fitting. For each complex, the total 27 binding free energy is obtained by summing up the contributions of each residue in the receptor 28 (pentamer) and the ligand (vaccine) to the free energy^{8, 9}. 29





Figure S3 Refined 3D structure from the Galaxy refine web server (a) and structure validation (b, c) of model2A β_{1-14} . (b) ProSA validation of predicted structure with Z score of -1.23, (c) Ramachandran plot analysis indicates 100% of residues are present in the most favored regions, 0% of residues are found in the allowed regions.



Figure S4 Refined 3D structure from the Galaxy refine web server (a) and structure validation (b, c) of model3Aβ₁₋₁₄. (b) ProSA validation of predicted structure with Z score of -1.99, (c) Ramachandran plot analysis indicates 100% of residues are present in the most favored regions, 0% of residues are found in the allowed regions.



8Figure S6 Docked complexes of TAPAS and modeli'A $β_{1-14}$ (i'=1 and 2) vaccines to Aβ receptors. (a) and (b) are9docked complexes of TAPAS docked with receptors A $β_{1-42}$ and A $β_{4-42}$, respectively; (c) and (d) stand for the10docked complexes of model1A $β_{1-14}$ docked with the two receptors, respectively; (e) and (f) refer to the docked11complexes of model2A $β_{1-14}$ docked with two receptors, respectively. TAPAS, model1A $β_{1-14}$, model2A $β_{1-14}$, A $β_{1-42}$ 12and A $β_{4-42}$ are represented in magenta, red, blue, slate and cyan, respectively.13











Figure S12 Structure validation of model2Aβ₁₋₁₅. (a) ProSA validation of predicted structure with Z score of -0.14, (b) Ramachandran plot analysis indicates 83.3% of residues are present in the most favored regions, 16.7% of residues are found in the allowed regions.



Figure S13 Structure validation of model3A β_{1-15} . (a) ProSA validation of predicted structure with Z score of - 0.77, (b) Ramachandran plot analysis indicates 100% of residues are present in the most favored regions, 0% of residues are found in the allowed regions.



Figure S14 Top 3 positions of two Aβ pentamers (fAβ and tAβ) for vaccines (M'1 and M'3) docking, in
which the three top poses of the vaccine are highlighted in red for Top 1, green for Top 2, and blue for Top 3,
respectively.





Figure S16 SASA results of the four complexes.





Figure S18 Interaction residues and corresponding distances on the vaccine-receptor contact interface. The
 symbols of A-E in parenthesis indicate the serial number of five chains in the Aβ pentameric receptors. F in the
 parenthesis stands for the vaccine. Hydrogen bond and salt bridges are represented by dotted lines in green and red,
 respectively.



2	
3	Figure S19 Fitted 3D conformations for model1A β_{1-15} and model3A β_{1-15} , where model1A β_{1-15} and
4	model3A β_{1-15} are represented in red and blue, respectively, and the labels of residues 1-15 are represented in
5	green.
6	



7	
~	

- Figure S20 Fitted 3D conformation for model j'A β_{1-15} (j'=1 and 3) and TAPAS. TAPAS and model j'A β_{1-15} are represented in magenta, red and blue, respectively.

Figure S21 The 3D structure of the free TAPAS

	immunogeni	icity	antigenicity	allergen		toxic
	0.14		VaxiJen 2.0 0.61 > 0.40	Non-allergen	ic	non-toxic
			Table S2 Physicocl	hemical properties of $A\beta_{1-14}$		
8	Number of amino acids	Molecular weight	Theoretical pI	Estimated half-life	Aliphatic index	GRAVY
	14	1676.76	5.73	 1.1 hours (mammalian reticulocytes, in vitro). 3 min (yeast, in vivo). >10 hours (Escherichia coli, in vivo). 	7.14	-1.25
	Table S3	Parameters after	fitting model $iA\beta_{1-1}$	$_4$ (<i>i</i> =1, 2 and 3) structure to the	3D structure	of TAPAS
	Model		RMSD(Å)	TM-score		Identity
	1		1.36	0.78		92%
						020/
	2		1.20	0.81		92%
	2 3		1.20 2.93	0.81 0.53		92% 8%
	2 3		1.20 2.93	0.81 0.53		92% 8%
	2 3	Tabl	1.20 2.93 e S4 Cluster scores c	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp	lex	92% 8%
	2 3 Cluster	Tabl	1.20 2.93 e S4 Cluster scores of lembers	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative	lex Weigl	92% 8%
	2 3 Cluster 1	Tabl M	1.20 2.93 e S4 Cluster scores of lembers 213	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center	lex Weigl -7	92% 8% nted Score 710.10
	2 3 Cluster 1	Tabl M	1.20 2.93 e S4 Cluster scores of lembers 213	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy	lex Weigl -7 -8	92% 8% nted Score 710.10 817.90 734.90
	2 3 Cluster 1 2	Tabl M	1.20 2.93 e S4 Cluster scores c lembers 213 184	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy	lex Weigl -7 -8 -7 -7	92% 8% nted Score 710.10 817.90 734.90 795.40
	2 3 Cluster 1 2	Tabl M	1.20 2.93 e S4 Cluster scores of lembers 213 184	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center	lex Weigl -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7	92% 8% nted Score 710.10 817.90 734.90 795.40 795.40
	2 3 Cluster 1 2 3	Tabl M	1.20 2.93 e S4 Cluster scores of lembers 213 184 180	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy	lex 	92% 8% Atted Score 710.10 817.90 734.90 795.40 793.20 793.20
	2 3 Cluster 1 2 3	Tabl M	1.20 2.93 e S4 Cluster scores of lembers 213 184 180	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy	lex Weig -7 -7 -7 -7 -7	92% 8% nted Score 710.10 817.90 734.90 795.40 793.20 793.20
	2 3 Cluster 1 2 3 (Cluster	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers	0.81 0.53 of docked TAPAS-Aβ _{1.42} comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy Center Lowest Energy	lex Weigl -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7	92% 8% hted Score 710.10 817.90 734.90 795.40 793.20 793.20 293.20
	2 3 Cluster 1 2 3 3	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy of docked TAPAS-Aβ ₄₋₄₂ comp Representative Center	lex Weigl -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7	92% 8% ated Score 710.10 817.90 734.90 793.20 793.20 793.20 rted Score 808.90
	2 3 Cluster 1 2 3 3 Cluster 1	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers 273	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy of docked TAPAS-Aβ ₄₋₄₂ comp Representative Center Lowest Energy	lex Weigl -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7 -7	92% 8% hted Score 710.10 817.90 734.90 795.40 793.20 793.20 793.20 hted Score 808.90 019.40
	2 3 Cluster 1 2 3 3 Cluster 1	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers 273	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy of docked TAPAS-Aβ ₄₋₄₂ comp Representative Center Lowest Energy Center Center	lex Weigl -7 -7 -7 -7 -7 -7 -7 -7 -7 -7	92% 8% ated Score 710.10 317.90 734.90 793.20 793.20 793.20 ated Score 308.90 919.40 776.60
	2 3 Cluster 1 2 3 Cluster 1 2	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers 273 235	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy of docked TAPAS-Aβ ₄₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy Center Lowest Energy	lex Weigl 	92% 8% hted Score 710.10 317.90 734.90 795.40 793.20 793.20 793.20 10 10 10 10 10 10 10 10 10 1
	2 3 Cluster 1 2 3 Cluster 1 2 3	Tabl M Tabl	1.20 2.93 e S4 Cluster scores of lembers 213 184 180 e S5 Cluster scores of lembers 273 235 158	0.81 0.53 of docked TAPAS-Aβ ₁₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy of docked TAPAS-Aβ ₄₋₄₂ comp Representative Center Lowest Energy Center Lowest Energy Center Lowest Energy Center Lowest Energy Center Lowest Energy Center	lex Weigl 	92% 8% hted Score 710.10 317.90 734.90 795.40 793.20 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.40 795.20 795.20 795.20

Table S6 Cluster scores of docked M1fA β complex

Cluster	Members	Representative	Weighted Score
1	412	Center	-663.90
I	415	Lowest Energy	-774.90
2	125	Center	-637.20
Z	125	Lowest Energy	-692.90
2	06	Center	-684.10
3	90	Lowest Energy	-684.10

Table S7 Cluster scores of docked M1tA β complex

 Cluster	Members	Representative	Weighted Score
1	210	Center	-610.80
1	312	Lowest Energy	-717.10
2	275	Center	-609.50
Z	275	Lowest Energy	-712.70
2	220	Center	-621.00
3	229	Lowest Energy	-702.20

	Table S8 Cluster s	cores of docked M2fA β complex	
Cluster	Members	Representative	Weighted Score
1	215	Center	-635.90
I	213	Lowest Energy	-678.70
2	145	Center	-583.40
2	143	Lowest Energy	-652.40
2	127	Center	-562.80
	15/	Lowest Energy	-635.80

	Table S9 Cluster sco	res of docked M2tAβ complex	
Cluster	Members	Representative	Weighted Score
1	212	Center	-610.80
1	312	Lowest Energy	-717.10
_		Center	-609.50

Lowest Energy

Center

Lowest Energy

-712.70

-621.00

-702.20

0
ð

Table S10 Contribution of each residue in the $A\beta_{1.42}$ when binding to TAPAS

Residue name	Num.	probability
VAL	30	0.37
ALA	16	0.20
ILE	11	0.14
GLY	9	0.11
LEU	7	0.09
ASP	5	0.06
GLU	3	0.04

Residue name	Num.	probability
 HIS	22	0.33
ASP	11	0.17
PHE	10	0.15
CVS	8	0.12
GLV	5	0.02
	5	0.08
	2	0.08
AKU	3	0.04
SEK	Ζ	0.03
Table S12 Contribution	on of each residue in the $A\beta_{4-42}$ wh	en binding to TAPAS
Residue name	Num.	probability
PHE	23	0.20
ILE	19	0.16
VAL	16	0.14
HIS	14	0.12
ASP		0.08
GLN	8	0.07
LVS	7	0.07
ΔΙΔ	6	0.00
TVD	Л	0.05
	-+ /	0.05
ULI	4	0.03
CED		0.03
SER	3	0.03
SER ARG GLU Table S13 Contribution Residue name	of each residue in the TAPAS who	en binding to the A $\beta_{4.42}$
SER ARG GLU Table S13 Contribution Residue name	of each residue in the TAPAS when Num.	$\frac{0.03}{0.02}$ en binding to the A β_{4-42} probability 0.26
SER ARG GLU Table S13 Contribution Residue name HIS PHF	of each residue in the TAPAS who Num.	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR	of each residue in the TAPAS who Num. 24 15 14	$0.02 \\ 0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP	of each residue in the TAPAS who Num. 24 15 14 11	$ \begin{array}{r} 0.03 \\ 0.02 \\ 0.01 \end{array} $ en binding to the A $\beta_{4.42}$ probability $ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \end{array} $
 SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SEP	s 2 1 1 of each residue in the TAPAS who Num. 24 15 14 11 9	$ \begin{array}{r} 0.02 \\ 0.01 \\ en binding to the A \beta_{4.42} \\ \hline $
 SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU	5 2 1 1 0 of each residue in the TAPAS who Num. 24 15 14 11 9 6	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06$
 SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLV	5 2 1 1 0 of each residue in the TAPAS who Num. 24 15 14 11 9 6 5	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA	5 2 1 1 1 1 1 1 1 1 2 4 15 14 11 9 6 5 4	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS	3 2 1 1 0 of each residue in the TAPAS who Num. 24 15 14 11 9 6 5 4 2	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.02$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS APG	3 2 1 1 of each residue in the TAPAS who Num. 24 15 14 11 9 6 5 4 3 2	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG	3 2 1 n of each residue in the TAPAS who Num. 24 15 14 11 9 6 5 4 3 2	$\begin{array}{r} 0.03 \\ 0.02 \\ 0.01 \end{array}$ en binding to the A $\beta_{4.42}$ probability $\begin{array}{r} 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG	$\frac{3}{2}$ 1 of each residue in the TAPAS who Num. $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the AB, to when	$0.02 \\ 0.01$ en binding to the A $\beta_{4.42}$ probability $0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02$ binding to model2A $\beta_{1.14}$
 SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name	$\frac{3}{2}$ 1 of each residue in the TAPAS who Num. $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the A $\beta_{1.42}$ when Num.	$0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.02 \\ 0.02 \\ 0.02 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.01 \\ 0.01 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.02 \\ 0.01 \\ 0.02 \\ $
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name	$\frac{3}{2}$ 1 of each residue in the TAPAS when $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the A β_{1-42} when $\frac{125}{2}$	$0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.02 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ 0.02 \\ 0.04 \\ 0.03 \\ 0.02 \\ $
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE	$\frac{3}{2}$ 1 of each residue in the TAPAS when $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the A β_{1-42} when $\frac{125}{23}$	$0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.01 \\ 0.02 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ $
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET	$\frac{3}{2}$ 1 of each residue in the TAPAS when $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the A β_{1-42} when $\frac{11}{25}$ 23	$\begin{array}{r} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1.14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ \hline \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS	$\frac{3}{2}$ 1 of each residue in the TAPAS when $\frac{24}{15}$ 14 11 9 6 5 4 3 2 of each residue in the A β_{1-42} when $\frac{11}{25}$ 23 11 10	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ \hline \\ binding to model2 A \beta_{1.14} \\ \hline \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ \hline \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS DUT	$\begin{array}{r} & \begin{array}{c} & \begin{array}{c} & \begin{array}{c} & \begin{array}{c} & \\ & \begin{array}{c} & \\ \end{array} \\ \hline $ \\ \hline \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \\ \hline \end{array} \\ \hline \\ \hline \\ \hline \end{array} \\ \hline \\ \hline \\ \hline \end{array} \\ \hline \end{array} \\ \hline \\ \hline \\ \hline \end{array} \\ \hline \end{array} \\ \hline \end{array} \\ \hline \\ \hline \end{array} \\ \hline \\ \hline \end{array} \\ \hline \\ \hline \end{array} \\ \hline \\ \\ \hline \\ \hline } \\ \\ } \\ } \\ } \\ } \\ } \\ } \\ } \\ } \\ } }	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1-14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ 0.02 \\ \hline \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS PHE CIV	$ \begin{array}{r} 3 \\ 2 \\ 1 1 0 of each residue in the TAPAS whomology 1 1 1 $	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1-14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ 0.09 \\ 0.02 \\ \hline \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS PHE GLY	$ \begin{array}{r} 3 \\ 2 \\ 1 \end{array} $ 1 of each residue in the TAPAS whom Num. 24 15 14 11 9 6 5 4 3 2 of each residue in the Aβ ₁₋₄₂ when Num. 25 23 11 9 6 5 4 3 2 0f each residue in the Aβ ₁₋₄₂ when 10 9 8 6 5 23 11 10 9 8 6 11 10 11	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1-14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ 0.09 \\ 0.08 \\ \hline \\ $
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS PHE GLY SER	$ \begin{array}{r} 3 \\ 2 \\ 1 \end{array} $ of each residue in the TAPAS when	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1-14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ 0.09 \\ 0.08 \\ 0.06 \\ \hline \end{array}$
SER ARG GLU Table S13 Contribution Residue name HIS PHE TYR ASP SER GLU GLY ALA CYS ARG Table S14 Contribution Residue name ILE VAL MET LYS PHE GLY SER ASN	$ \begin{array}{r} 3 \\ 2 \\ 1 0 of each residue in the TAPAS when $	$\begin{array}{c} 0.03 \\ 0.02 \\ 0.01 \\ \hline \\ \hline \\ en binding to the A \beta_{4.42} \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.16 \\ 0.15 \\ 0.12 \\ 0.10 \\ 0.06 \\ 0.05 \\ 0.04 \\ 0.03 \\ 0.02 \\ \hline \\ \hline \\ binding to model2 A \beta_{1-14} \\ \hline \\ \hline \\ \hline \\ probability \\ \hline \\ 0.26 \\ 0.23 \\ 0.11 \\ 0.10 \\ 0.09 \\ 0.08 \\ 0.06 \\ 0.05 \\ \hline \\ \end{array}$

Resi	due nume	Num.		probabil	ity
	ASP	16		0.21	
	HSE	15		0.19	
	TYR	15		0.19	
	SER	9		0.12	
	GLU	5		0.06	
	ALA	5		0.06	
	ARG	5		0.06	
	GLY	4		0.05	
	CYS	3		0.04	
	PHE	1		0.01	
1	able S16 Contri	oution of each residue in the A	$A\beta_{4-42}$ when binding t	to model2A β_{1-1}	4
Resi	due name	Num.		probabil	ity
	VAL	20		0.19	
	ILE	18		0.17	
	PHE	16		0.15	
	HIS	16		0.15	
		10		0.15	
		1		0.07	
	GLN	6		0.06	
	GLY	5		0.05	
	GLU	4		0.04	
	ALA	4		0.04	
	ASP	3		0.03	
	ARG	3		0.03	
	LEU	1		0.01	
	SER	1		0.01	
Ta Resi	ble S17 Contribu due name	tion of each residue in the mo Num.	$del2A\beta_{1-14}$ when bin	iding to the Aβ. probabil	1-42 ity
Ta Resi	ble S17 Contribu due name HIS	tion of each residue in the mo Num. 17	odel2A β_{1-14} when bin	iding to the Aβ. probabil 0.22	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR	tion of each residue in the mo Num. 17 15	odel2A β_{1-14} when bin	ding to the Aβ. probabil 0.22 0.19	4-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE	tion of each residue in the mo Num. 17 15 12	odel2A β_{1-14} when bin	ding to the Aβ. probabil 0.22 0.19 0.15	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP	tion of each residue in the mo Num. 17 15 12 8	odel2Aβ ₁₋₁₄ when bin	ding to the Aβ. probabil 0.22 0.19 0.15 0.10	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER	tion of each residue in the mo Num. 17 15 12 8 8 8	odel2Aβ ₁₋₁₄ when bin	dding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER GLY	tion of each residue in the mo Num. 17 15 12 8 8 5	odel2Aβ ₁₋₁₄ when bin	ding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5	odel2Aβ ₁₋₁₄ when bin	ding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06	ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5 4	odel2Aβ ₁₋₁₄ when bin	ading to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05	1-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5 5 4 4 4	odel2Aβ ₁₋₁₄ when bin	ding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05 0.05	4-42 ity
Ta Resi	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5 5 4 4 4 18 Immunogenicity, antigenio	odel2Aβ ₁₋₁₄ when bin	ding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05 0.05 y of Aβ ₁₋₁₅	1-42 ity
Ta Resi immunog	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S genicity	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5 5 4 4 4 18 Immunogenicity, antigenic antigenicity	odel2Aβ ₁₋₁₄ when bin city, allergen, toxicit allerge	ading to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05 0.05 y of Aβ ₁₋₁₅	toxic
Ta Resi immunog	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S genicity	tion of each residue in the mo Num. 17 15 12 8 8 5 5 5 4 4 4 18 Immunogenicity, antigenic antigenicity VaxiJen 2.0	odel2Aβ ₁₋₁₄ when bin	ading to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05 0.05 y of Aβ ₁₋₁₅	toxic
Ta Resi immunog	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S genicity	tion of each residue in the mo Num. 17 15 12 8 8 5 5 4 4 4 18 Immunogenicity, antigenic antigenicity VaxiJen 2.0 0.56 > 0.4	odel2Aβ ₁₋₁₄ when bin city, allergen, toxicit allerge non-aller	ding to the Aβ. probabil 0.22 0.19 0.15 0.10 0.10 0.06 0.06 0.05 0.05 y of Aβ ₁₋₁₅ en	toxic
Ta Resi immunog 0.30	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S genicity	tion of each residue in the mo Num. 17 15 12 8 8 5 5 4 4 4 18 Immunogenicity, antigenic antigenicity VaxiJen 2.0 0.56 > 0.4 Table S19 Physicochemica	city, allergen, toxicit allerge non-aller	ading to the Aβ. probabil 0.22 0.19 0.15 0.10 0.06 0.06 0.05 0.05 y of Aβ ₁₋₁₅ en	toxic
Ta Resi immunog 0.30	ble S17 Contribu due name HIS TYR PHE ASP SER GLY GLU CYS ARG Table S genicity 4 Molecular weight	tion of each residue in the mo Num. 17 15 12 8 8 8 5 5 4 4 4 18 Immunogenicity, antigenic antigenicity VaxiJen 2.0 0.56 > 0.4 Table S19 Physicochemica Theoretical pI	odel2Aβ ₁₋₁₄ when bin city, allergen, toxicit allerge non-aller l properties of Aβ ₁₋₁₂ Estimated half-life	$ding to the A\beta.$ probabil 0.22 0.19 0.15 0.10 0.06 0.06 0.05 0.05 y of A β_{1-15} en rgen	toxic Non-Toxin

Table S15 Contribution of each residue in the model2A $\beta_{1\text{-}14}$ when binding to the A $\beta_{1\text{-}42}$

Table S20 Cluster scores of docked vaccine $M'1fA\beta$ complex

Cluster	Members	Representative	Weighted Score
1	500	Center	-636.60
I	288	Lowest Energy	-749.00
2	156	Center	-647.60
2		Lowest Energy	-719.70
		Center	-660.90
3	50	Lowest Energy	-636.60

	Table S21 Cluster scores o	f docked vaccine M'1tAβ complex	i
ster	Members	Representative	We

 Cluster	Members	Representative	Weighted Score
1	267	Center	-711.00
1		Lowest Energy	-780.70
2	189	Center	-701.00
2		Lowest Energy	-813.90
2	105	Center	-703.30
3	185	Lowest Energy	-853.90

	Table S22 Cluster scores of docked vaccine M'3fA β complex			
Cluster	Members	Representative	Weighted Score	
1	270	Center	-591.80	
1	379	Lowest Energy	-690.30	
2	210	Center	-590.50	
2	318	Lowest Energy	-748.60	
2	100	Center	-586.40	
3	109	Lowest Energy	-661.40	

Table S23 Cluster scores of docked vaccine M'3tA β complex

Cluster	Members	Representative	Weighted Score
1	455	Center	-641.00
1	435	Lowest Energy	-793.30
2	2/5	Center	-687.90
2	265	Lowest Energy	-779.20
		Center	-669.00
3	175	Lowest Energy	-704.80

Table S24 Contribution o	f each resid	due in the A	β_{1-42} when bi	inding to model	$A\beta_{1-15}$
--------------------------	--------------	--------------	------------------------	-----------------	-----------------

Residue name	Num.	probability
VAL	25	0.29
LYS	17	0.20
ILE	10	0.12
MET	9	0.11
PHE	9	0.11
GLY	8	0.09
SER	3	0.03
HIS	3	0.03
ALA	1	0.01

_		111	5 8	
	Residue name	Num.	pro	bability
	HIS	15		0.20
	TYR	13		0.18
	VAL	8		0.11
	ASP	7		0.10
	GLN	7		0.10
	SER	6		0.08
	PHF	ő		0.08
	GLV	4		0.00
		3		0.03
		2		0.07
	ARG	2		0.03
_	Table S26 Contribu	tion of each residue in the $A\beta_{4-42}$ whe	n binding to model1.	Αβ ₁₋₁₅
	Residue name	Num.	pro	bability
	HIS	21		0.19
	PHE	20		0.18
	ARG	16		0.15
	ILE	12		0.11
	VAL	11		0.10
	ALA	6		0.06
	GLN	6		0.06
	ASP	Š		0.05
	SED	5		0.05
	I VS	5		0.05
		5		0.03
	UL I	I		0.01
	Table S27 Contribution	on of each residue in the model1A β_{1-1}	5 when binding to the	e Aβ ₄₋₄₂
	Residue name	Num.	pro	bability
	HIS	15		0.20
	TYR	13		0.18
	VAL	8		0.11
	ASP	7		0.10
	GLN	7		0.10
	SER	6		0.08
	PHE	6		0.08
	GLV	4		0.00
		4		0.05
		2		0.05
	ALA	3		0.05 0.04
	ALA GLU	3 2		0.05 0.04 0.03
	ALA GLU ARG	3 2 2		0.05 0.04 0.03 0.03
	ALA GLU ARG	3 2 2		0.05 0.04 0.03 0.03
	ALA GLU ARG Table S28 Parat	3 2 2	el1A β_{1-15} and model ²	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅
_	ALA GLU ARG Table S28 Parat RMSD	3 2 2 neters of fitted 3D structures for mode TM-score	el1A β_{1-15} and model2	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity
	ALA GLU ARG Table S28 Parar RMSD 0.71	neters of fitted 3D structures for mode TM-score 0.87	el1Aβ ₁₋₁₅ and model3	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100%
	ALA GLU ARG Table S28 Parar RMSD 0.71	aneters of fitted 3D structures for mode TM-score 0.87	el1A β_{1-15} and model:	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100%
	ALA GLU ARG Table S28 Paran RMSD 0.71 Table S29 Paramet	3 2 2 neters of fitted 3D structures for mode TM-score 0.87 ers of fitted 3D structures for modelj'.	el1Aβ ₁₋₁₅ and model? e Aβ ₁₋₁₅ (<i>j</i> '=1 and 3) an	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100%
	ALA GLU ARG Table S28 Parar RMSD 0.71 Table S29 Paramet Model	3 2 2 neters of fitted 3D structures for model TM-score 0.87 ers of fitted 3D structures for modelj', RMSD	el1A β_{1-15} and model? e A β_{1-15} (j'=1 and 3) an TM-score	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity
	ALA GLU ARG Table S28 Parar RMSD 0.71 Table S29 Paramet Model Model model1Aβ ₁₋₁₅	a neters of fitted 3D structures for model TM-score 0.87 ers of fitted 3D structures for modelj'. RMSD 1.11	el1A β_{1-15} and model? e A β_{1-15} (j'=1 and 3) an TM-score 0.65	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity 85%
	ALA GLU ARG Table S28 Parar RMSD 0.71 0.71 Table S29 Paramet Model Model model1Aβ ₁₋₁₅ model3Aβ ₁₋₁₅	a a a a a a a a a a a a a a	el1Aβ ₁₋₁₅ and model2 e Aβ ₁₋₁₅ ($j'=1$ and 3) an TM-score 0.65 0.59	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity 85% 85%
	ALA GLU ARG Table S28 Paran RMSD 0.71 Table S29 Paramet Model model1Aβ ₁₋₁₅ model3Aβ ₁₋₁₅	a a a a a a a a a a a a a a	el1A β_{1-15} and model? e A β_{1-15} (<i>j</i> '=1 and 3) an TM-score 0.65 0.59	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity 85% 85%
_ _ _ _	ALA GLU ARG Table S28 Paran RMSD 0.71 Table S29 Paramet Model model1Aβ ₁₋₁₅ model3Aβ ₁₋₁₅	a a a a a a a a a a a a a a	el1Aβ ₁₋₁₅ and model2 e Aβ ₁₋₁₅ ($j'=1$ and 3) an TM-score 0.65 0.59	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity 85% 85%
_ _ _ _	ALA GLU ARG Table S28 Paran RMSD 0.71 Table S29 Paramet Model model1Aβ ₁₋₁₅ model3Aβ ₁₋₁₅	a a a a a a a a a a a a a a	el1Aβ ₁₋₁₅ and model2 e Aβ ₁₋₁₅ ($j'=1$ and 3) an TM-score 0.65 0.59	0.05 0.04 0.03 0.03 3Aβ ₁₋₁₅ Identity 100% d TAPAS Identity 85% 85%

1		References
2	1.	M. U. Rahman, H. Liu, A. Wadood and H. F. Chen, <i>Mol Biosyst</i> , 2016, 12 , 3280-3293.
3	2.	H. Yu, Y. Fang, X. Lu, Y. Liu and H. Zhang, Chem. Biol. Drug. Des., 2014, 83, 89-105.
4 5	3.	T. D. Martin, E. H. Hill, D. G. Whitten, E. Y. Chi and D. G. Evans, <i>Langmuir</i> , 2016, 32 , 12542-12551.
6 7	4.	E. Wang, H. Sun, J. Wang, Z. Wang, H. Liu, J. Z. H. Zhang and T. Hou, <i>Chem. Rev</i> , 2019, 119 , 9478-9508.
8 9	5.	Yj. Sheng, Yw. Yin, Yq. Ma and Hm. Ding, <i>Journal of Chemical Information and Modeling</i> , 2021, 61 , 2454-2462.
10 11	6.	K. Huang, S. Luo, Y. Cong, S. Zhong, J. Z. H. Zhang and L. Duan, <i>Nanoscale</i> , 2020, 12 , 10737-10750.
12 13	7.	L. Duan, X. Liu and J. Z. H. Zhang, <i>Journal of the American Chemical Society</i> , 2016, 138 , 5722-5728.
14	8.	M. R. Lee, Y. Duan and P. A. Kollman, Proteins, 2000, 39, 309-316.
15 16	9.	R. Kumari, R. Kumar and A. Lynn, J. Chem. Inf. Model, 2014, 54, 1951-1962.
17 18 19		
• •		