Three novel mutations I65S, R66S and G86R divulges significant conformational variations in the PTB domain of IRS1 gene

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Supplementary Tables:

Table S1: Genetic analysis of IRS1 gene in type 2 diabetic patients showing the identified mutations and their reflection in amino acid changes.

GenBank ID	Mutation	Codon Change	Amino acid change
KF725072	T-G	ATC-AGC	I65S
KF725073	G-C	GGG-CGG	G86R
KF725074	G-C	AGG-AGC	R66S

Table S2: PDBSum analysis of wild type and mutated IRS1 structures explaining the conformational variations due to mutations.

IRS structure	Z-Rank score	Z-dock score (kcal/mol)	No Pi Interactions	No Hydrogen Bonds	Ligand Contact Surface Area ($Å^2$)	Receptor Contact Surface Area ($Å^2$)
Wild Type	-110.73	15.72	3	10	623.36	625.47
I65S	-106.76	15.74	2	11	557.90	511.86
R66S	-111.94	20.30	3	12	887.66	929.33
G86R	-107.26	18.06	3	14	835.59	811.33

Table S3: Protein-protein docking of IRS1 wild type and mutated structures explaining affinity and bonding pattern variations against IR protein.

IRS structure	Z-Rank score	Z-dock score (kcal/mol)	No Pi Interactions	No Hydrogen Bonds	Ligand Contact Surface Area (Å²)	Receptor Contact Surface Area (Å²)
Wild Type	-110.73	15.72	3	10	623.36	625.47
I65S	-106.76	15.74	2	11	557.90	511.86
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Table S4: Analysis of intermolecular interactions through Z-dock. The hydrogen bonds and pi-interactions formed between IR and IRS1-wild type and mutant models were shown.

IRS1 Protein	Hydrogen bonds			Pi-interactions		
	IR residues	IRS1 residues	Distance (Å)	IR residues	IRS1 residues	Distance (Å)
Wild Type	ALA356	ASN198	2.19	TRP559	MET156	5.40
	GLU355	GLU200	2.31	PHE518	CYS186	4.04
	SER290	GLN175	2.13	PHE518	PHE160	5.13
	SER290	GLN175	2.58			
	SER619	SER261	2.67			
	PHE518	PRO158	2.31			
	SER290	LYS171	1.83			
	GLU355	SER199	2.19			
	PRO617	SER261	2.74			
	PRO617	SER261	2.39			
I65S	GLY623	GLY174	2.24	PRO307	PHE264	5.28
	THR530	GLN175	2.20	TYR507	LEU173	4.29
	THR516	ARG213	1.38			
	ASP519	GLY234	2.45			
	GLN521	THR231	2.60			
	GLY623	GLY174	2.84			

	THR516	ARG213	2.78			
	ASP519	PRO233	1.94			
	THR530	PRO233	2.91			
	GLY291	PHE264	2.66			
	GLY291	PHE264	2.47			
R66S	ARG86	SER217	2.54	TYR91	TRP237	4.45
	ARG118	PRO170	2.69	PHE88	LYS169	4.78
	ARG118	PRO170	2.04	ARG118	TRP237	5.05
	ASN348	ALA159	1.90			
	SER528	PHE264	1.86			
	GLN328	TRP164	2.73			
	GLN521	LYS190	1.55			
	PHE88	TRP237	1.72			
	GLY347	PHE160	2.15			
	ASN348	LYS161	2.90			
	GLU120	GLY172	2.66			
	GLN521	LYS190	2.39			
G86R	ARG86	ASP241	1.67	PHE89	GLU162	4.29
	ARG118	GLN165	3.04	PHE89	TRP164	4.87
	GLN328	CYS214	1.63	PHE89	TRP164	4.04
	ASN348	ILE211	2.49			
	PHE89	GLN165	2.58			
	PHE89	GLN165	2.94			
	GLN521	ARG212	2.70			

	CYS524	SER228	2.82			
	CYS524	GLY232	2.64			
	GLY347	LEU208	2.09			
	CYS524	GLY232	2.11			
	ALA523	PRO233	2.91			
	GLY525	PRO233	2.10			
	GLU329	GLU251	2.51			

Supplementary Figures

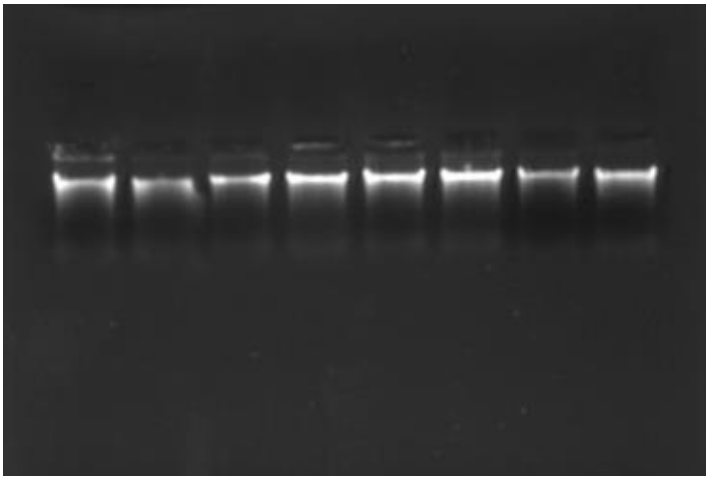

Figure S1: Agarose gel electrophoresis gel showing the genomic DNA isolated from normal controls and type 2 diabetic patients

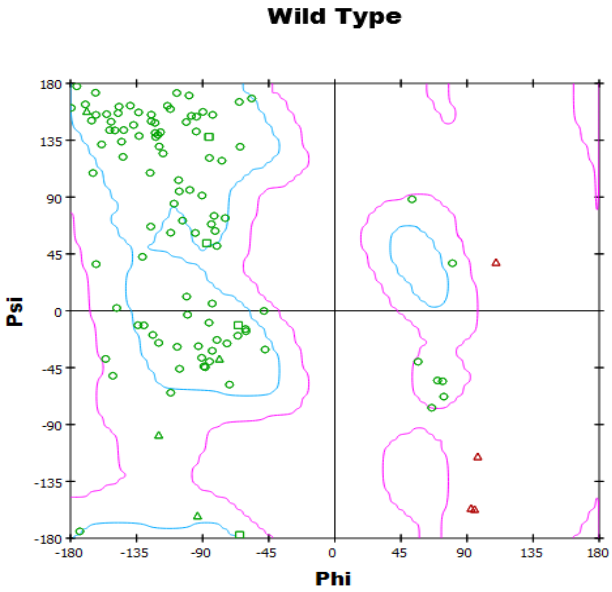

Figure S2: Ramachandran plot explaining the stereo chemical quality of molecular dynamics simulated wild type IRS1 structure.

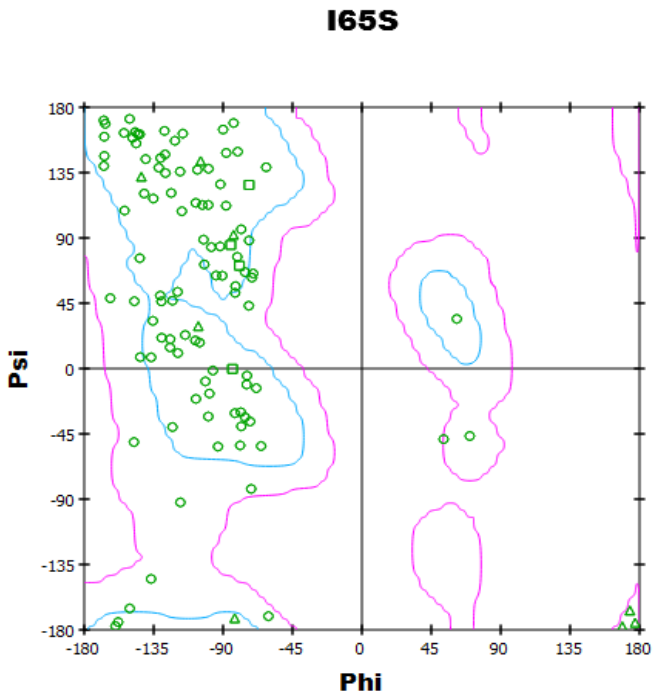

Figure S3: Ramachandran plot explaining the stereo chemical quality of molecular dynamics simulated I65S mutant IRS1 structure.

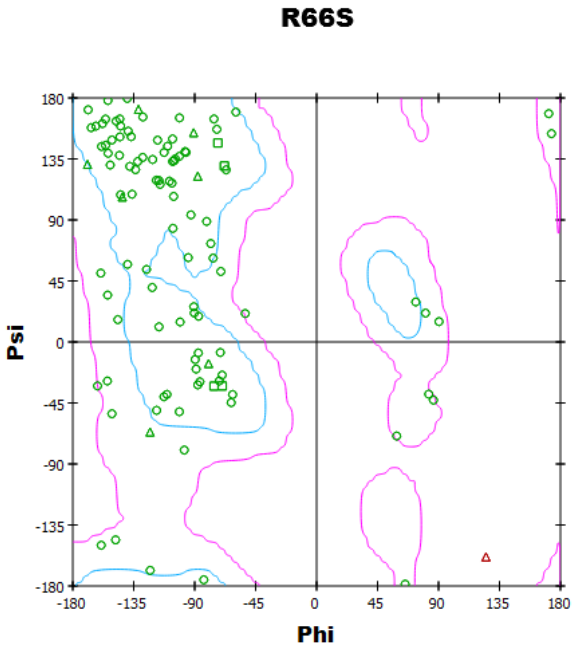

Figure S4: Ramachandran plot explaining the stereo chemical quality of molecular dynamics simulated R66S mutant IRS1 structure.

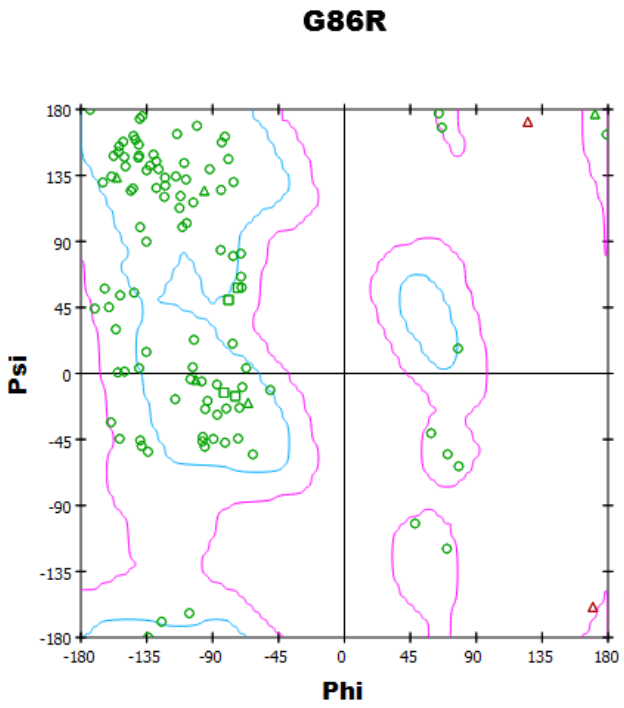

Figure S5: Ramachandran plot explaining the stereo chemical quality of molecular dynamics simulated G86R mutant IRS1 structure.

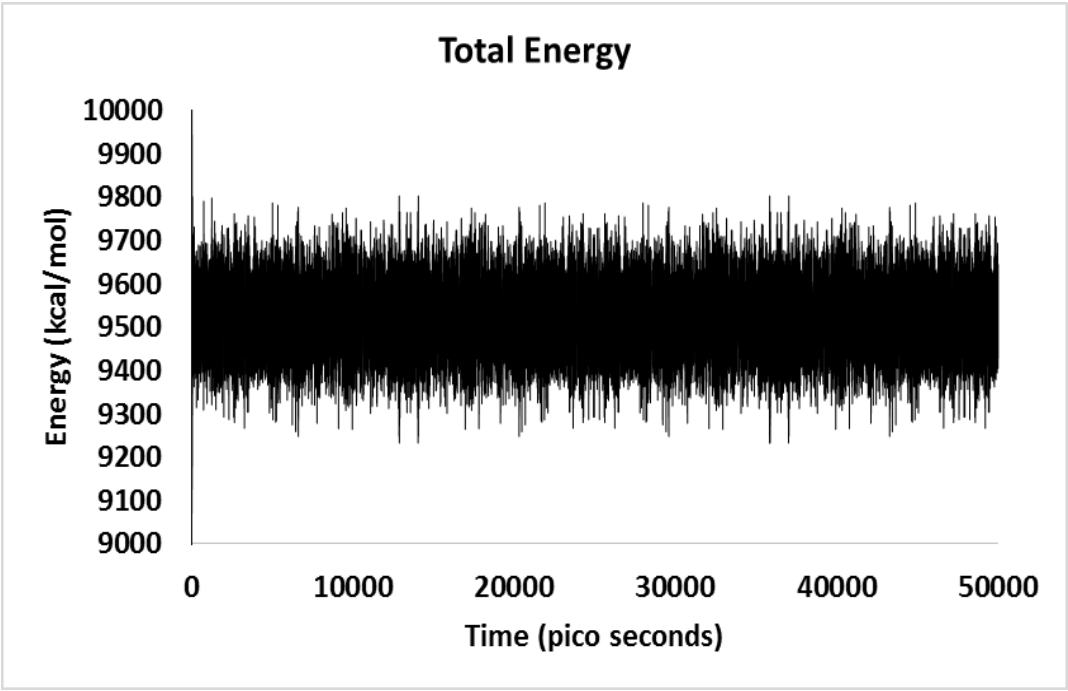

Figure S6: Total energy plot of Insulin receptor (IR) generated from 50000 ps molecular dynamics simulations showing the stabilised nature of energy at 9500 kcal/mol/.

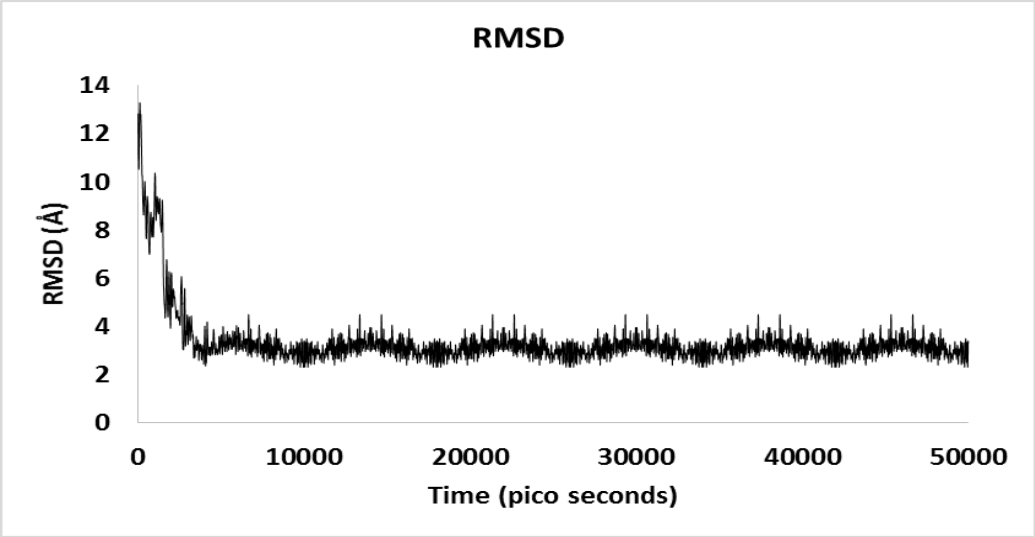

Figure S7: RMSD plot of Insulin receptor (IR) generated from 50000 ps molecular dynamics simulations showing the stabilized nature of RMSD at 3Å.