**Supporting information**

**Identifying potential GluN2B subunit containing N-Methyl-d-aspartate receptor inhibitors: An integrative *in silico* and molecular modeling approach**

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**Fig. S1.** KNIME workflow for drug likeliness filter.



**Fig. S2.** KNIME workflow by RD Kit to remove PAINS.



**Fig S3.** Distribution of the compounds according to (a) cLogP, (b) a number of rotatable bonds, (c)TPSA, (d) number of HBD, (e) molecular weight and (f) number of HBA (compounds in groups highlighted with darker blue shades were selected).



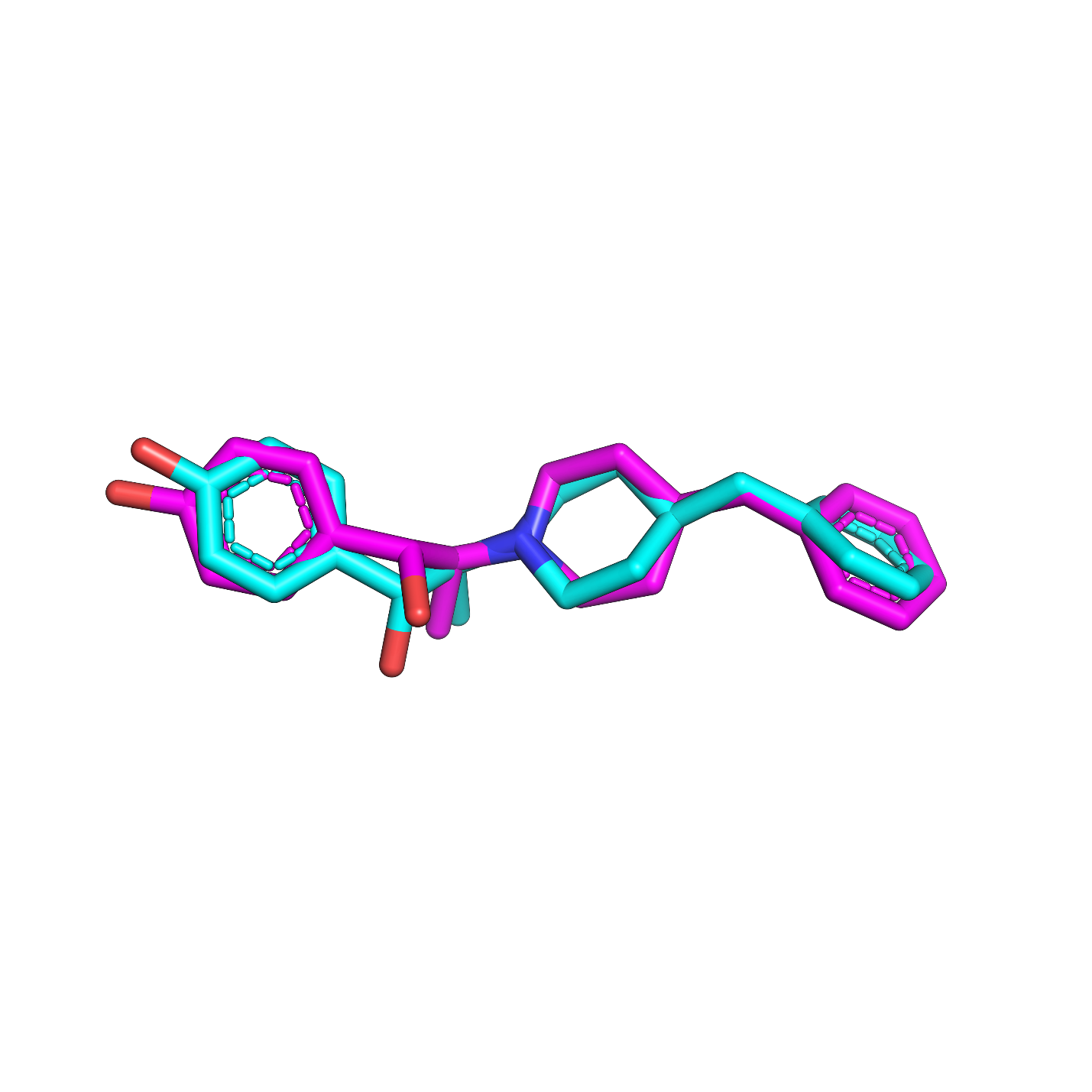
**Fig. S4.** Homology model validation (a) Global QMEAN quality score. The white area in the bar plots (values near zero) indicate that the property is similar to what one would expect from experimental structure of similar size. Positive values indicate that the model scores higher than experimental structures on average. (b) Local quality plot for chain A (Blue color) and chain B (Red color). (c) Comparison plot of model quality scores of homology model related to scores obtained for experimental structures of similar size.

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**Fig. S5.** Ramachandran plot of homology model indicating 4 residues in disallowed region (Marked red).

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**Fig. S6.** Plot of potential energy of protein during energy minimisation in vacuum



**Fig. S7**. Superimposition of co-crystallised (magenta) and docked ifenprodil (turquoise)

**Fig. S8**. Scatter plot representing the distribution of filtered ligands according to binding energy and cluster size (in percentage) after SP docking (ifenprodil is represented in orange colour). The compounds having higher cluster size and lower binding energy than ifenprodil were selected for XP docking (represented in the blue box).



**Fig. S9**. (a) Plot of energy minimsation of ZINC257261614-protein complex. (b) Plot of temperature of the ZINC257261614-protein complex system. (c) Plot of density of the ZINC257261614-protein complex system (d) RMSD plots of ZINC257261614-protein complex during equilibration.



**Fig. S10**. (a) Plot of energy minimsation of ZINC95977857-protein complex. (b) Plot of temperature of the ZINC95977857-protein complex system. (c) Plot of density of the ZINC ZINC95977857-protein complex system (d) RMSD plots of ZINC ZINC95977857-protein complex during equilibration.

**Table**

**Table T1.** Summary of energy minimization steps for protein preparation.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Stage | Maximum number of steps (steepest descent) | Maximum number of steps (conjugate gradient) | Weight for the positional restraints. (in kcal/mol-Å2) | Restrained elements |
| 1 | 2000 | 3000 | 500 | Protein except hydrogen |
| 2 | 1000 | 4000 | 500 | Protein except side chain |
| 3 | 1000 | 4000 | 50 | Protein except hydrogen |
| 4 | 1000 | 4000 | 5 | Protein except hydrogen |
| 5 | 1000 | 4000 | 0.5 | Protein except hydrogen |
| 6 | 1000 | 4000 | 0 | No restraint |

**Table T2.** Summary of parameters used for docking studies.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Type of docking study | Number of compound subjected to docking | Number of compounds obtained | GA population size | Genetic algorithm run | Maximum number of energy evaluation |
| **HTVS** | 1607 | 192 | 75 | 20 | 250,000 |
| **SP** | 192 | 48 | 150 | 50 | 2,500,000 |
| **XP** | 48 | 10 | 150 | 100 | 25,000,000 |

**Table T3.** Summary of energy minimization steps for MM-GBSA and MD simulation of solvated system.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Stage | Maximum number of steps (steepest descent) | Maximum number of steps (conjugate gradient) | Weight for the positional restraints. (in kcal/mol-Å2) | Restrained elements |
| 1 | 2000 | 3000 | 500 | Protein except solute and water |
| 2 | 1000 | 4000 | 500 | Protein except hydrogen |
| 3 | 1000 | 4000 | 50 | Protein except side chain |
| 4 | 1000 | 4000 | 5 | Protein except hydrogen |
| 5 | 1000 | 4000 | 0.5 | Protein except hydrogen |
| 6 | 1000 | 4000 | 0 | No restraint |