Supplementary Information for

Identification of potential modulators of IFITM3 by *in-silico* modeling and virtual screening

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Short title: Drug-discovery for IFITM3

Supplementary Tables

Table S1: Top hits from FDA dataset

Rank as per ΔG (XP rank)	Compound	ΔG	Docking score (XP)	Activity
1 (10)	Fidaxomicin	-88.8	-8.735	Novel macrolide antibiotic used in the treatment of diarrhea
7 (122)	Eluxadoline	-74.57	-5.975	Mixed mu-opioid receptor agonist, kappa-opioid receptor agonist, and a-delta opioid receptor antagonist indicated for use in diarrhea-predominant irritable bowel syndrome
3 (498)	Itraconazole	-80.78	-4.066	Antifungal. A highly selective inhibitor of fungal cytochrome P-450 sterol C-14 α-demethylation via the inhibition of the enzyme cytochrome P450 14α-demethylase
10 (998)	Isavuconazonium	-73.53	0.717	Antifungal. Used for the treatment of invasive aspergillosis and mucormycosis.
15 (72)	Naloxegol	-71.03	-6.525	Peripherally-selective opioid antagonist
19 (100)	Valrubicin	-67.38	-6.193	Semisynthetic analog of the doxorubicin. Treatment of the bladder cancer
21 (321)	Thiethylperazine	-66.18	-4.746	A dopamine antagonist that is particularly useful in treating the nausea and vomiting associated with anaesthesia
22 (444)	Montelukast	-65.38	-4.328	Leukotriene receptor antagonist. used typically in addition to or complementary with the use of inhaled corticosteroids or other agents in asthma step therapy
24 (16)	Sacubitril	-65.14	-7.857	A prodrug neprilysin inhibitor used in combination with valsartan to reduce the risk of cardiovascular events in patients with chronic heart failure (NYHA Class II-IV) and reduced ejection fraction
27 (225)	Ertugliflozin	-64.74	-5.163	Potent and selective inhibitors of the sodium-dependent glucose cotransporters (SGLT), specifically the type 2 which is responsible for about 90% of the glucose reabsorption from glomerulus

14 (429)	Ledipasvir	-71.17	-4.316	Antiviral. Inhibits NS5A of HCV
41 (221)	Atazanavir	-62.35	-5.064	Antiviral. HIV-1 protease inhibitor
45 (530)	Telaprevir	-61.65	-3.922	Antiviral. Inhibitor of NS3/4a protease of HCV
47 (333)	Aprepitant	-61.44	-4.620	Antagonist of P/neurokinin 1 (NK1) receptor. Antiemetic agent.
48 (508)	Indinavir	-61.41	-4.019	Antiviral. Inhibits HIV protease
55 (52)	Fusidic acid	-60.01	-6.748	Antibiotic. Interferes with bacterial protein synthesis
68 (55)	Hesperidin	-57.08	-6.668	Bioflavonoid. Effective in blood vessel disorders
79 (792)	Elbasvir	-55.65	-3.109	Antiviral. Inhibits NS5A of HCV
80 (179)	Mitoxantrone	-55.64	-5.402	Used in multiple sclerosis. Inhibits topoisomerase II
84 (92)	Tafenoquine	-55.30	-6.186	Treatment for relapsing vivax malaria
85 (388)	Roflumilast	-55.26	-4.465	Inhibitor of phosphodiesterase-4 (PDE-4). Used against chronic obstructive pulmonary disease (COPD) exacerbations.
95 (256)	Riboflavin	-54.19	-4.904	Vitamin B2
99 (54)	Cephaloglycin	-53.87	-6.697	Antibiotic. Inhibits cell wall synthesis.
716 (1)	Amikacin	-26.25	-10.464	Antibiotic. Binds to bacterial 30S ribosomal subunit.

Table S2: Top hits from SNDB dataset

Rank as per ΔG (XP rank)	Compound	ΔG	Docking score (XP)
1 (628)	SN00224572	-100.79	-8.312
2 (16)	SN00342783	-98.98	-12.06
3 (374)	SN00249458	-98.56	-9.071
4 (143)	SN00328659	-97.01	-10.167
5 (278)	SN00226205	-94.52	-9.428
9 (2)	SN00244021	-93.78	-13.621
13 (823)	SN00164639	-92.38	-7.884
27 (675)	SN00239590	-90.23	-8.202
37 (2429)	SN00323932	-87.60	-3.242
41 (1069)	SN00265483	-86.84	-7.373
57 (1572)	SN00286991	-84.05	-6.489
69 (38)	SN00280809	-83.14	-11.317
73 (111)	SN00274576	-82.75	-10.498
115 (1422)	SN00287660	-80.2	-6.753
116 (502)	SN00379347	-80.15	-8.639
167 (450)	SN00306006	-77.50	-8.783
187 (1278)	SN00029983	-76.61	-7.026

247 (312)	SN00374092	-73.92	-9.334
268 (408)	SN00274346	-72.76	-8.924
273 (279)	SN00226238	-72.36	-9.427
279 (642)	SN00242218	-72.19	-8.291
298 (511)	SN00226669	-71.59	-8.608
318 (1853)	SN00304961	-70.67	-5.817
345 (515)	SN00318481	-69.53	-8.602

Supplementary Figures

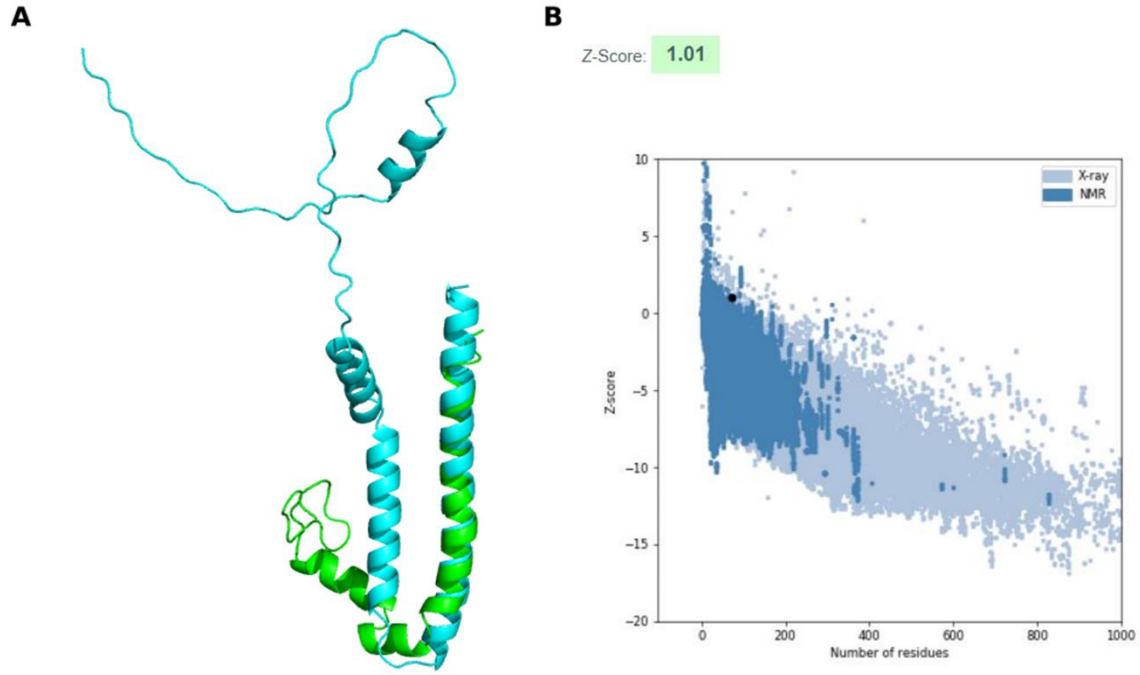
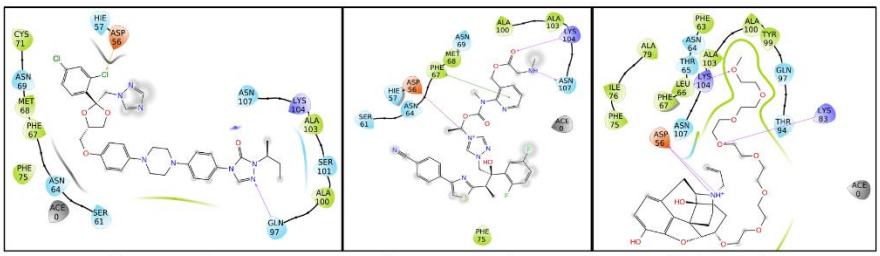
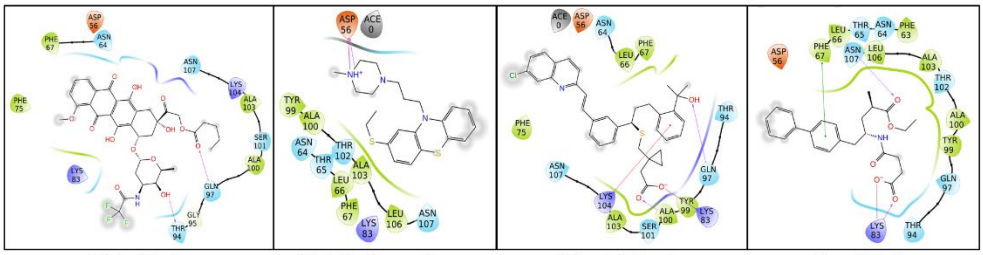


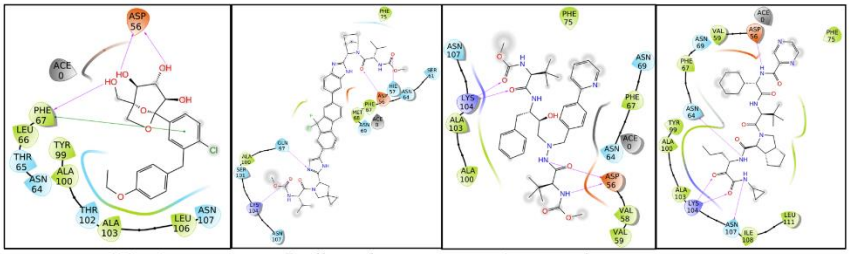
Figure S1: (A) Comparison of modelled IFITM3 modelled structure (Green) with AlphaFold model (Cyan) (**B**) Overall model quality of IFITM3 assessed by ProSA-web. The Z-score of all experimentally determined protein structures in PDB solved by X-ray (Light blue) or NMR (Dark blue). The Z-score of IFITM3 is represented by black dot.



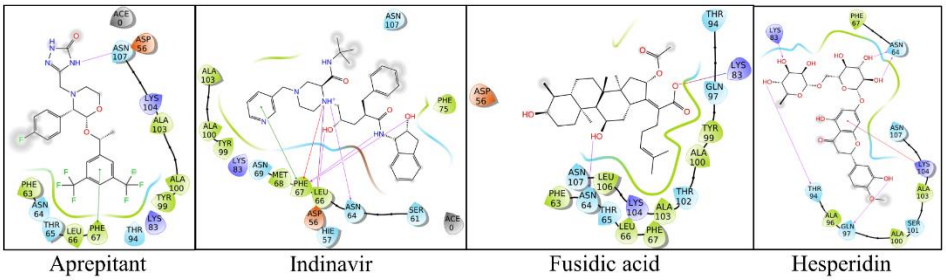
Itraconazole Isavuconazonium Naloxegol



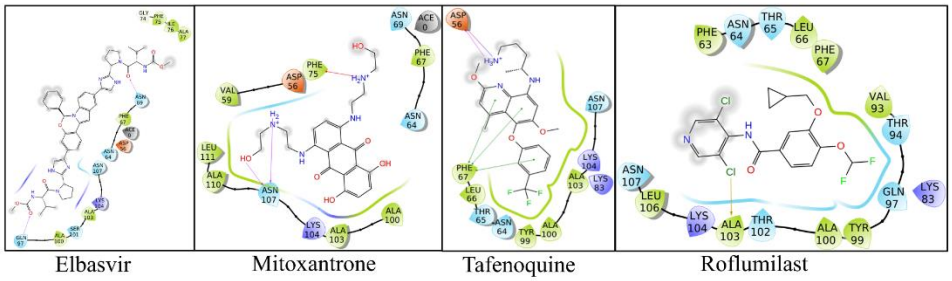
Valrubicin Thiethylperazine Montelukast Sacubitril



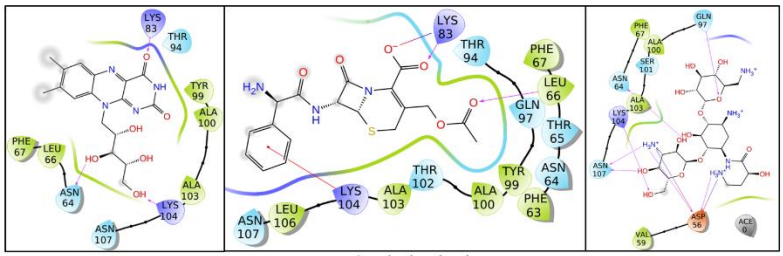
Ertugliflozin Ledipasvir Atazanavir Telaprevir



Aprepitant Indinavir Fusidic acid Hesperidin



Elbasvir Mitoxantrone Tafenoquine Roflumilast



Riboflavin Cephaloglycin Amikacin

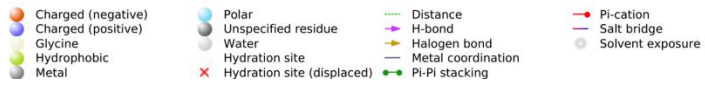


Figure S2: Interaction plot of top FDA ligands (XP docking pose) with IFITM3

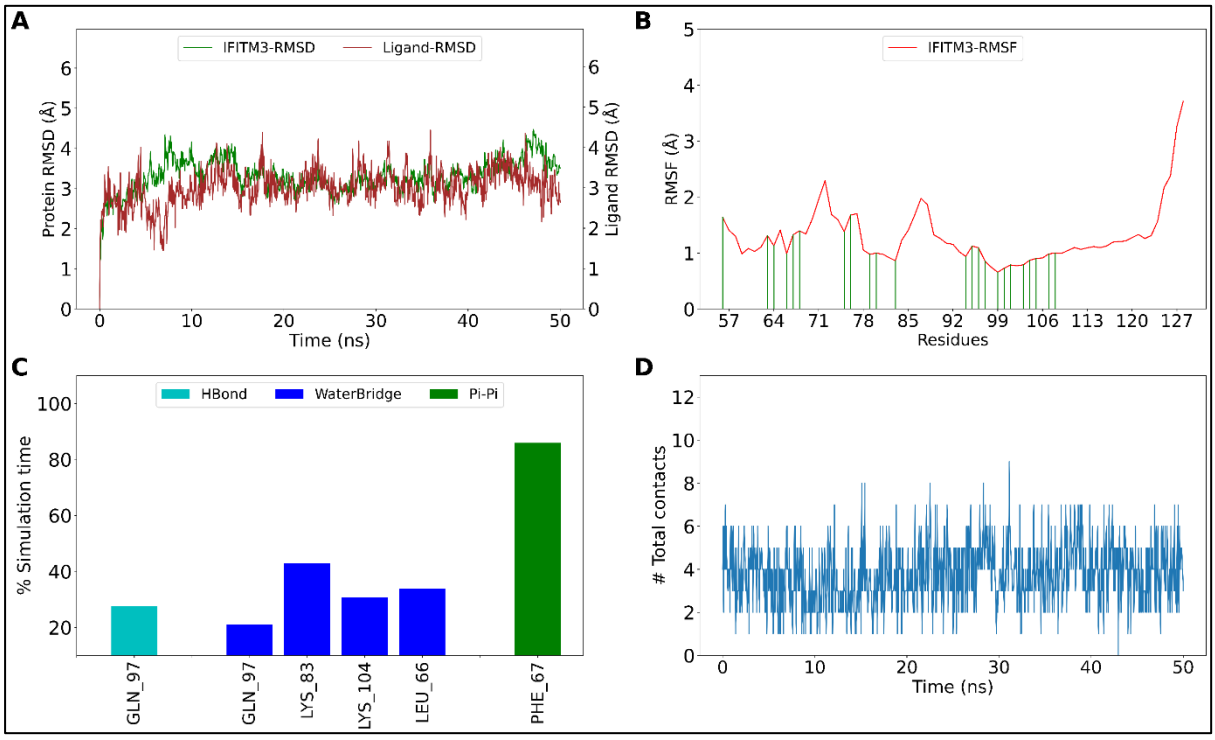


Figure S3: MD simulation of IFITM3-Valrubicin complex (**A**) RMSD of IFITM3 and Valrubicin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Valrubicin (**C**) Interactions between IFITM3 and Valrubicin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Valrubicin and IFITM3

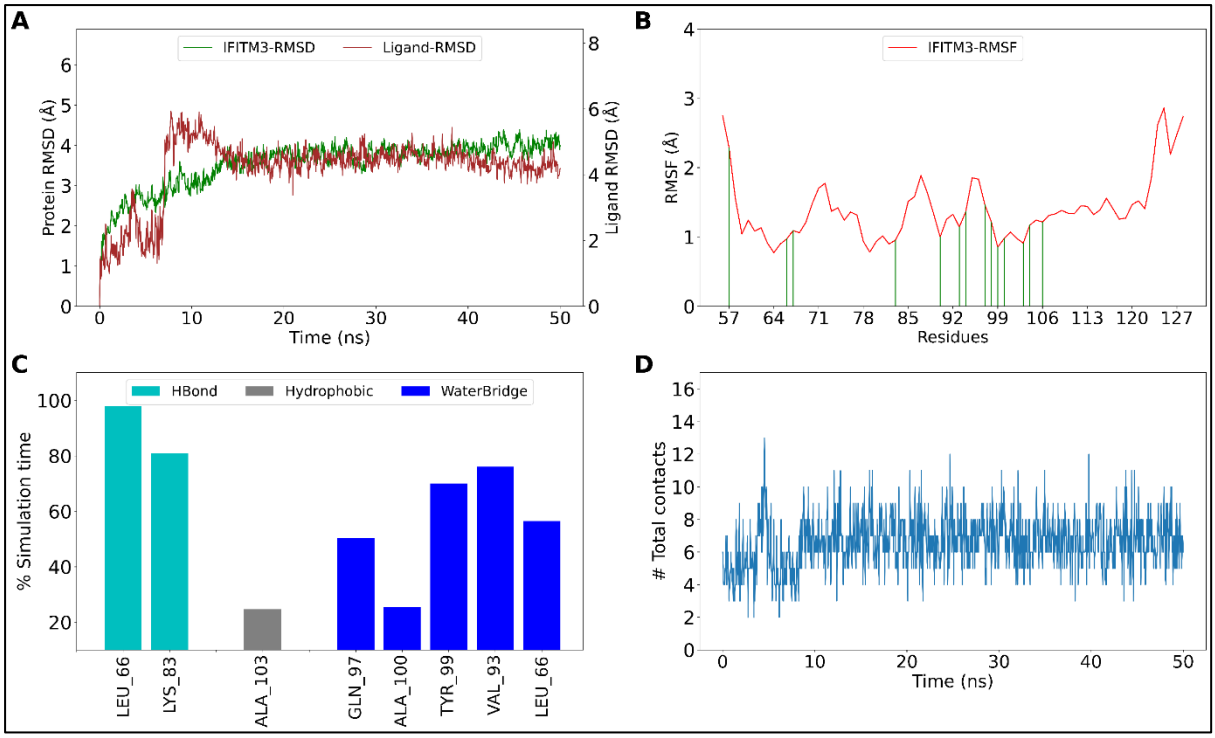


Figure S4: MD simulation of IFITM3-Sacubitril complex (**A**) RMSD of IFITM3 and Sacubitril fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Sacubitril (**C**) Interactions between IFITM3 and Sacubitril as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Sacubitril and IFITM3

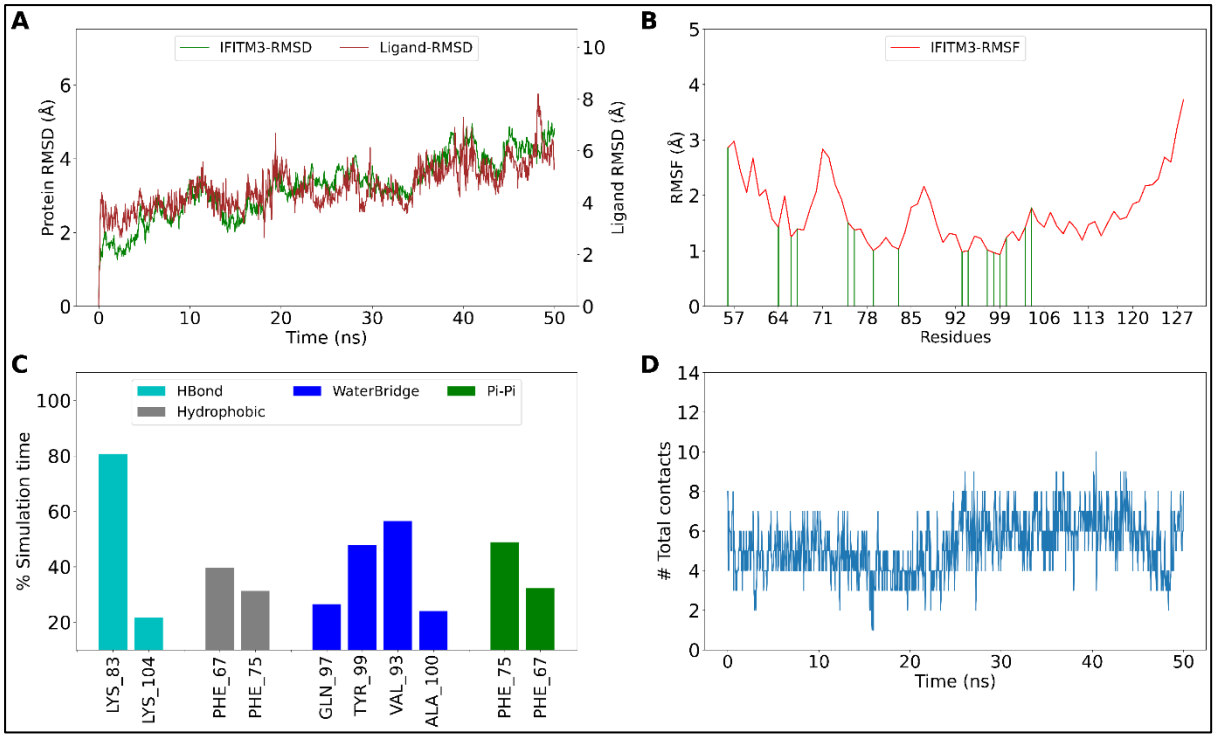


Figure S5: MD simulation of IFITM3-Montelukast complex (**A**) RMSD of IFITM3 and Montelukast fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Montelukast (**C**) Interactions between IFITM3 and Montelukast as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Montelukast and IFITM3

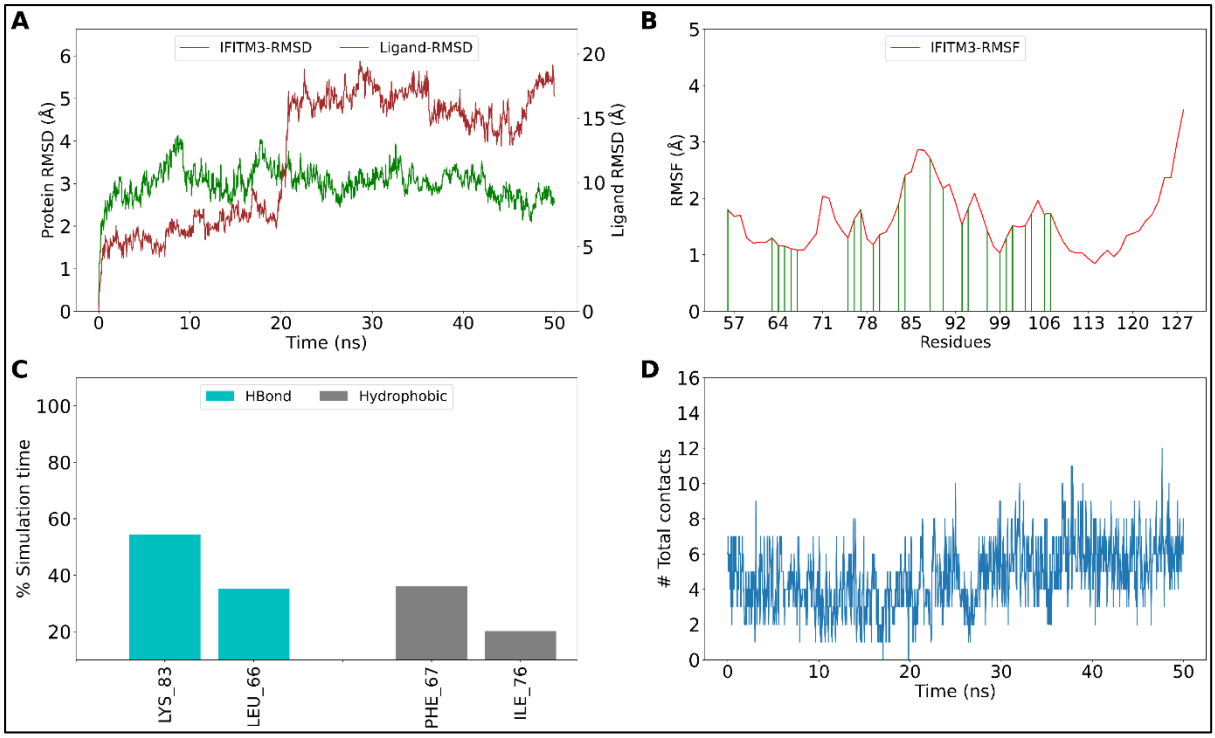


Figure S6: MD simulation of IFITM3-Naloxegol complex (**A**) RMSD of IFITM3 and Naloxegol fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Naloxegol (**C**) Interactions between IFITM3 and Naloxegol as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Naloxegol and IFITM3

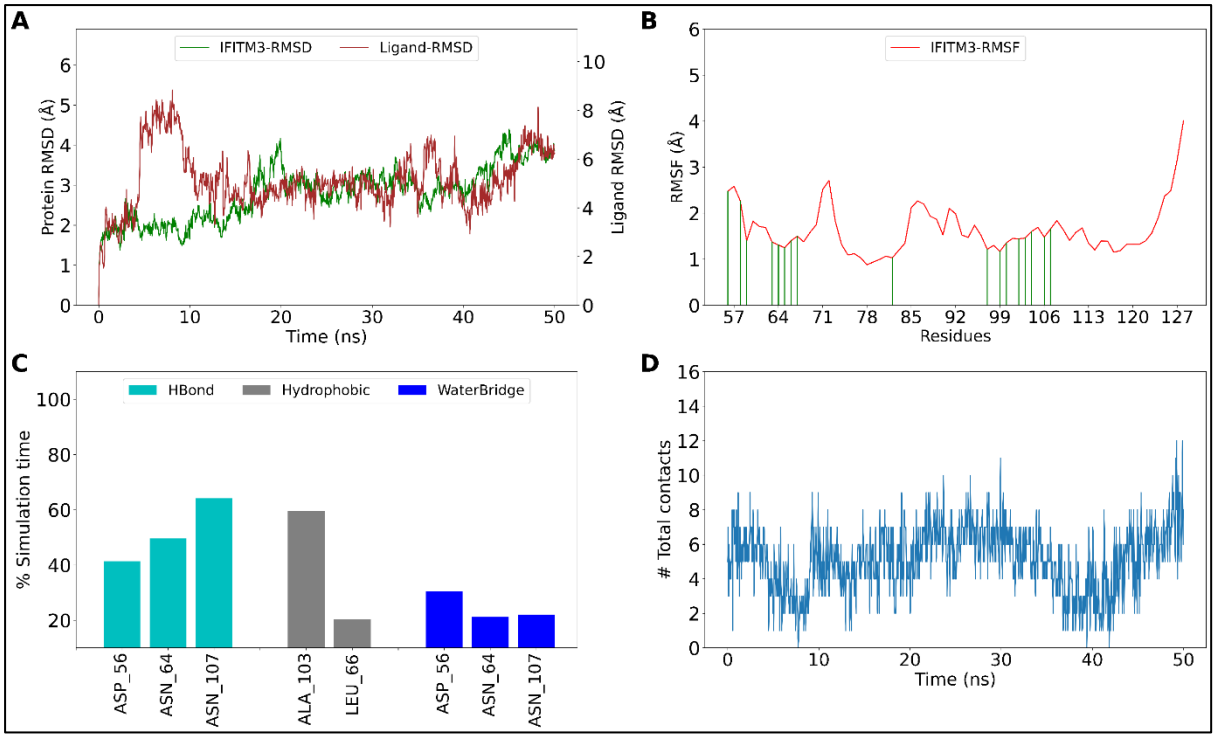


Figure S7: MD simulation of IFITM3-Ertugliflozin complex (**A**) RMSD of IFITM3 and Ertugliflozin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Ertugliflozin (**C**) Interactions between IFITM3 and Ertugliflozin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Ertugliflozin and IFITM3

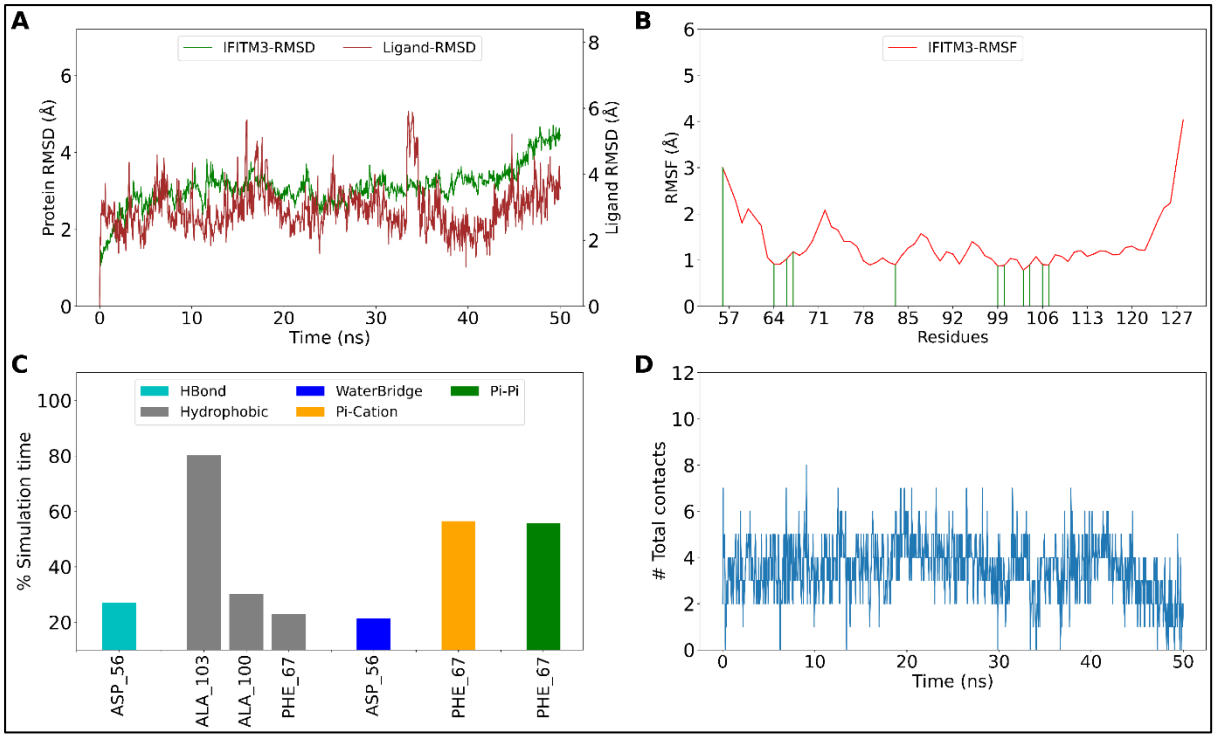


Figure S8: MD simulation of IFITM3-Thiethylperazine complex (**A**) RMSD of IFITM3 and Thiethylperazine fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Thiethylperazine (**C**) Interactions between IFITM3 and Thiethylperazine as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Thiethylperazine and IFITM3

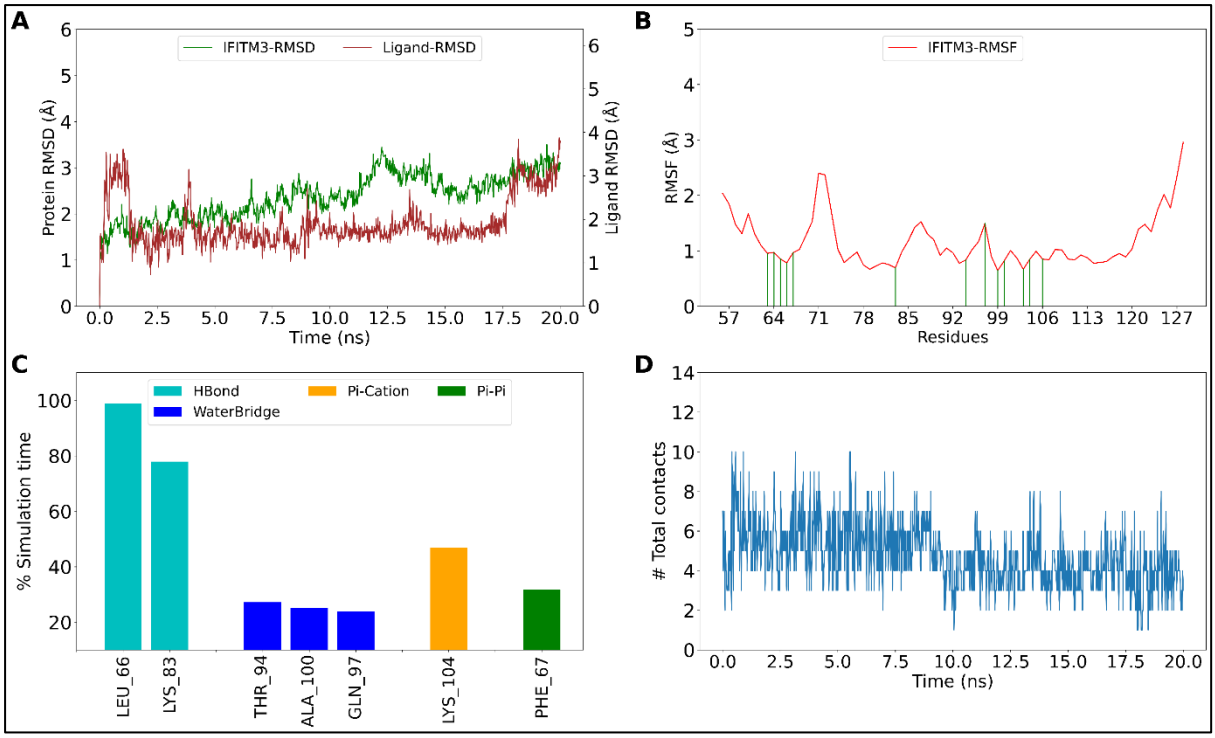


Figure S9: MD simulation of IFITM3-Cephaloglycin complex (**A**) RMSD of IFITM3 and Cephaloglycin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Cephaloglycin (**C**) Interactions between IFITM3 and Cephaloglycin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Cephaloglycin and IFITM3

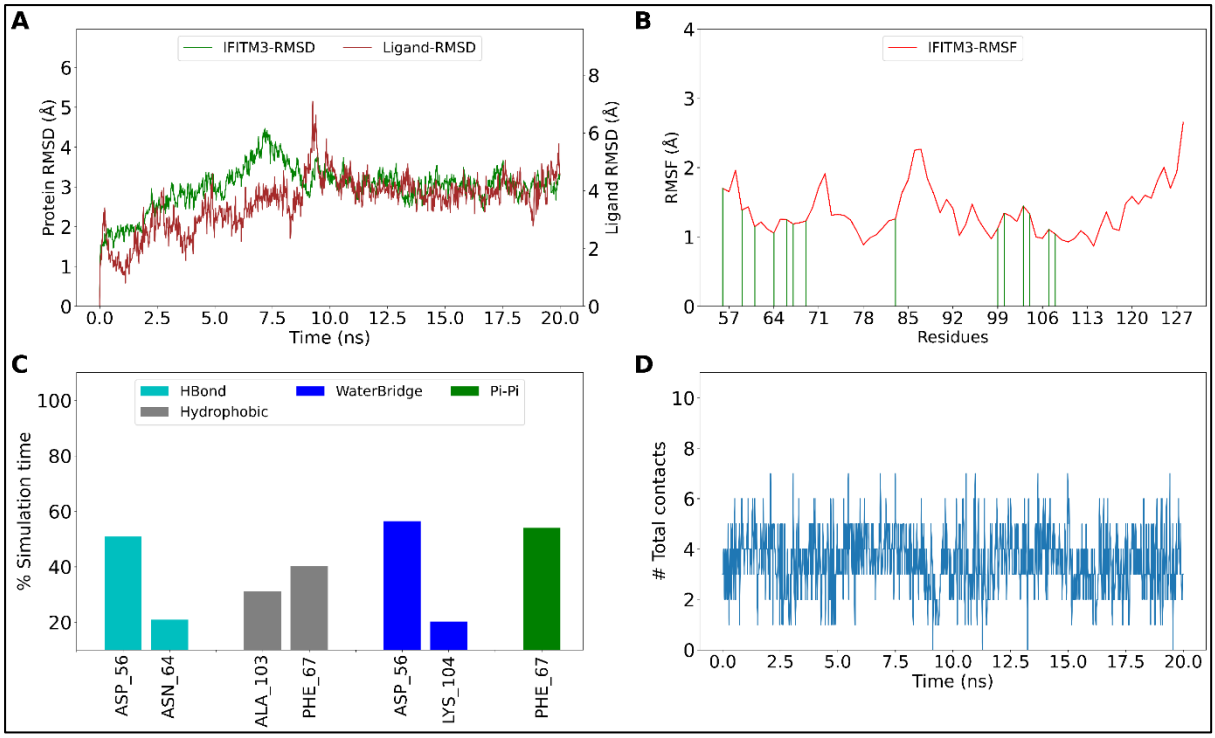


Figure S10: MD simulation of IFITM3-Aprepitant complex (**A**) RMSD of IFITM3 and Aprepitant fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Aprepitant (**C**) Interactions between IFITM3 and Aprepitant as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Aprepitant and IFITM3

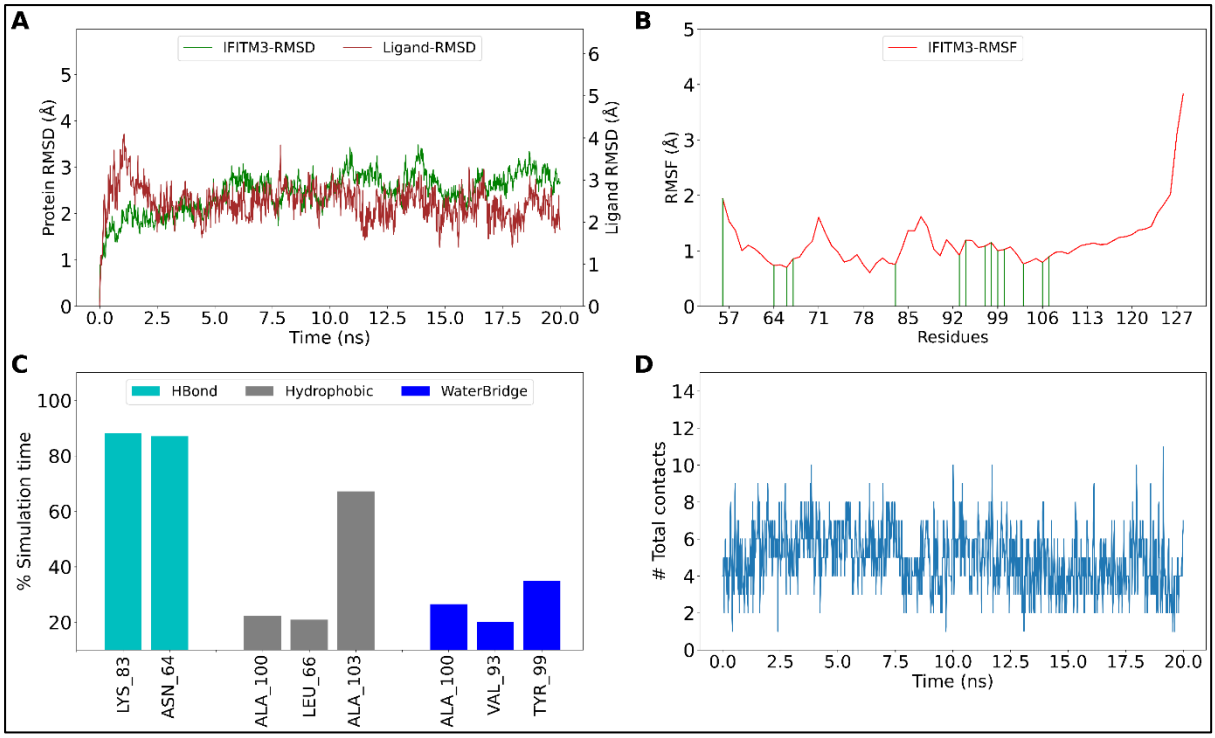


Figure S11: MD simulation of IFITM3-Fusidic acid complex (**A**) RMSD of IFITM3 and Fusidic acid fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Fusidic acid (**C**) Interactions between IFITM3 and Fusidic acid as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Fusidic acid and IFITM3

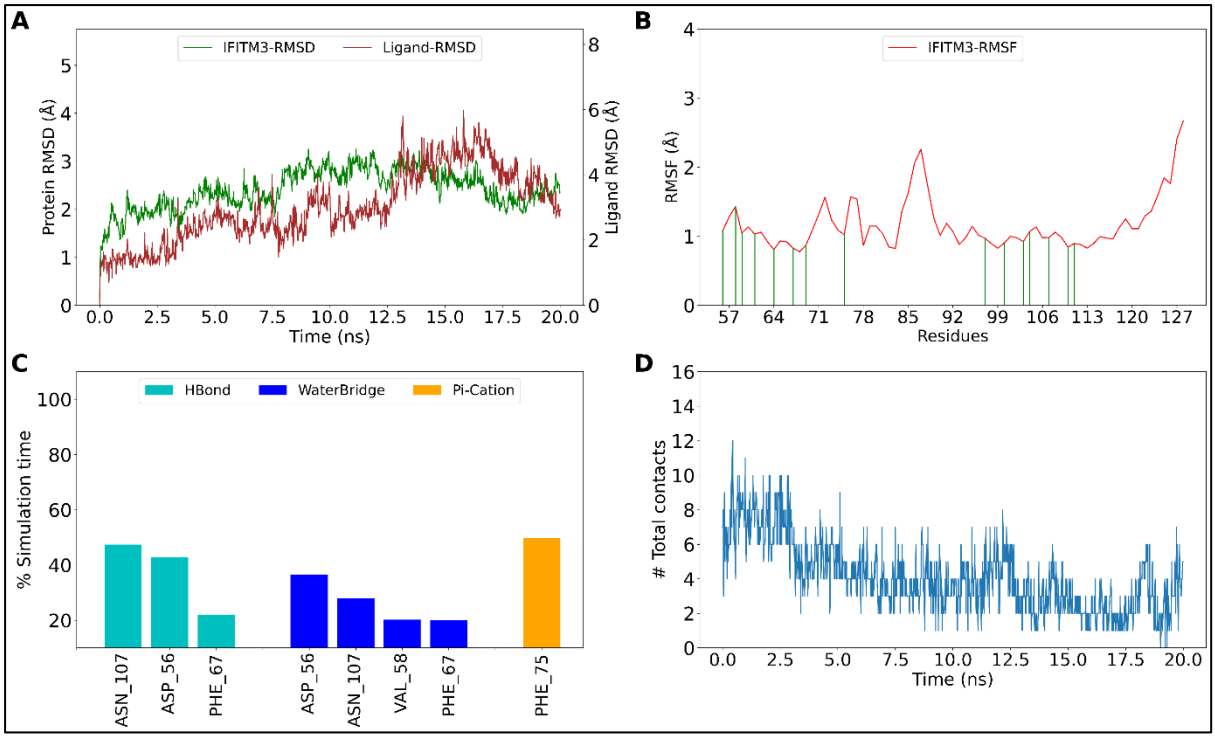


Figure S12: MD simulation of IFITM3-Mitoxantrone complex (**A**) RMSD of IFITM3 and Mitoxantrone fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Mitoxantrone (**C**) Interactions between IFITM3 and Mitoxantrone as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Mitoxantrone and IFITM3

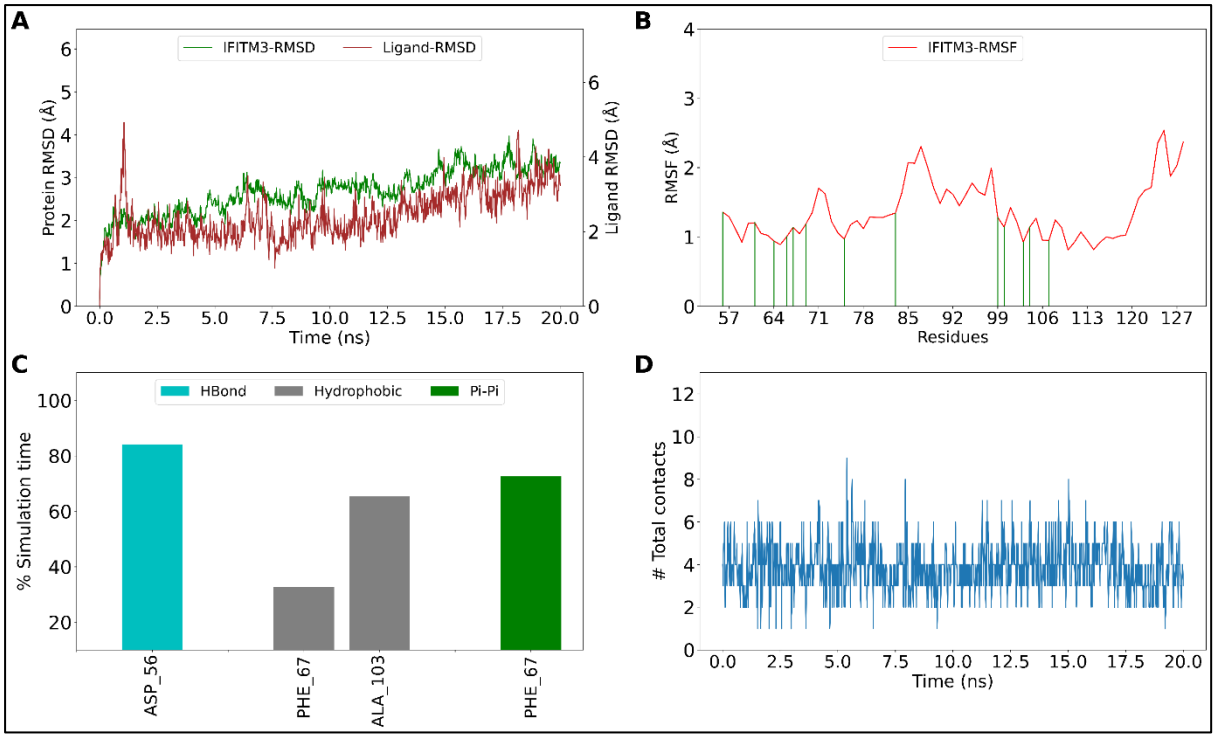


Figure S13: MD simulation of IFITM3-Tafenoquine complex (**A**) RMSD of IFITM3 and Tafenoquine fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Tafenoquine (**C**) Interactions between IFITM3 and Tafenoquine as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Tafenoquine and IFITM3

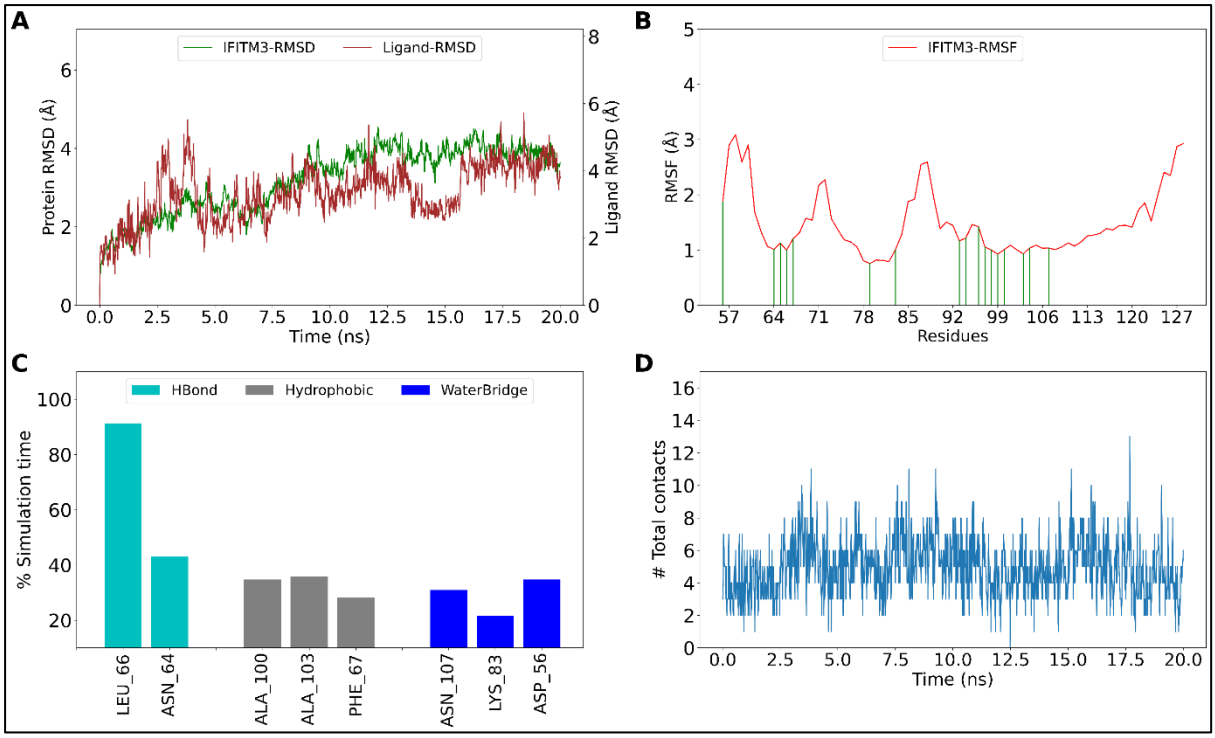


Figure S14: MD simulation of IFITM3-Riboflavin complex (**A**) RMSD of IFITM3 and Riboflavin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Riboflavin (**C**) Interactions between IFITM3 and Riboflavin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Riboflavin and IFITM3

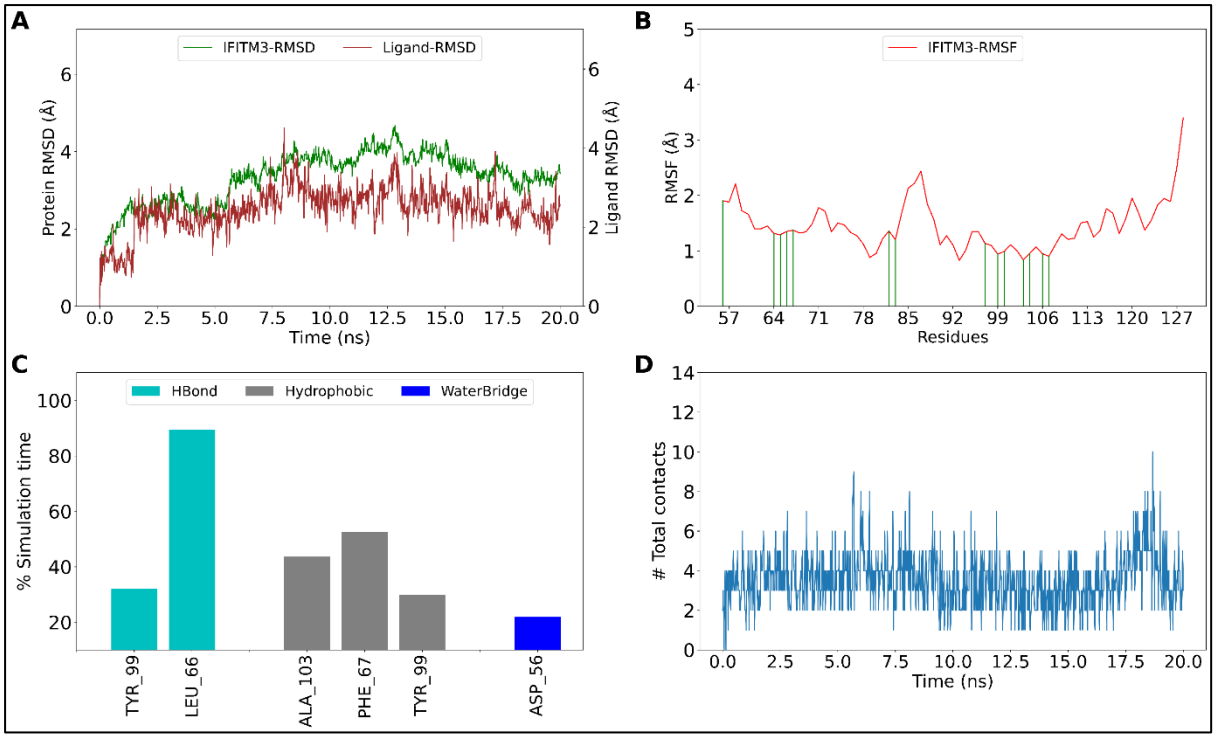


Figure S15: MD simulation of IFITM3-Roflumilast complex (**A**) RMSD of IFITM3 and Roflumilast fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Roflumilast (**C**) Interactions between IFITM3 and Roflumilast as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Roflumilast and IFITM3

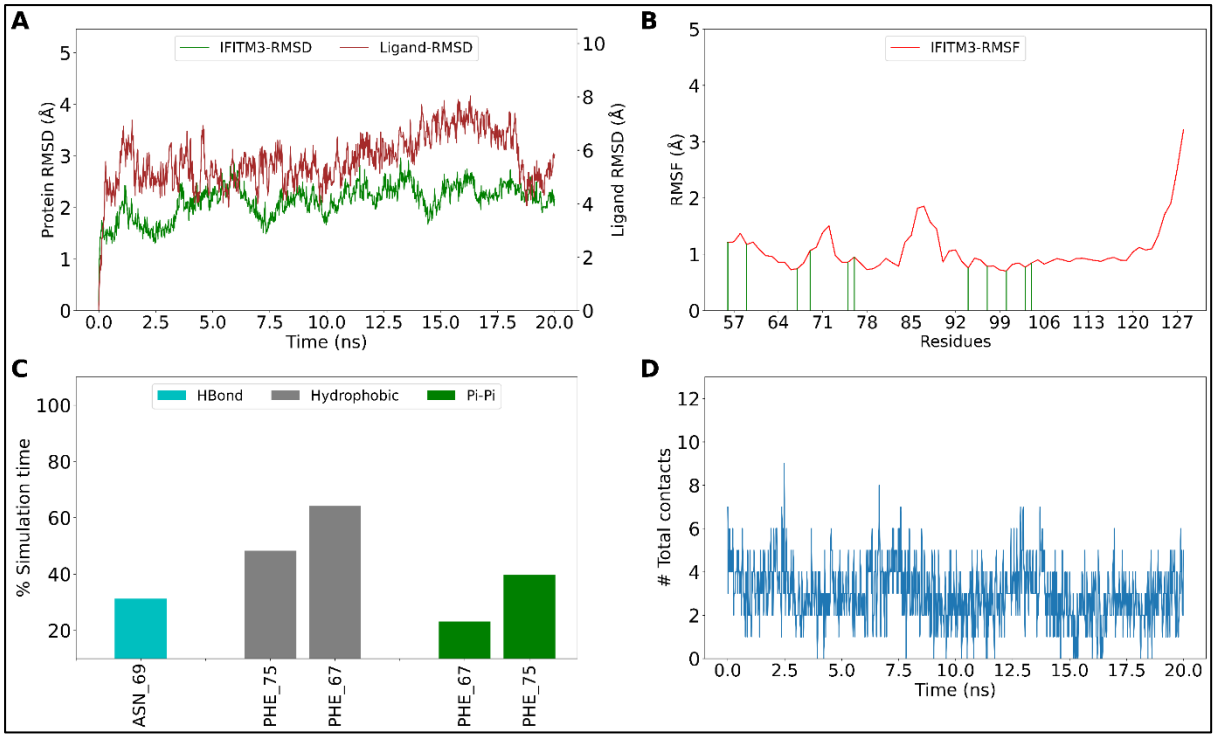


Figure S16: MD simulation of IFITM3-Atazanavir complex (**A**) RMSD of IFITM3 and Atazanavir fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Atazanavir (**C**) Interactions between IFITM3 and Atazanavir as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Atazanavir and IFITM3

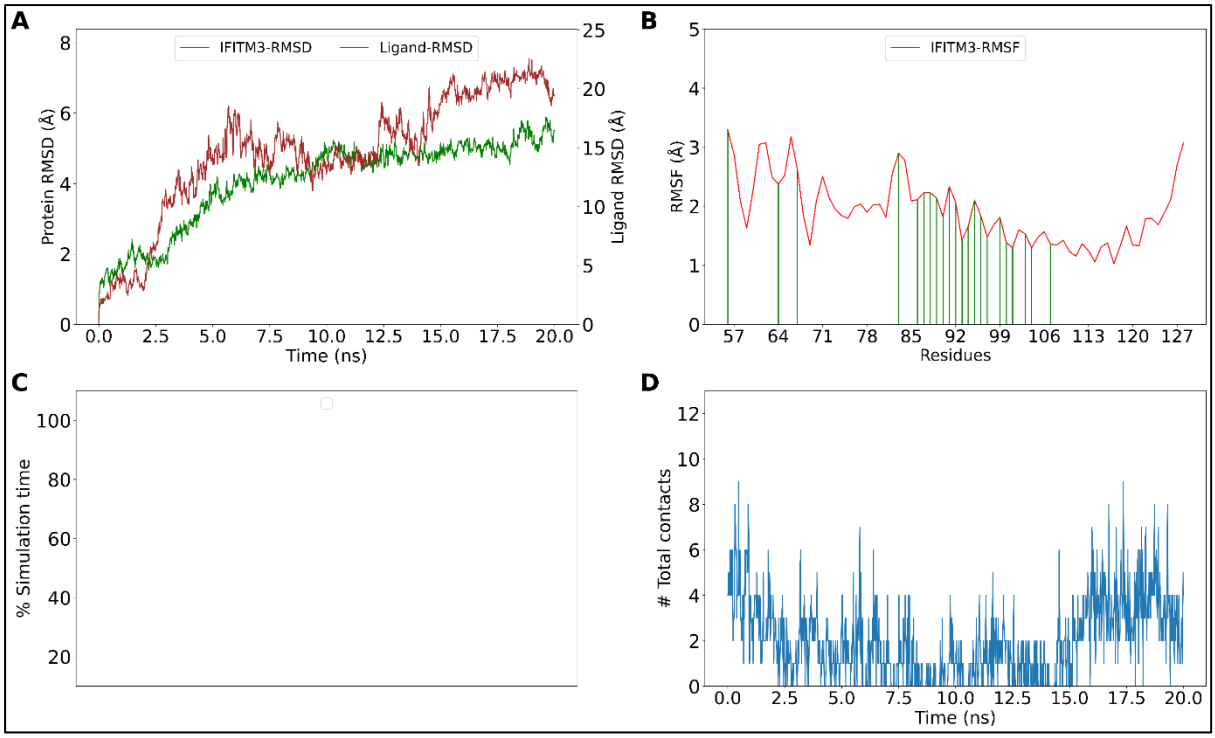


Figure S17: MD simulation of IFITM3-Hesperidin complex (**A**) RMSD of IFITM3 and Hesperidin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Hesperidin (**C**) Interactions between IFITM3 and Hesperidin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Hesperidin and IFITM3

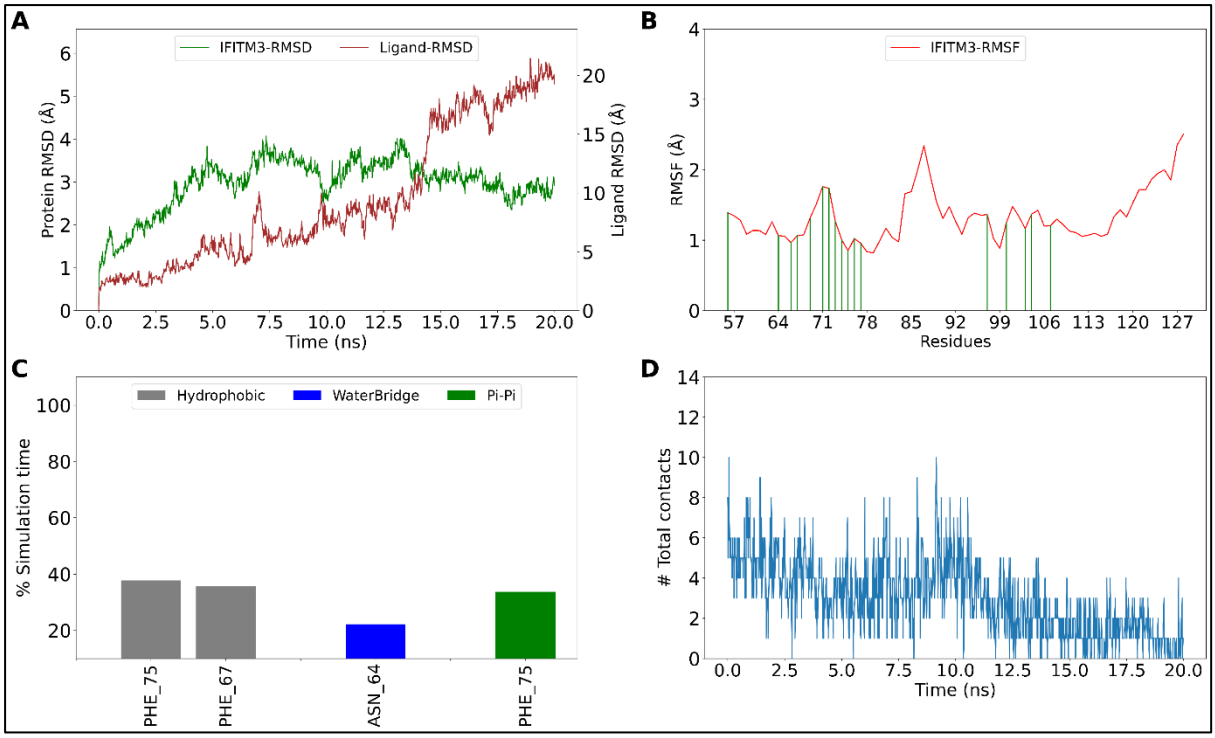


Figure S18: MD simulation of IFITM3-Elbasvir complex (**A**) RMSD of IFITM3 and Elbasvir fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Elbasvir (**C**) Interactions between IFITM3 and Elbasvir as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Elbasvir and IFITM3

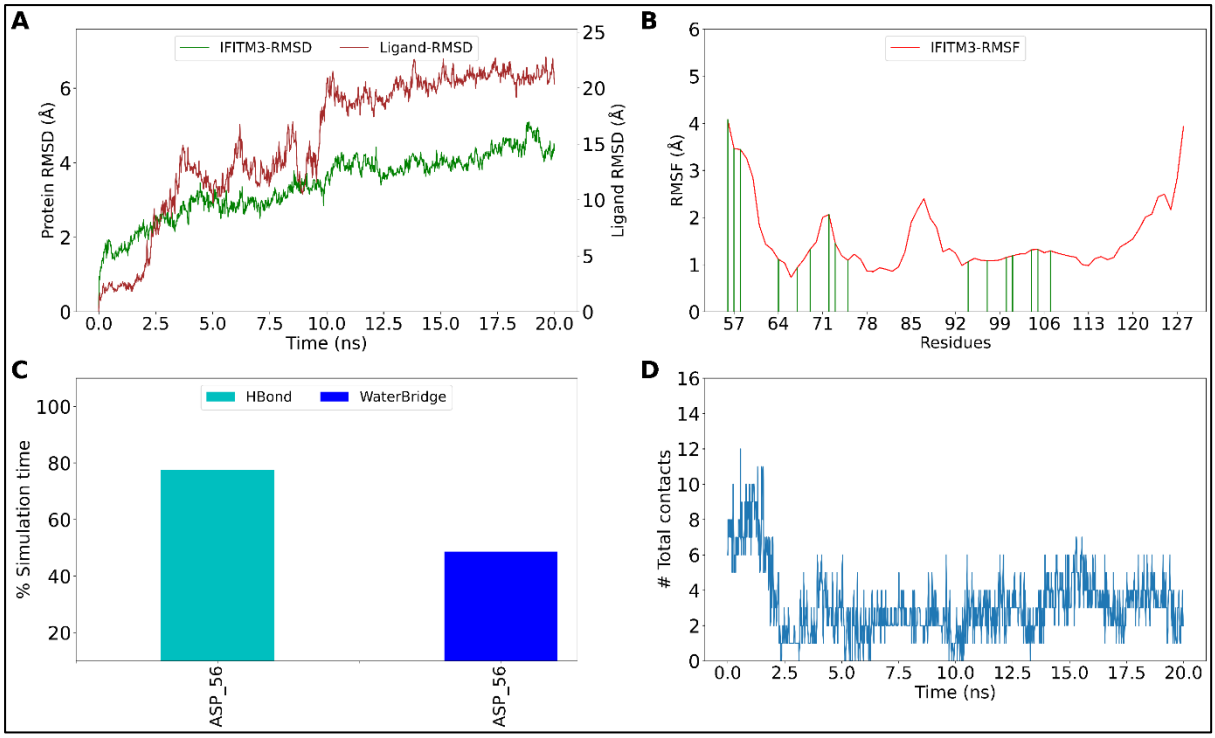
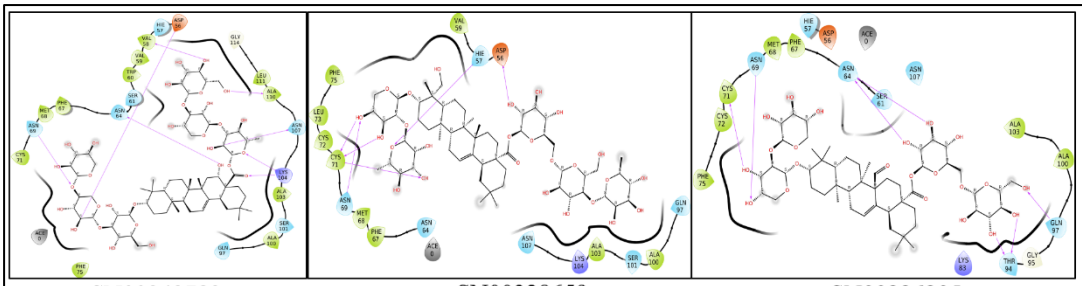


Figure S19: MD simulation of IFITM3-Amikacin complex (**A**) RMSD of IFITM3 and Amikacin fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Amikacin (**C**) Interactions between IFITM3 and Amikacin as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Amikacin and IFITM3



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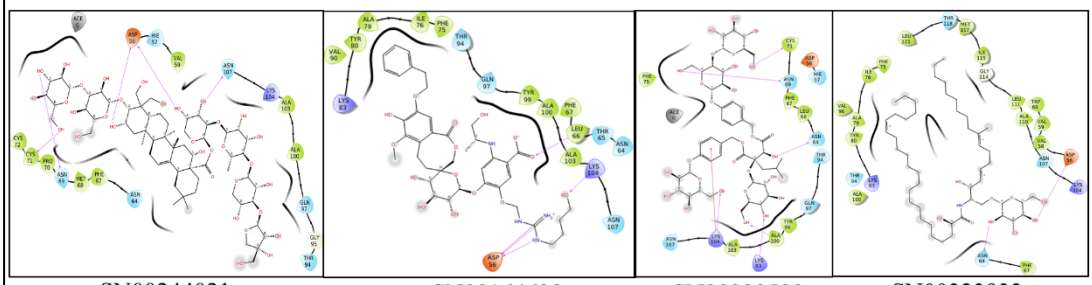

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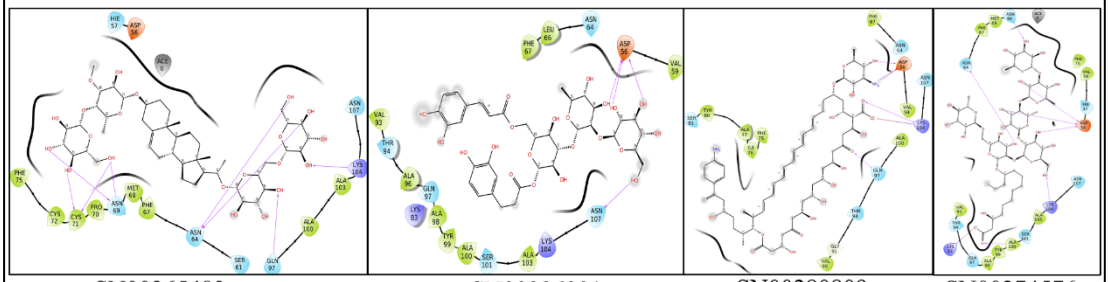

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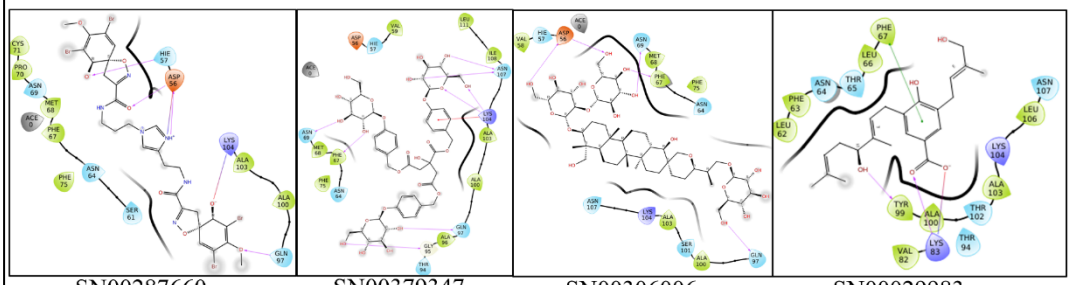

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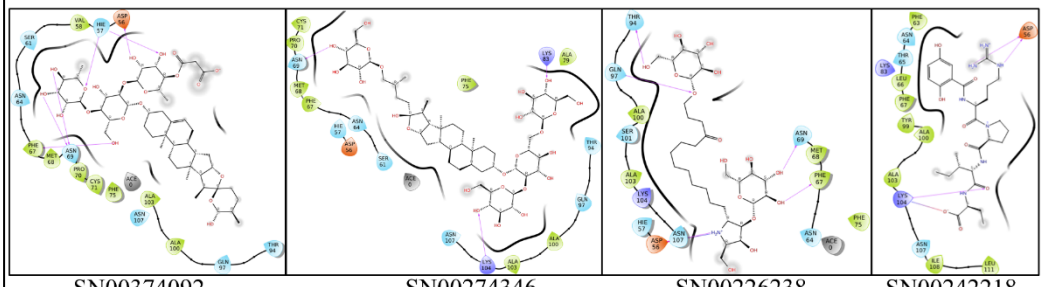
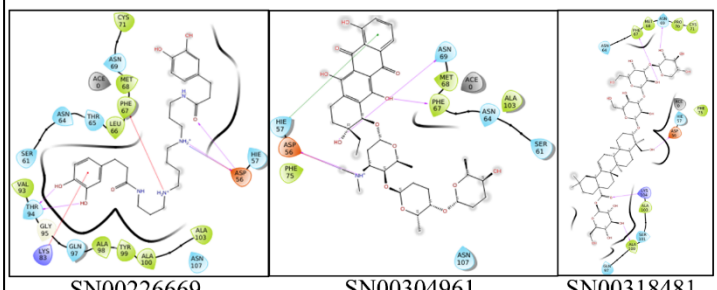


SN00374092 SN00274346 SN00226238 SN00242218



SN00226669 SN00304961 SN00318481

Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure

Figure S20: Interaction plot of SNDB ligands (XP docking pose) with IFITM3

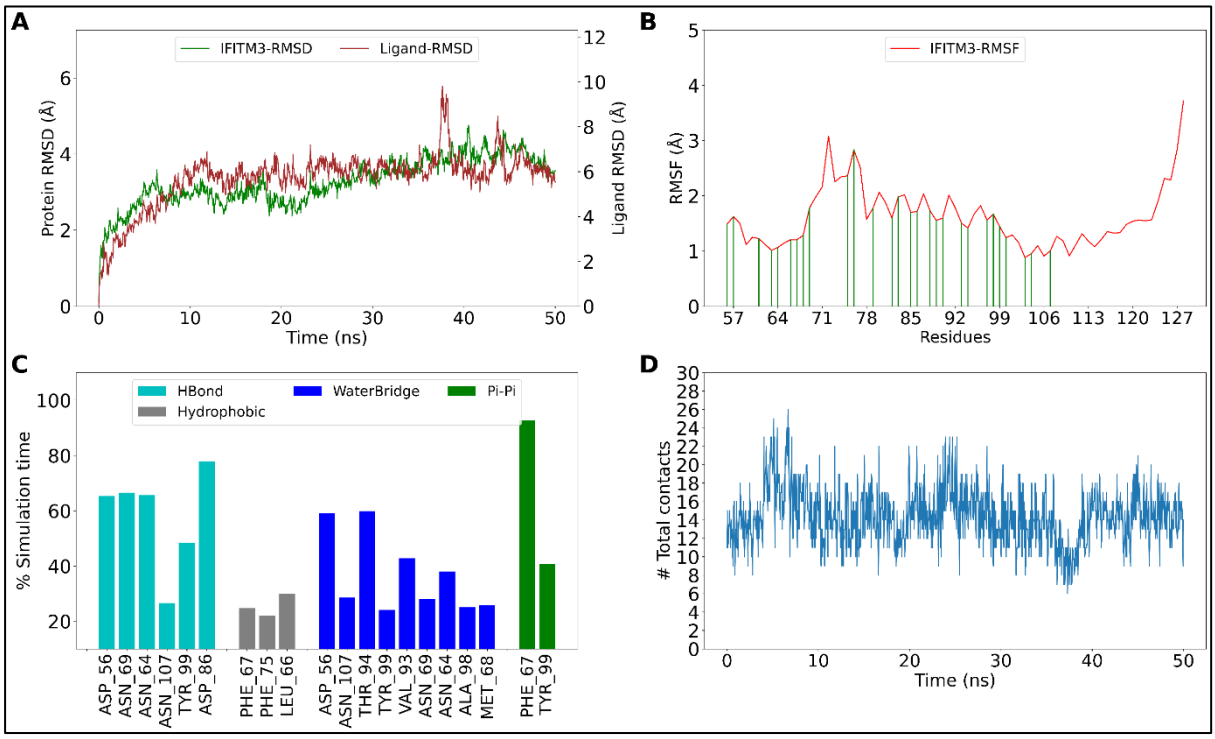


Figure S21: MD simulation of IFITM3-SN00249458 complex (**A**) RMSD of IFITM3 and SN00249458 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00249458 (**C**) Interactions between IFITM3 and SN00249458 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00249458 and IFITM3

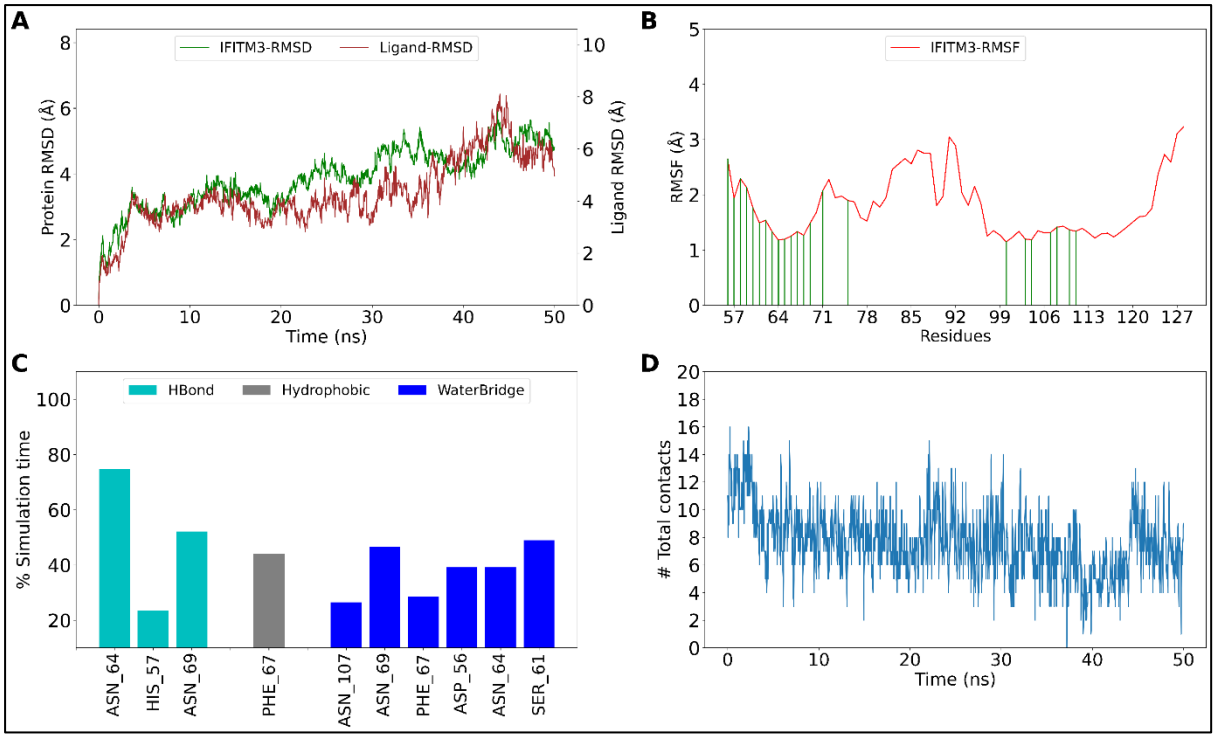


Figure S22: MD simulation of IFITM3-SN00342783 complex (**A**) RMSD of IFITM3 and SN00342783 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00342783 (**C**) Interactions between IFITM3 and SN00342783 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00342783 and IFITM3

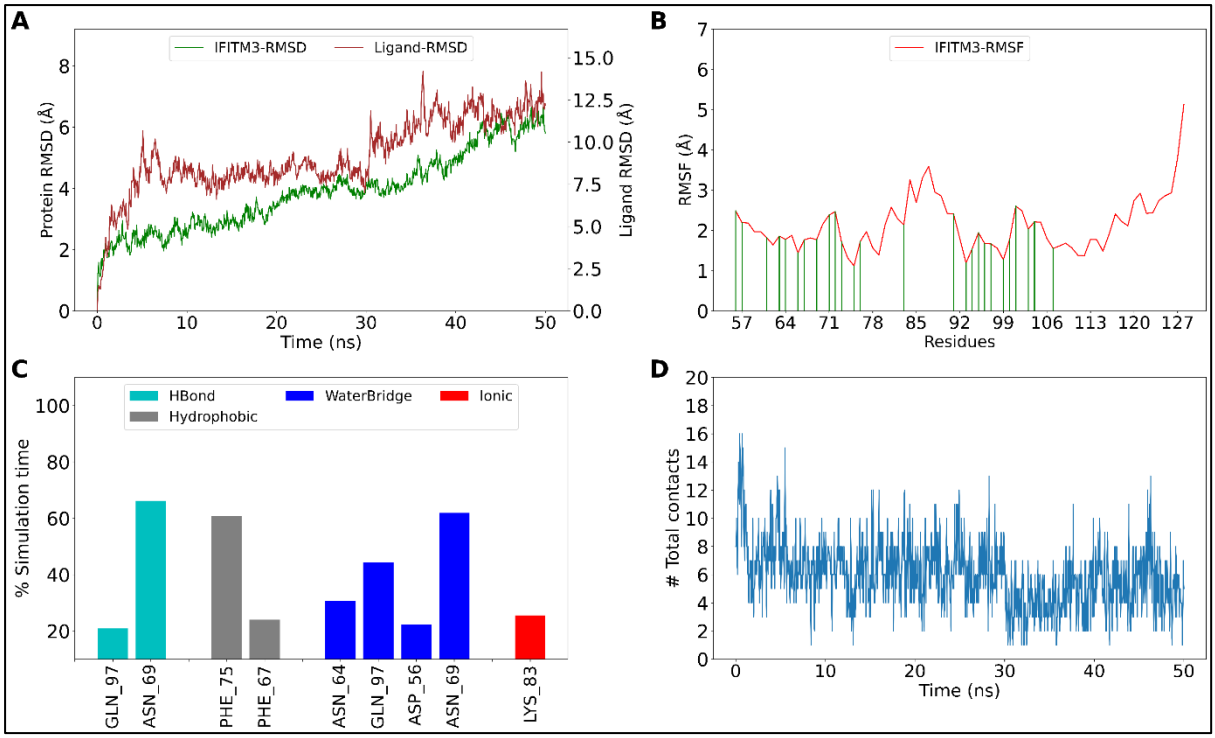


Figure S23: MD simulation of IFITM3-SN00328659 complex (**A**) RMSD of IFITM3 and SN00328659 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00328659 (**C**) Interactions between IFITM3 and SN00328659 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00328659 and IFITM3

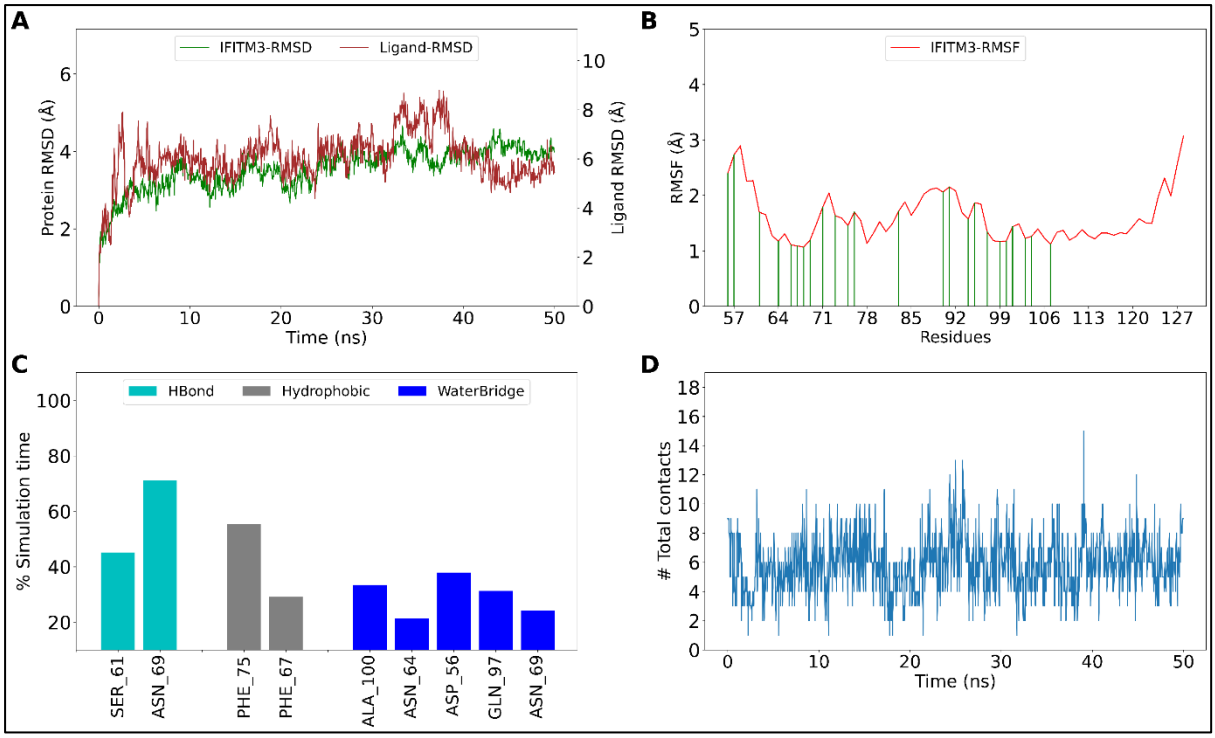


Figure S24: MD simulation of IFITM3-SN00226205 complex (**A**) RMSD of IFITM3 and SN00226205 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00226205 (**C**) Interactions between IFITM3 and SN00226205 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00226205 and IFITM3

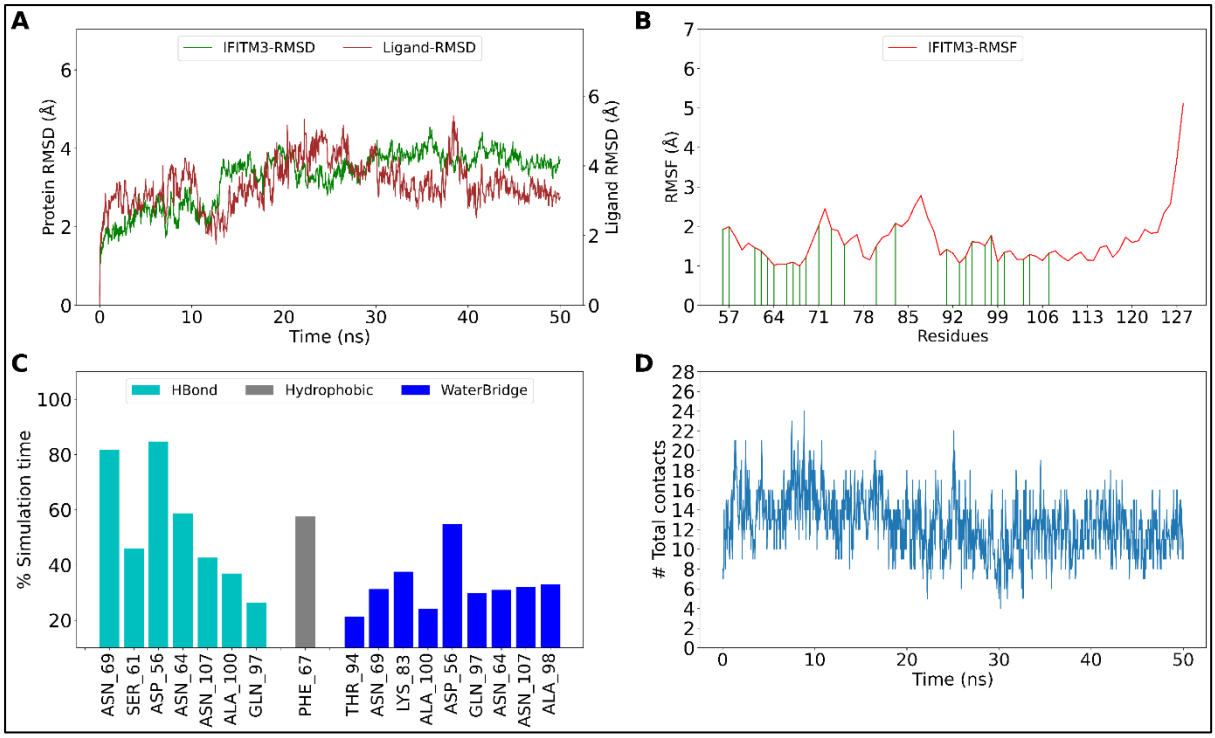


Figure S25: MD simulation of IFITM3-SN00244021complex (**A**) RMSD of IFITM3 and SN00244021 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00244021 (**C**) Interactions between IFITM3 and SN00244021 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00244021 and IFITM3

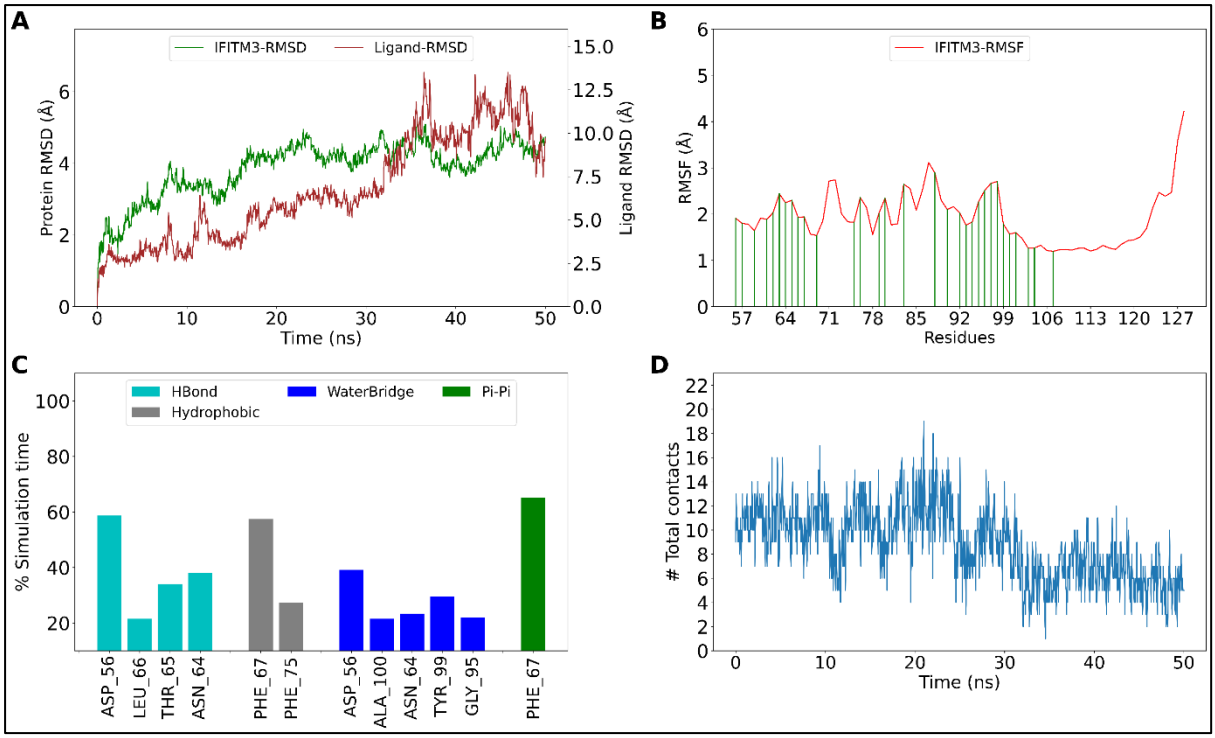


Figure S26: MD simulation of IFITM3-SN00164639 complex (**A**) RMSD of IFITM3 and SN00164639 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00164639 (**C**) Interactions between IFITM3 and SN00164639 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00164639 and IFITM3

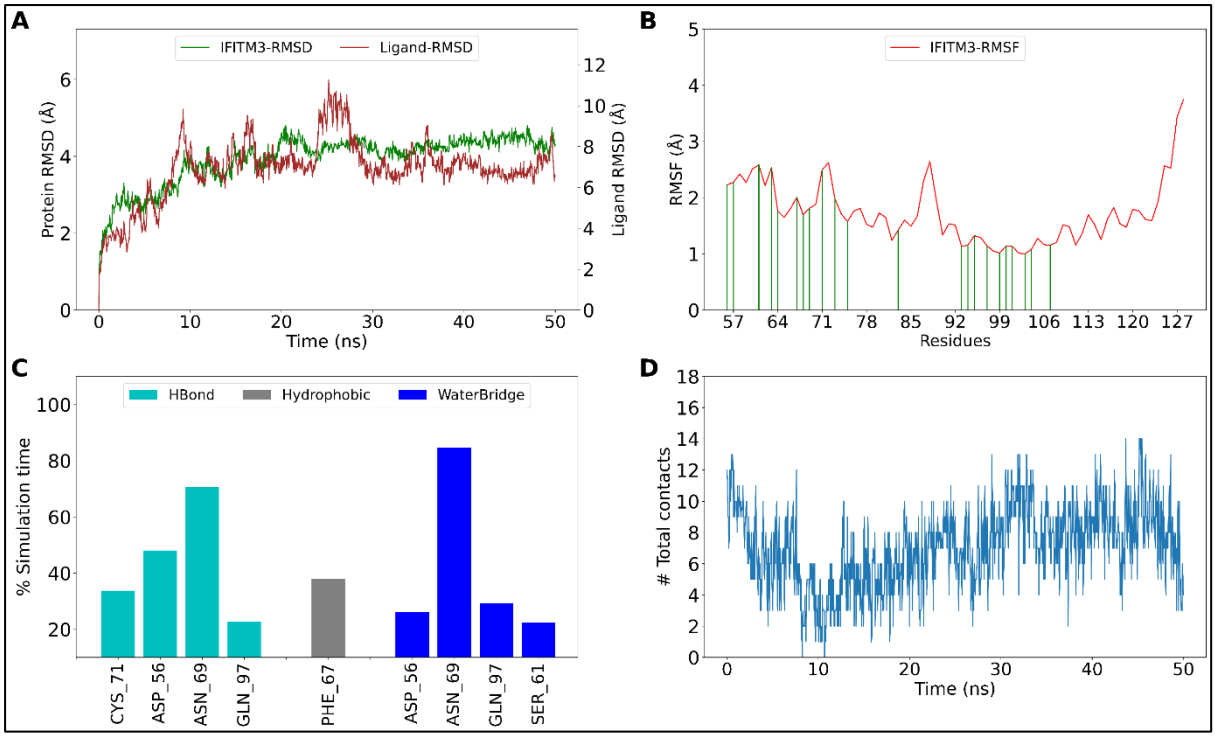


Figure S27: MD simulation of IFITM3-Periseoside D (SN00265483) complex (**A**) RMSD of IFITM3 and Periseoside D fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Periseoside D (**C**) Interactions between IFITM3 and Periseoside D as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Periseoside D and IFITM3

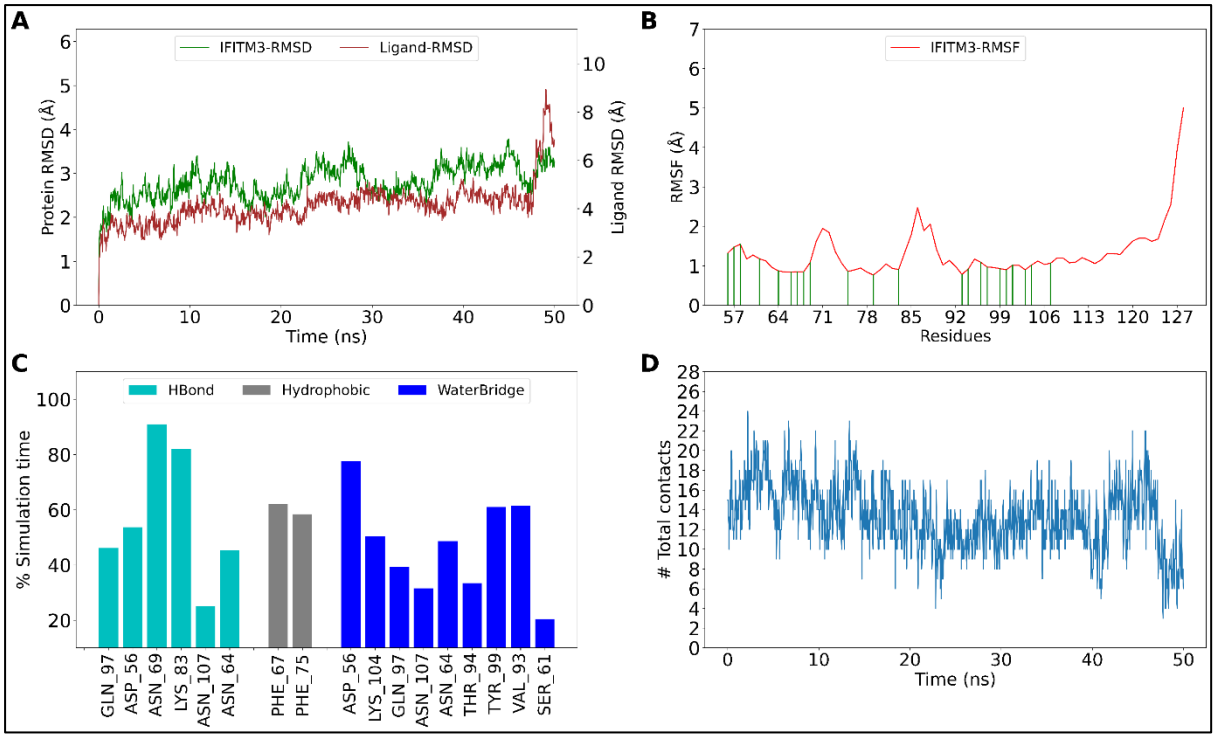


Figure S28: MD simulation of IFITM3-Pharbitic acid D (SN00274576) complex (**A**) RMSD of IFITM3 and Pharbitic acid D fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Pharbitic acid D (**C**) Interactions between IFITM3 and Pharbitic acid D as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Pharbitic acid D and IFITM3

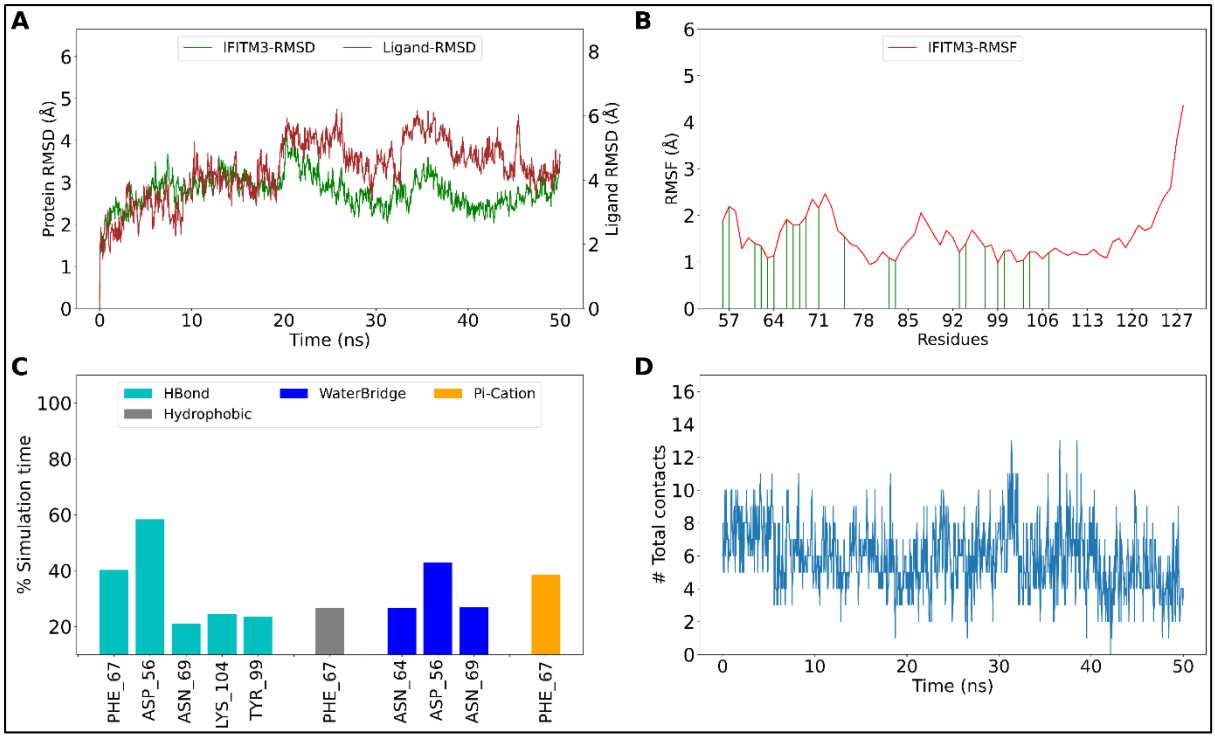


Figure S29: MD simulation of IFITM3-Pseudoceratinazole A (SN00287660) complex (**A**) RMSD of IFITM3 and Pseudoceratinazole A fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Pseudoceratinazole A (**C**) Interactions between IFITM3 and Pseudoceratinazole A as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Pseudoceratinazole A and IFITM3

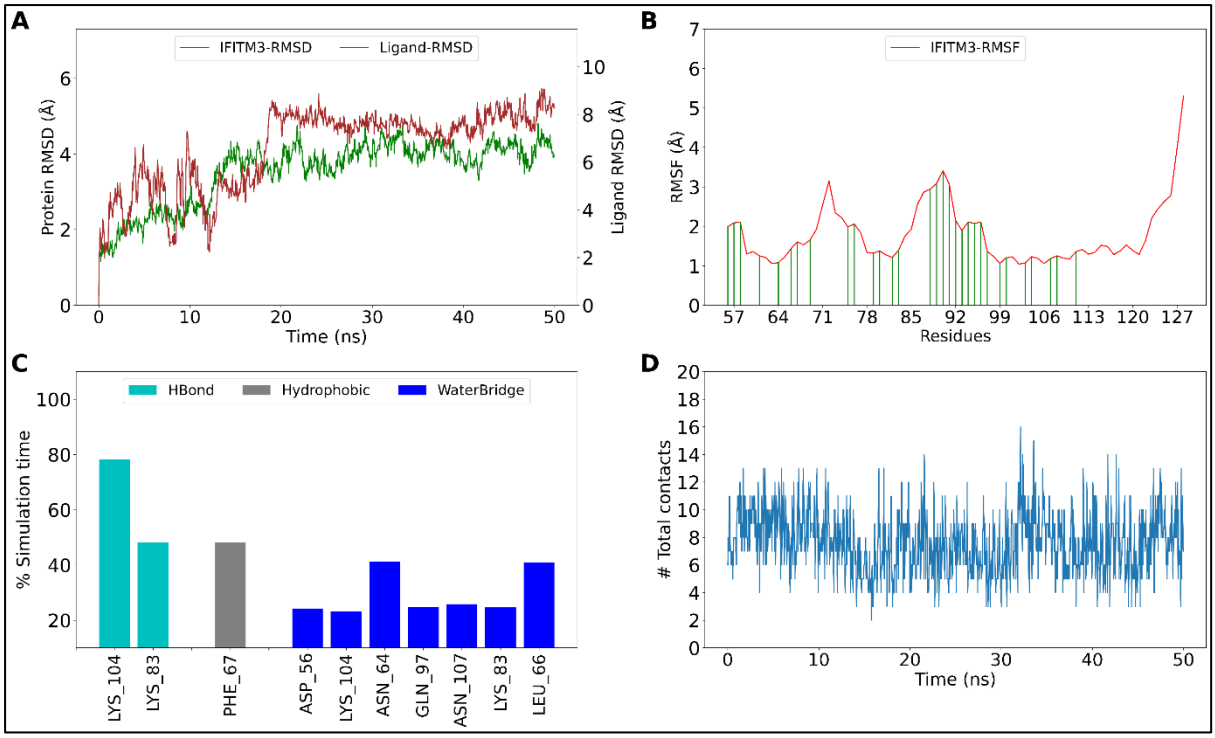


Figure S30: MD simulation of IFITM3-Parishin A (SN00379347) complex (**A**) RMSD of IFITM3 and Parishin A fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Parishin A (**C**) Interactions between IFITM3 and Parishin A as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Parishin A and IFITM3

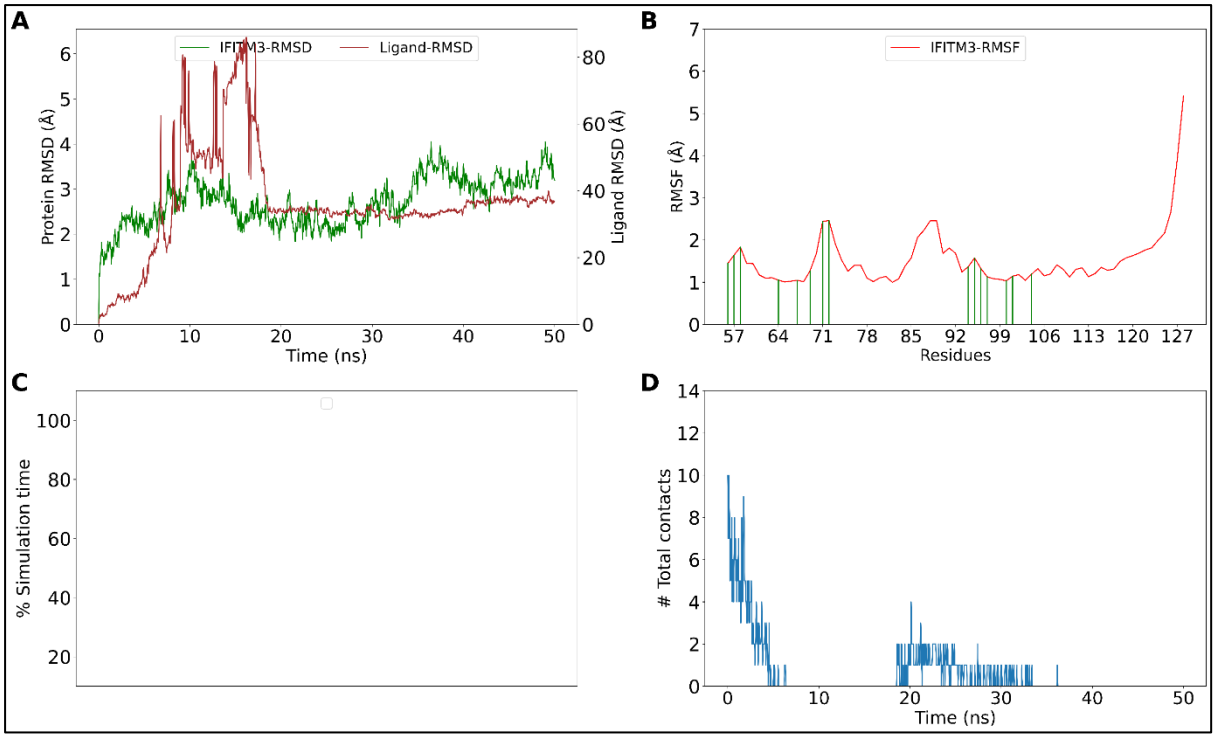


Figure S31: MD simulation of IFITM3-Hosenkoside B (SN00306006) complex (**A**) RMSD of IFITM3 and Hosenkoside B fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Hosenkoside B (**C**) Interactions between IFITM3 and Hosenkoside B as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Hosenkoside B and IFITM3

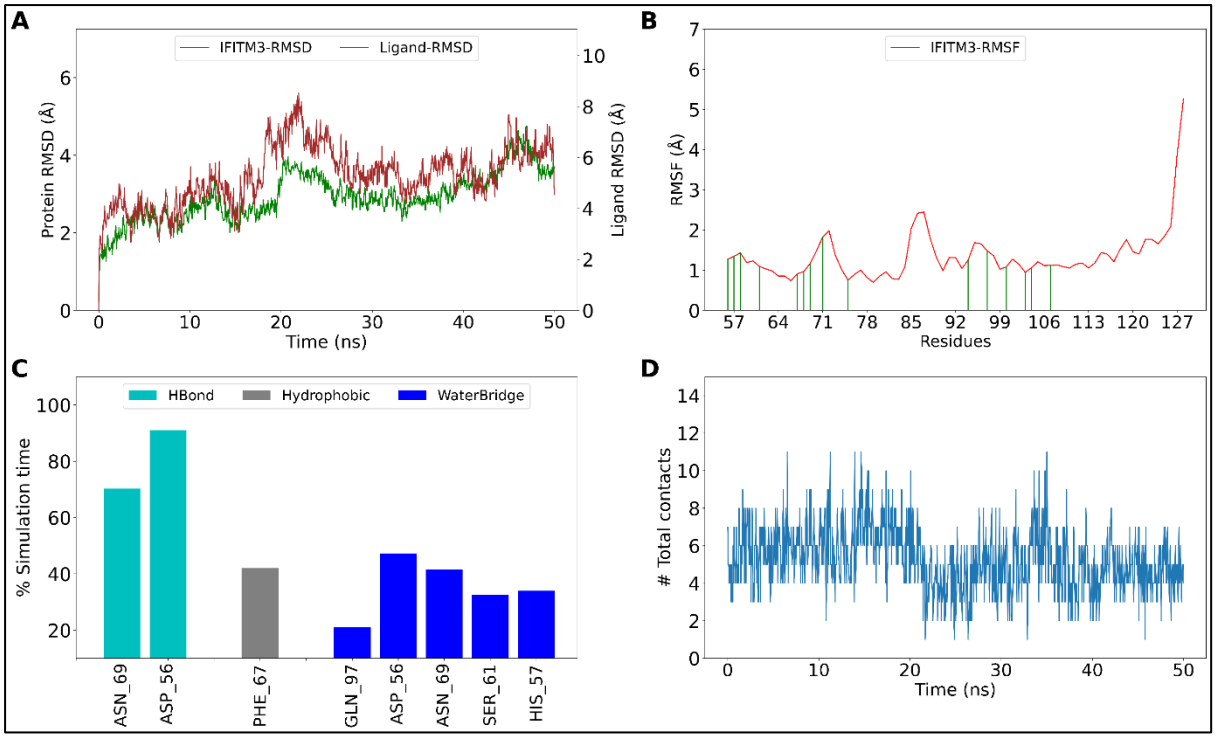


Figure S32: MD simulation of IFITM3-Anguivioside B (SN00374092) complex (**A**) RMSD of IFITM3 and Anguivioside B fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Anguivioside B (**C**) Interactions between IFITM3 and Anguivioside B as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Anguivioside B and IFITM3

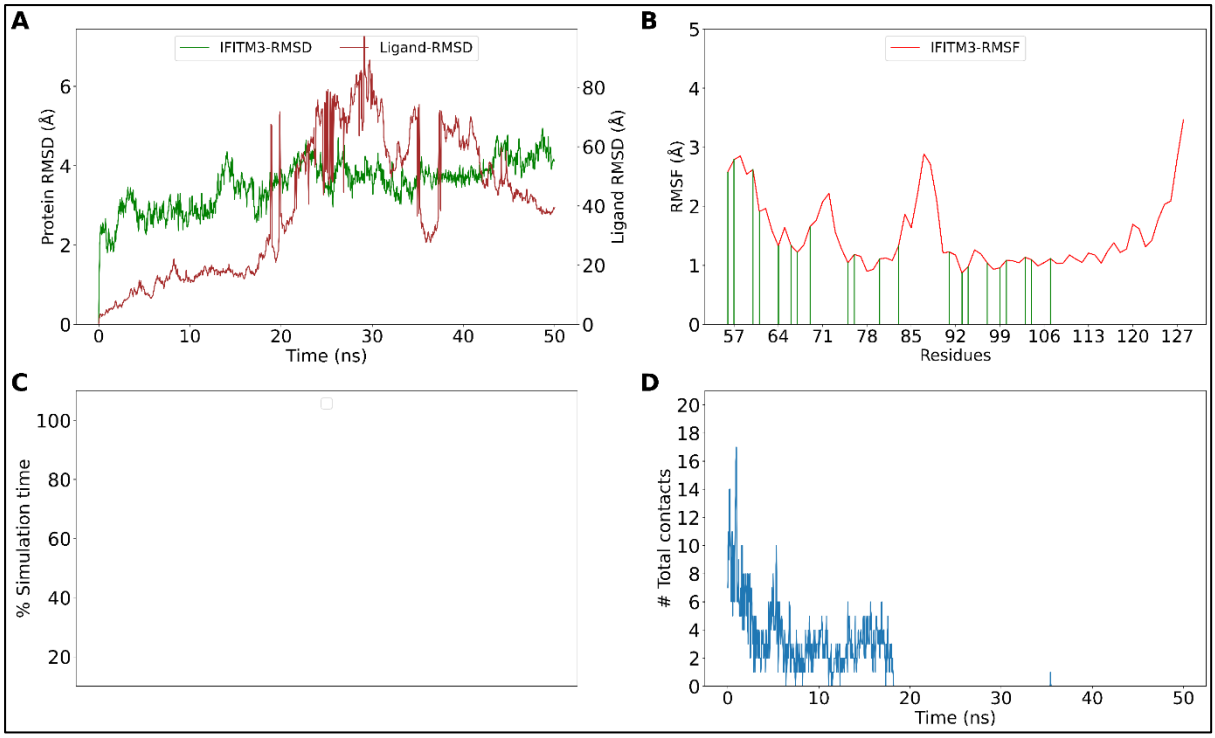


Figure S33: MD simulation of IFITM3-Disporoside D (SN00274346) complex (**A**) RMSD of IFITM3 and Disporoside D fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Disporoside D (**C**) Interactions between IFITM3 and Disporoside D as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Disporoside D and IFITM3

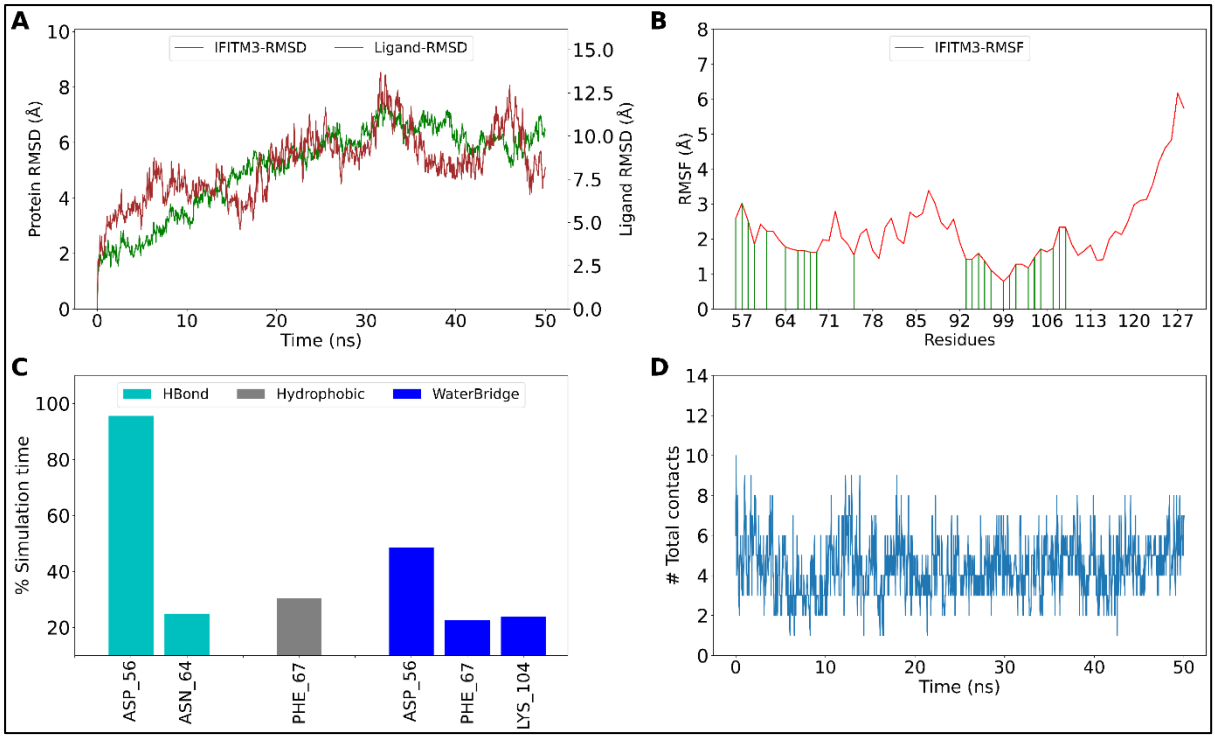


Figure S34: MD simulation of IFITM3-Broussonetine Q (SN00226238) complex (**A**) RMSD of IFITM3 and Broussonetine Q fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Broussonetine Q (**C**) Interactions between IFITM3 and Broussonetine Q as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Broussonetine Q and IFITM3

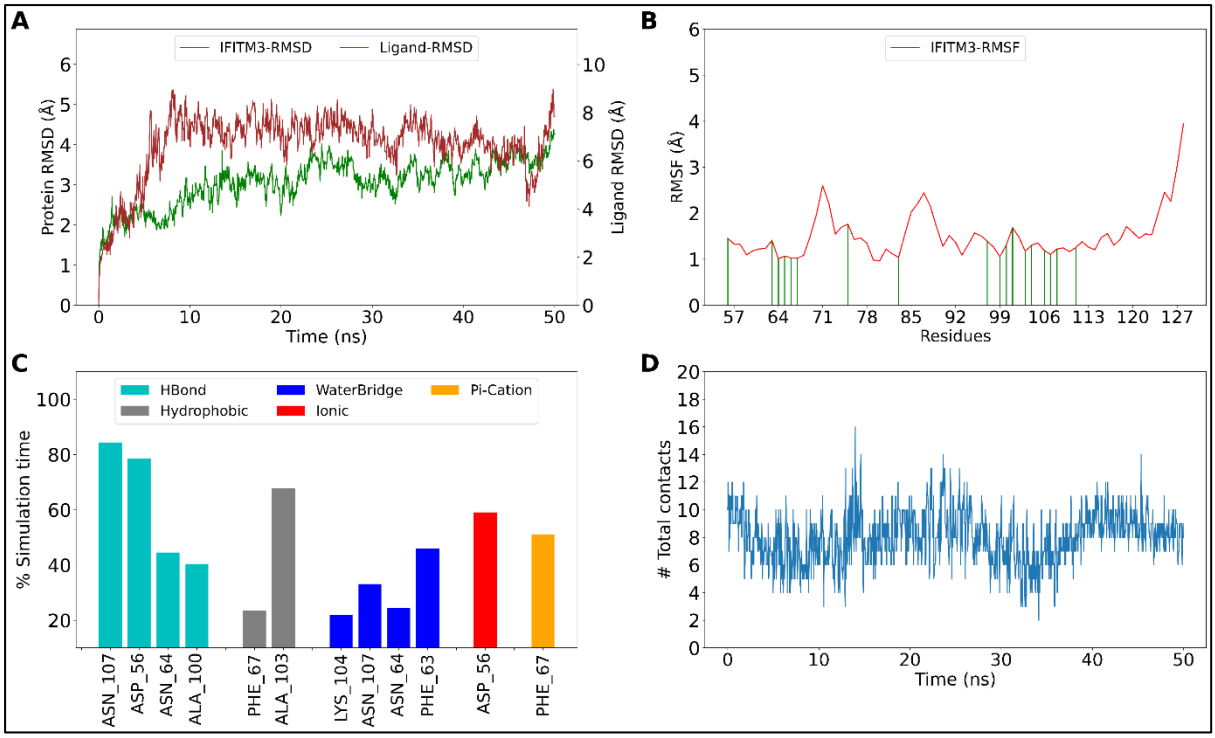


Figure S35: MD simulation of IFITM3-Nazumamide A (SN00242218) complex (**A**) RMSD of IFITM3 and Nazumamide A fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Nazumamide A (**C**) Interactions between IFITM3 and Nazumamide A as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Nazumamide A and IFITM3

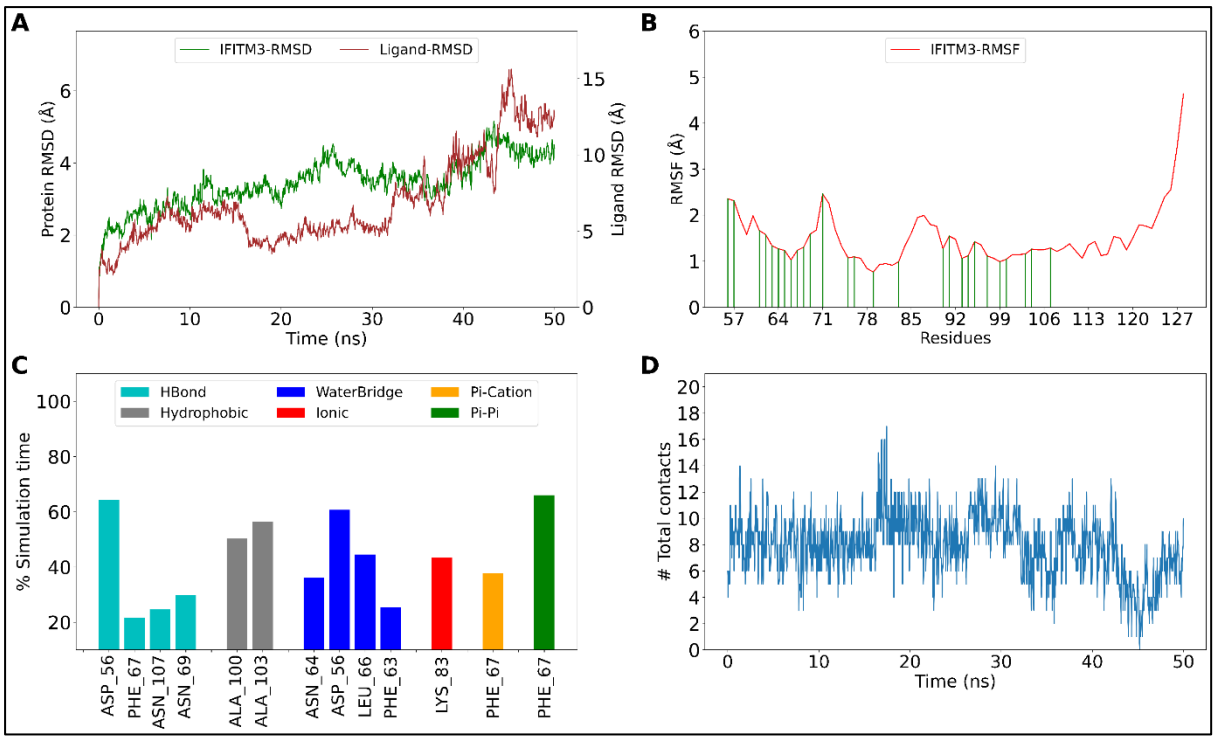


Figure S36: MD simulation of IFITM3-Kukoamine A (SN00226669) complex (**A**) RMSD of IFITM3 and Kukoamine A fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Kukoamine A (**C**) Interactions between IFITM3 and Kukoamine A as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Kukoamine A and IFITM3

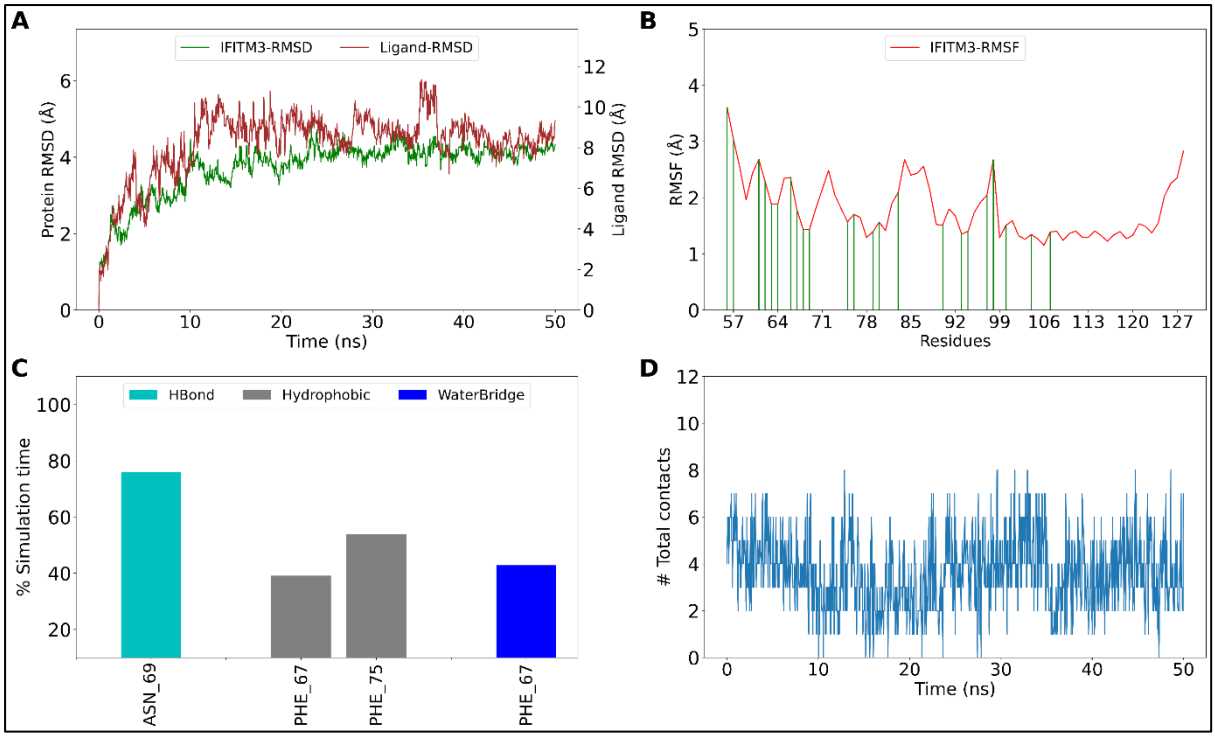


Figure S37: MD simulation of IFITM3-Rhodilunancin A (SN00304961) complex (**A**) RMSD of IFITM3 and Rhodilunancin A fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Rhodilunancin A (**C**) Interactions between IFITM3 and Rhodilunancin A as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Rhodilunancin A and IFITM3

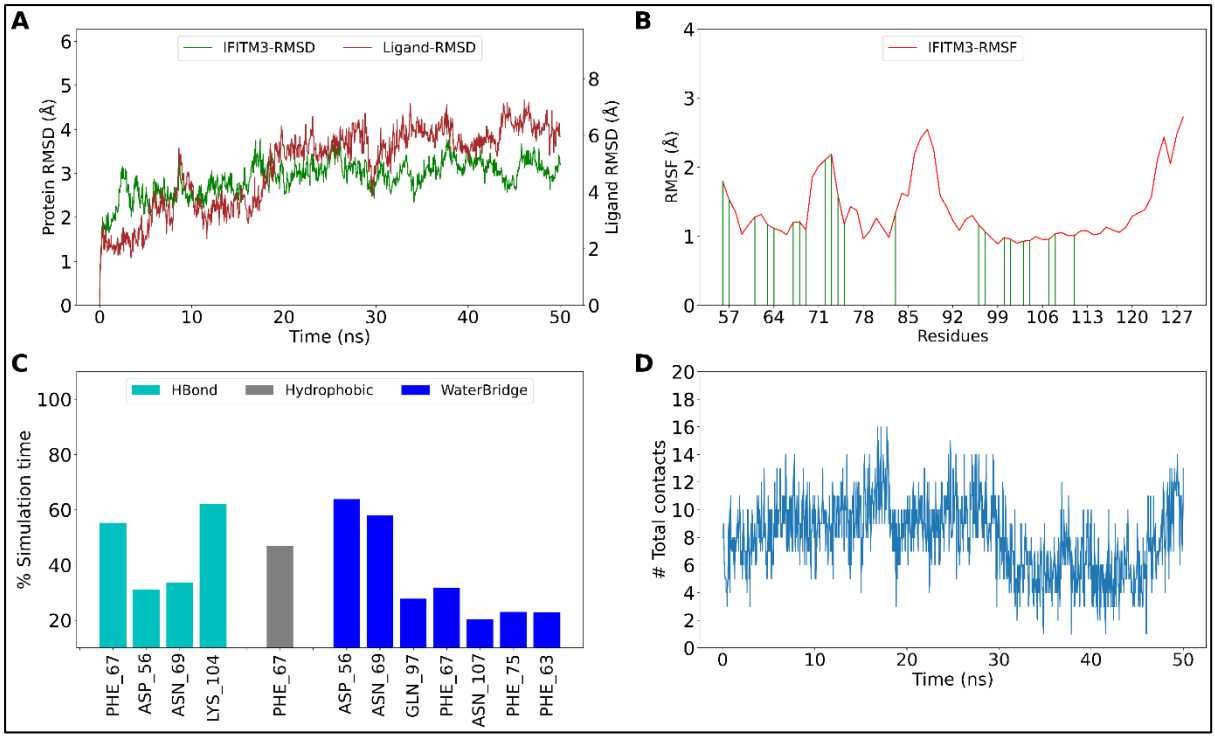


Figure S38: MD simulation of IFITM3-Caryocaroside II-12 (SN00318481) complex (**A**) RMSD of IFITM3 and Caryocaroside II-12 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Caryocaroside II-12 (**C**) Interactions between IFITM3 and Caryocaroside II-12 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Caryocaroside II-12 and IFITM3

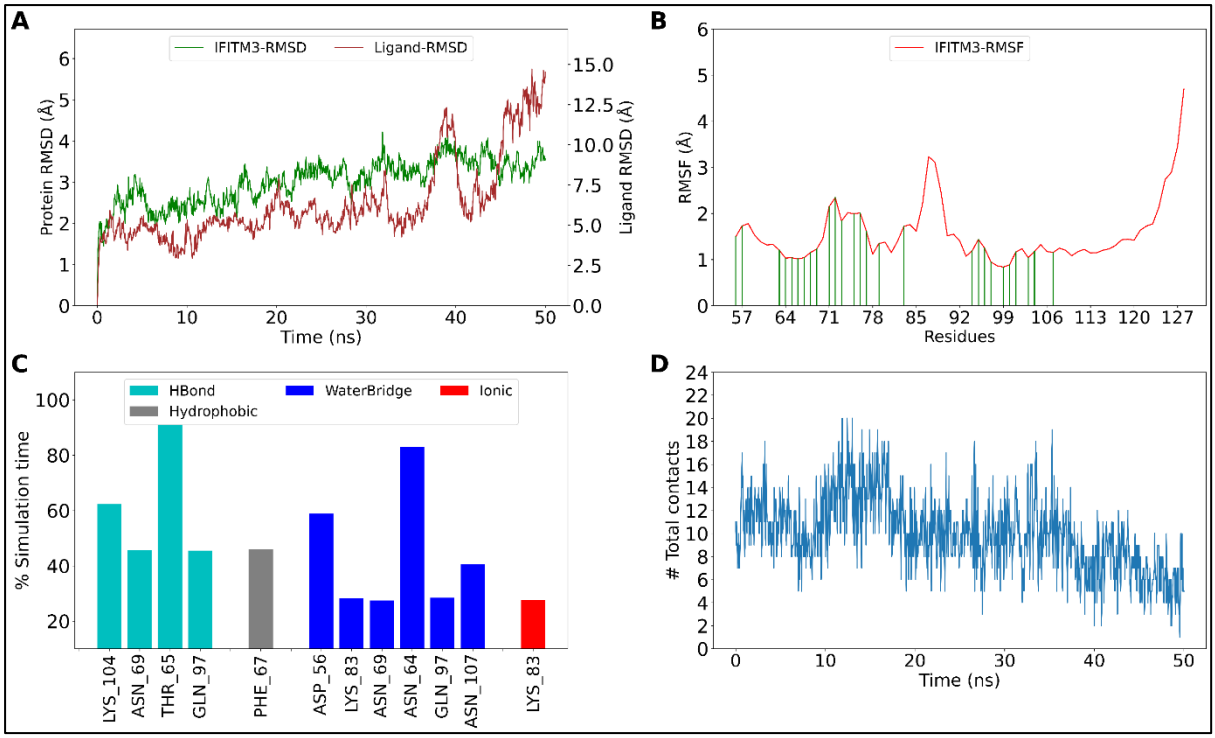


Figure S39: MD simulation of IFITM3-SN00239590 complex (**A**) RMSD of IFITM3 and SN00239590 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00239590 (**C**) Interactions between IFITM3 and SN00239590 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00239590 and IFITM3

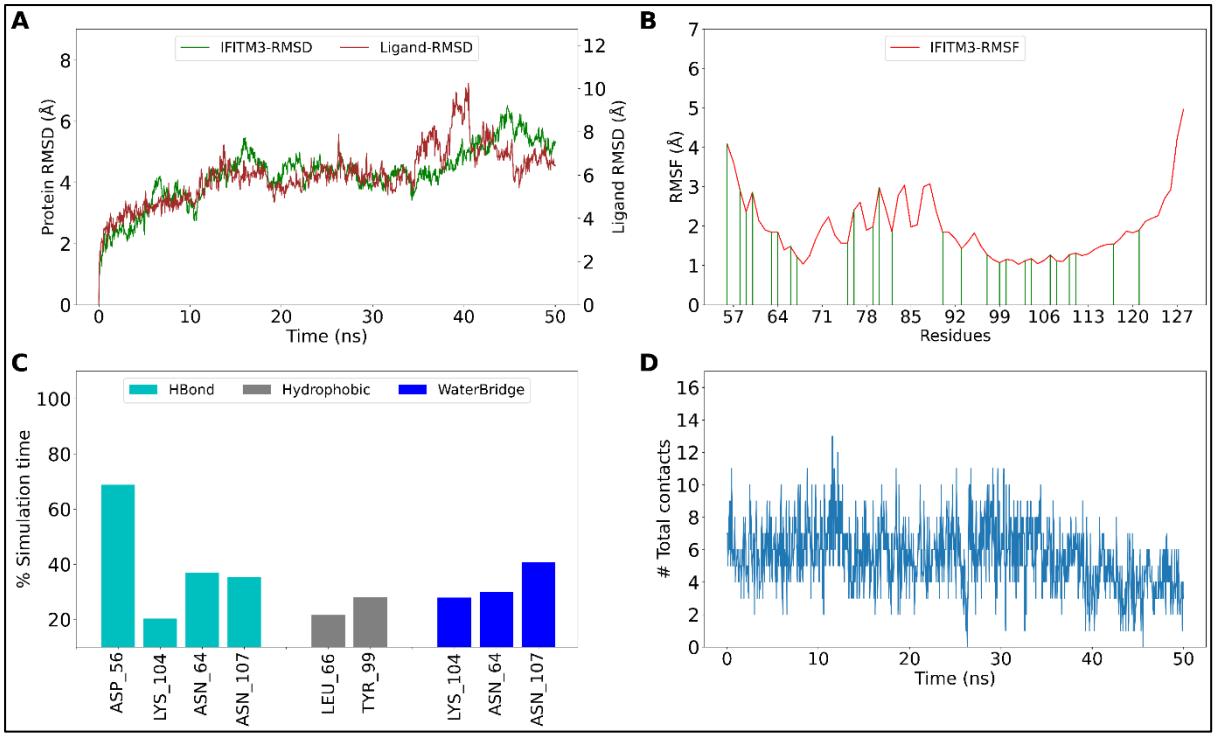


Figure S40: MD simulation of IFITM3-SN00323932 complex (**A**) RMSD of IFITM3 and SN00323932 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00323932 (**C**) Interactions between IFITM3 and SN00323932 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00323932 and IFITM3

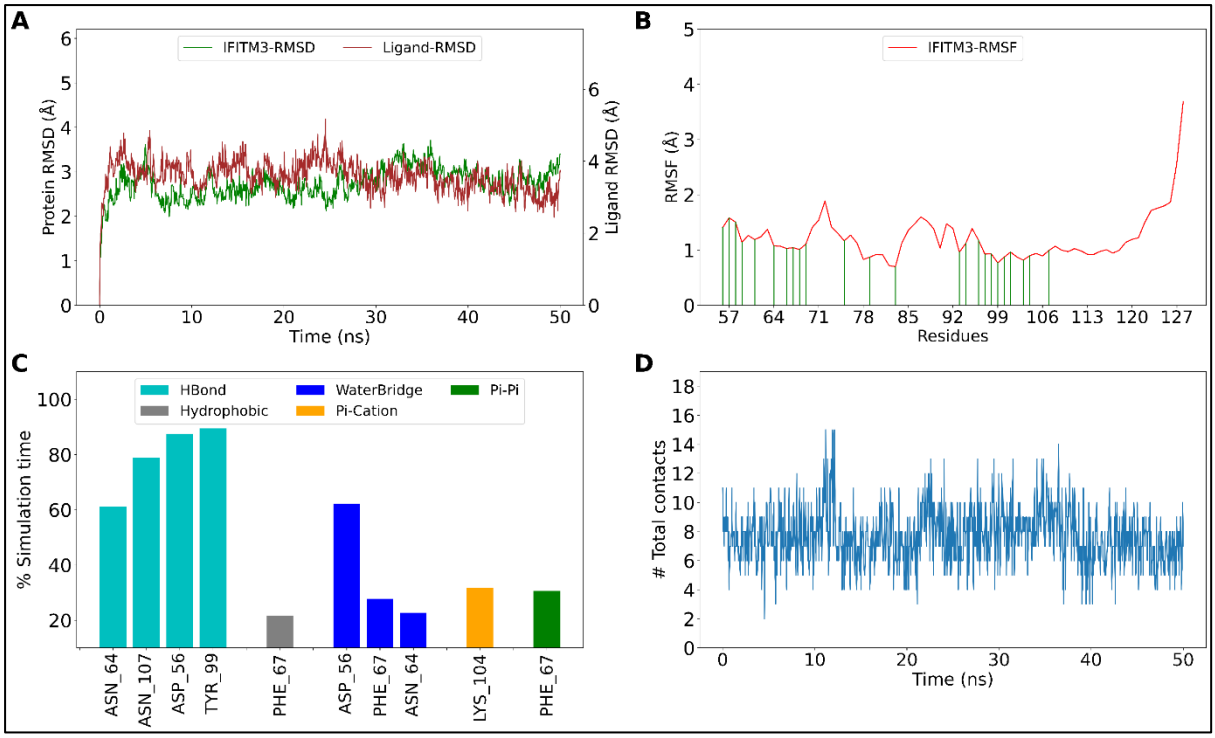


Figure S41: MD simulation of IFITM3-SN00286991 complex (**A**) RMSD of IFITM3 and SN00286991 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00286991 (**C**) Interactions between IFITM3 and SN00286991 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00286991 and IFITM3

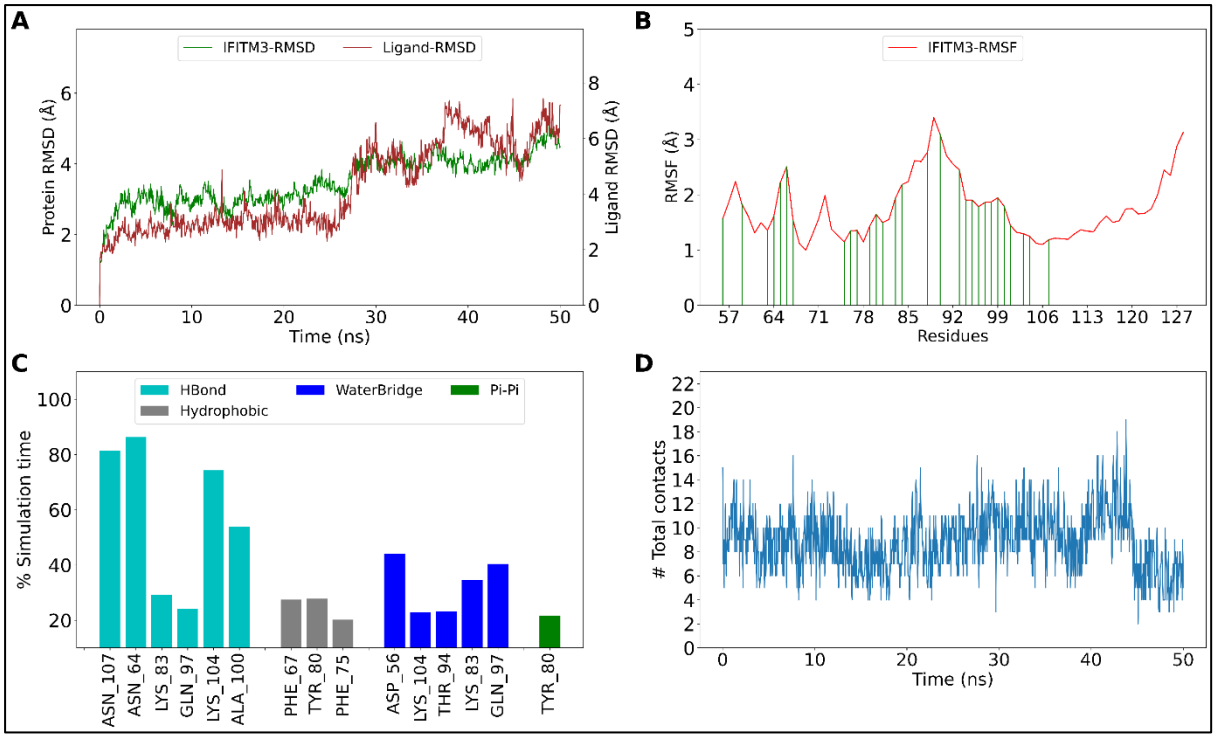


Figure S42: MD simulation of IFITM3-SN00280809 complex (**A**) RMSD of IFITM3 and SN00280809 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00280809 (**C**) Interactions between IFITM3 and SN00280809 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00280809 and IFITM3

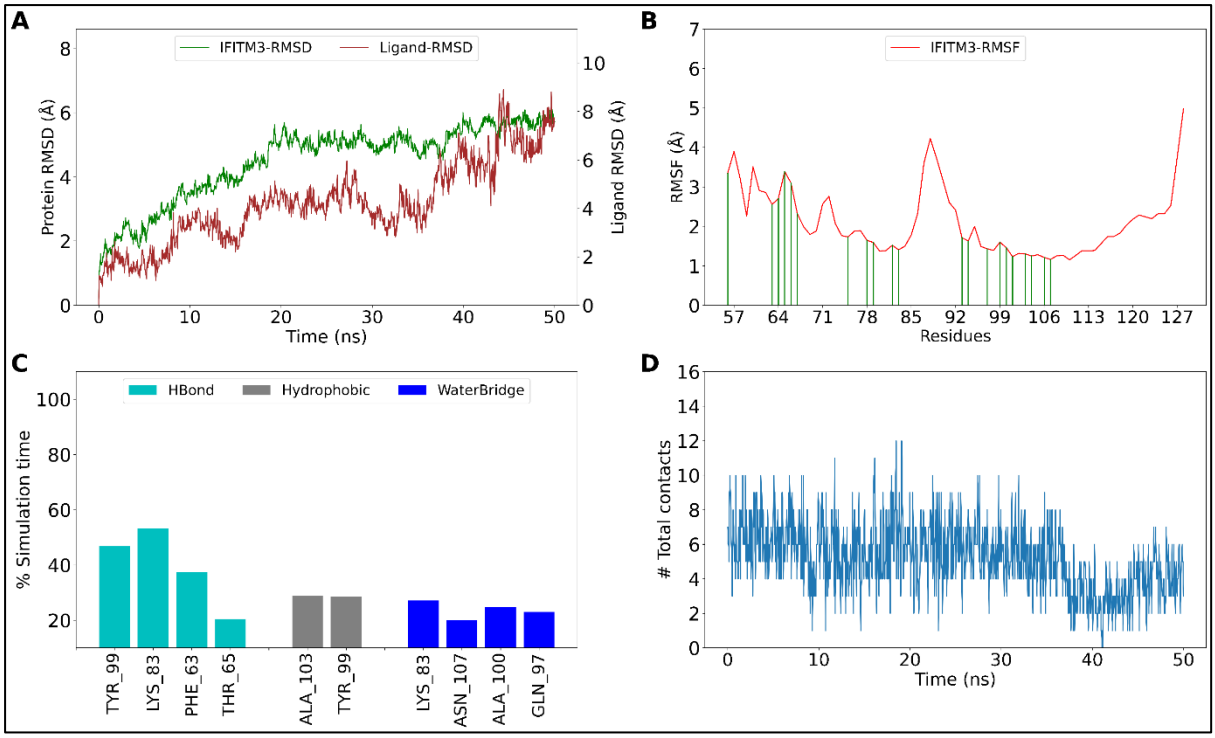


Figure S43: MD simulation of IFITM3-SN00029983 complex (**A**) RMSD of IFITM3 and SN00029983 fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with SN00029983 (**C**) Interactions between IFITM3 and SN00029983 as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between SN00029983 and IFITM3

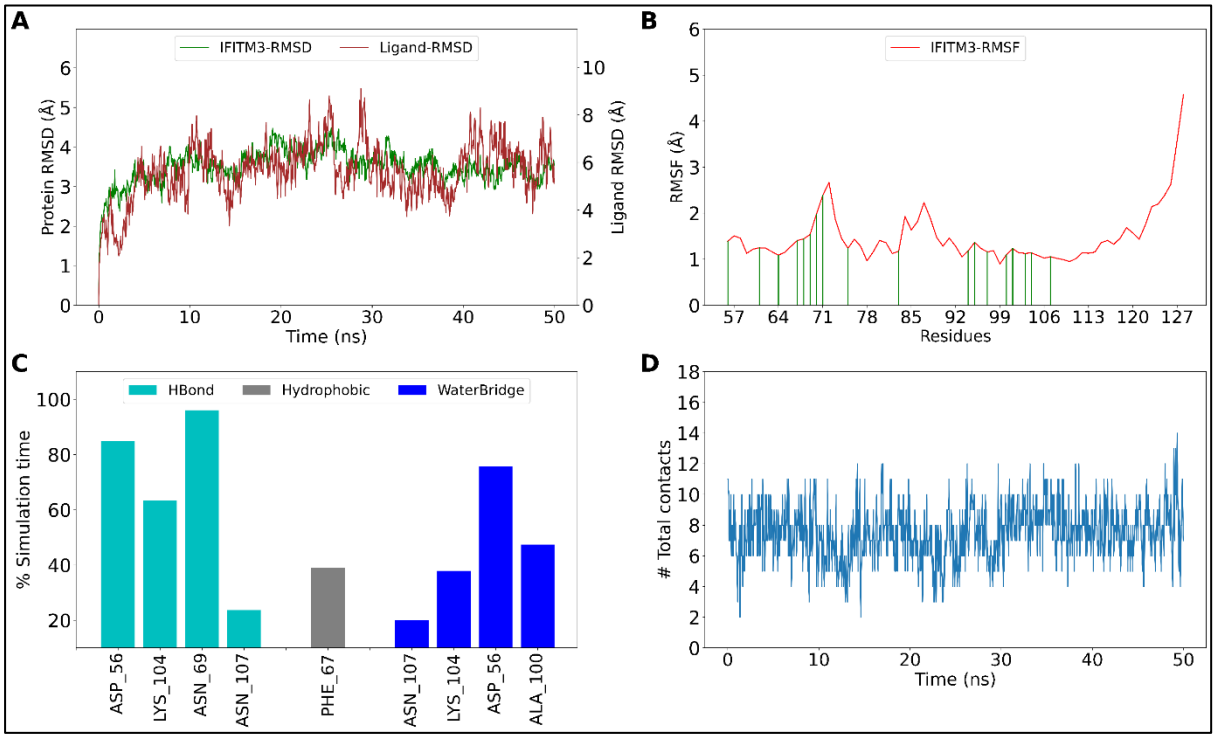


Figure S44: MD simulation of IFITM3-Amphotericin B complex (**A**) RMSD of IFITM3 and Amphotericin B fit on IFITM3 (Ligand-RMSD) (**B**) RMSF of IFITM3. Green lines indicate interactions with Amphotericin B (**C**) Interactions between IFITM3 and Amphotericin B as percentage of simulation time. Interactions that persist for more than 20% of simulation time have been shown (**D**) Total contacts (includes all interactions) between Amphotericin B and IFITM3