Electronic Supplementary Material (ESI) for RSC Advances.

Discovery of 8-Prenylnaringenin from Hop (*Humulus lupulus L.*) as a potent Monoacylglycerol Lipase Inhibitor for Treatments of Neuroinflammation and Alzheimer's Disease

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Supporting information

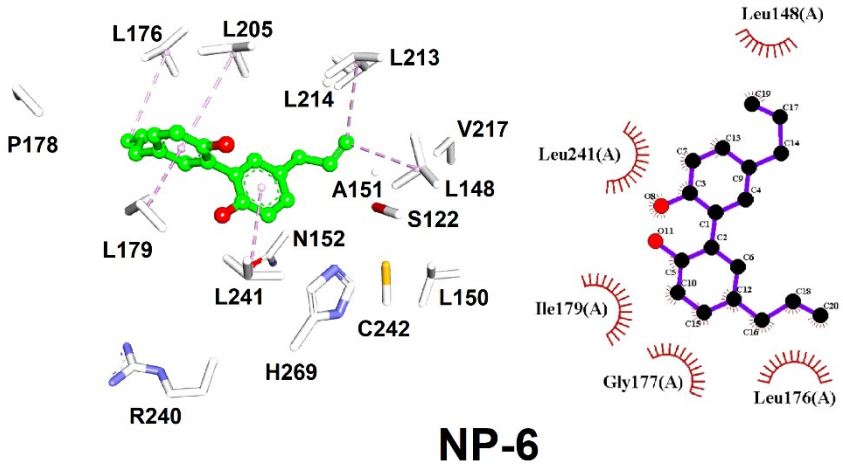

Fig. S1 The molecular interactions of hMAGL-NP-6. (The inhibitor was shown in ball-and-sticks (green); the active site residues were presented as white sticks. The dash lines indicate hydrogen-bond (green) and hydrophobic interactions (light-pink).)

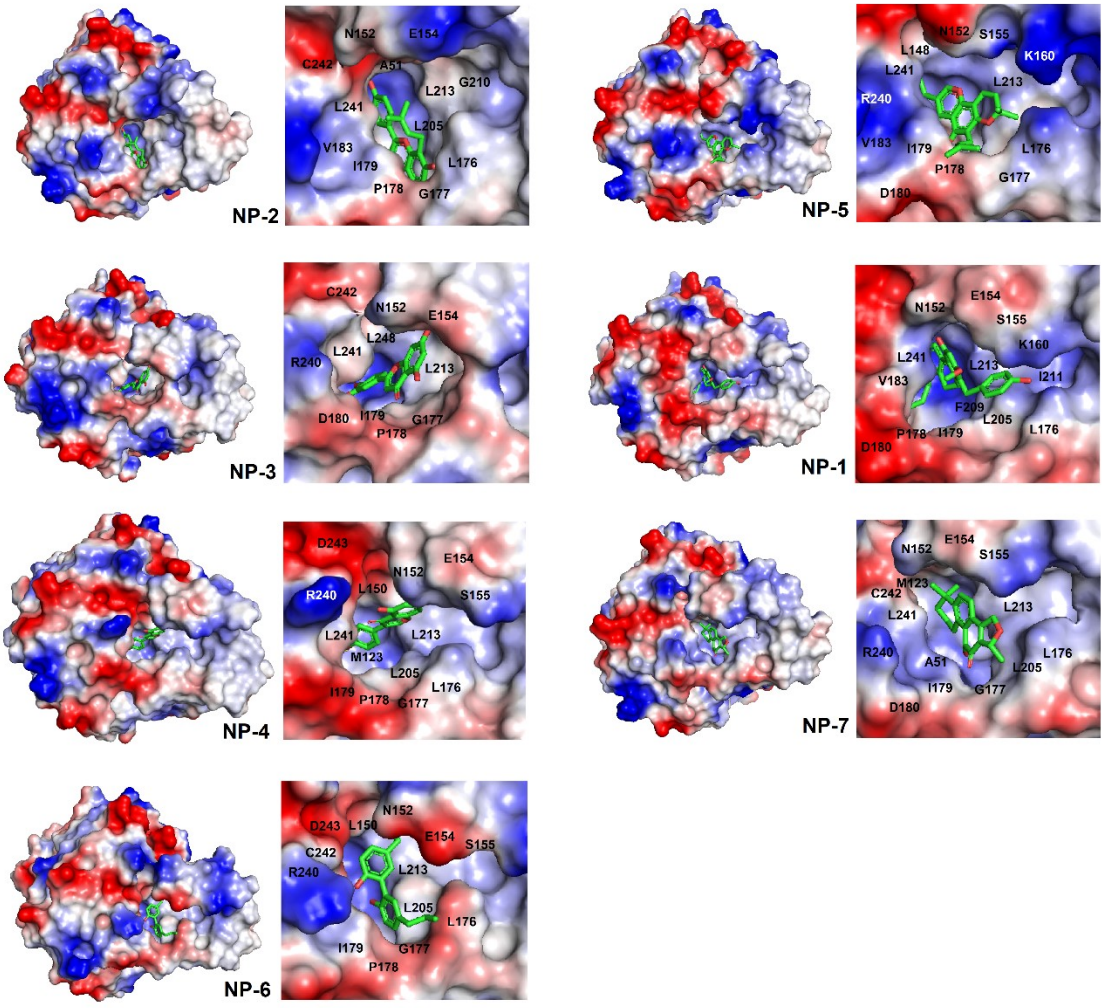

Figure S2. The orientations of the identified inhibitors in the active site of hMAGL. The structure of hMAGL is presented as electrostatic surface potential map and the inhibitors are shown in sticks (green). The active site residues which surround the inhibitors are labeled. The figure was made by using PyMOL2.3.4. (http:// www.pymol.org).

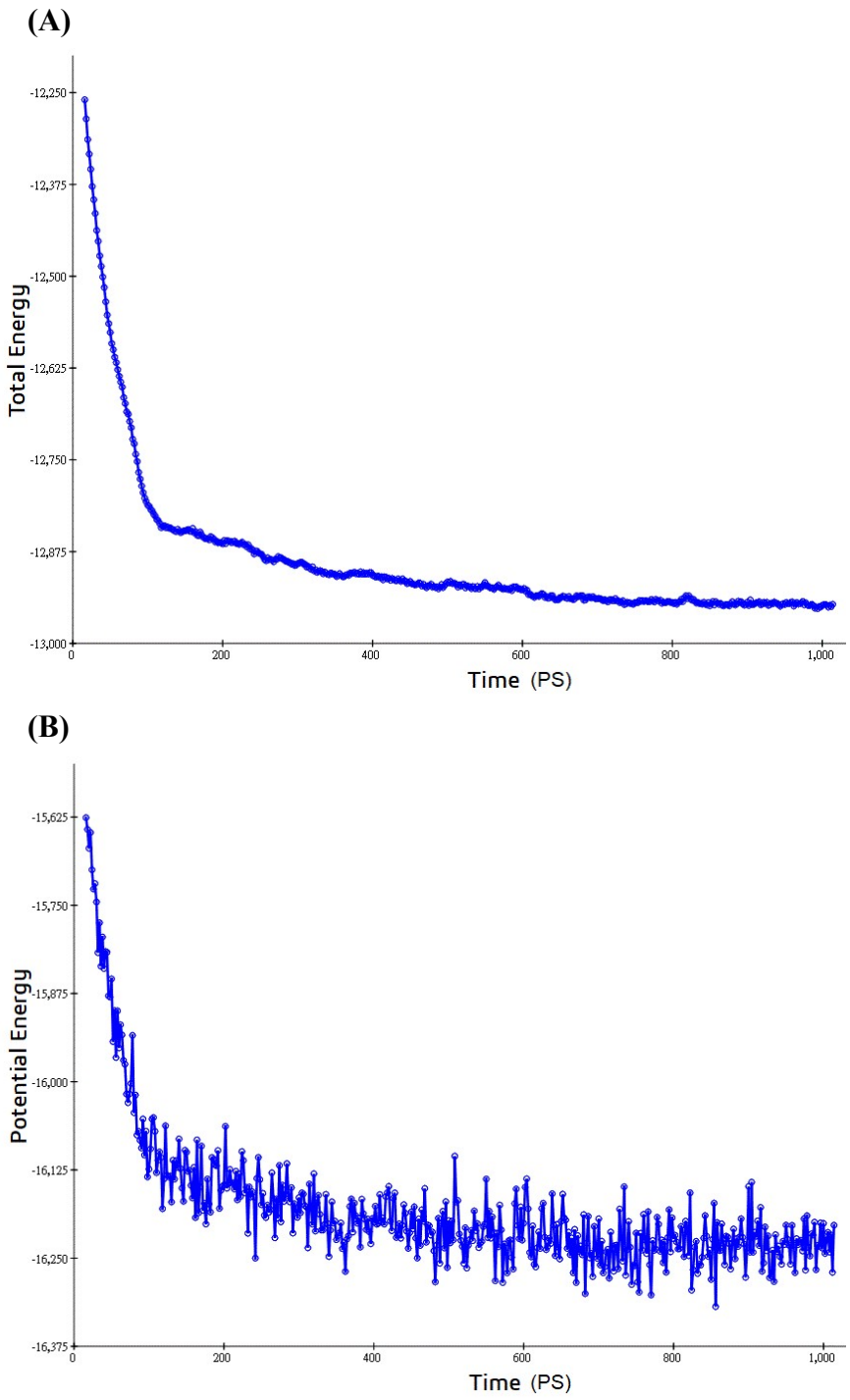

Figure S3. The molecular dynamics simulations of hMAGL-NP-1 complex.
(A) The total energy as a function of time. (B) The potential energy as a function of time.

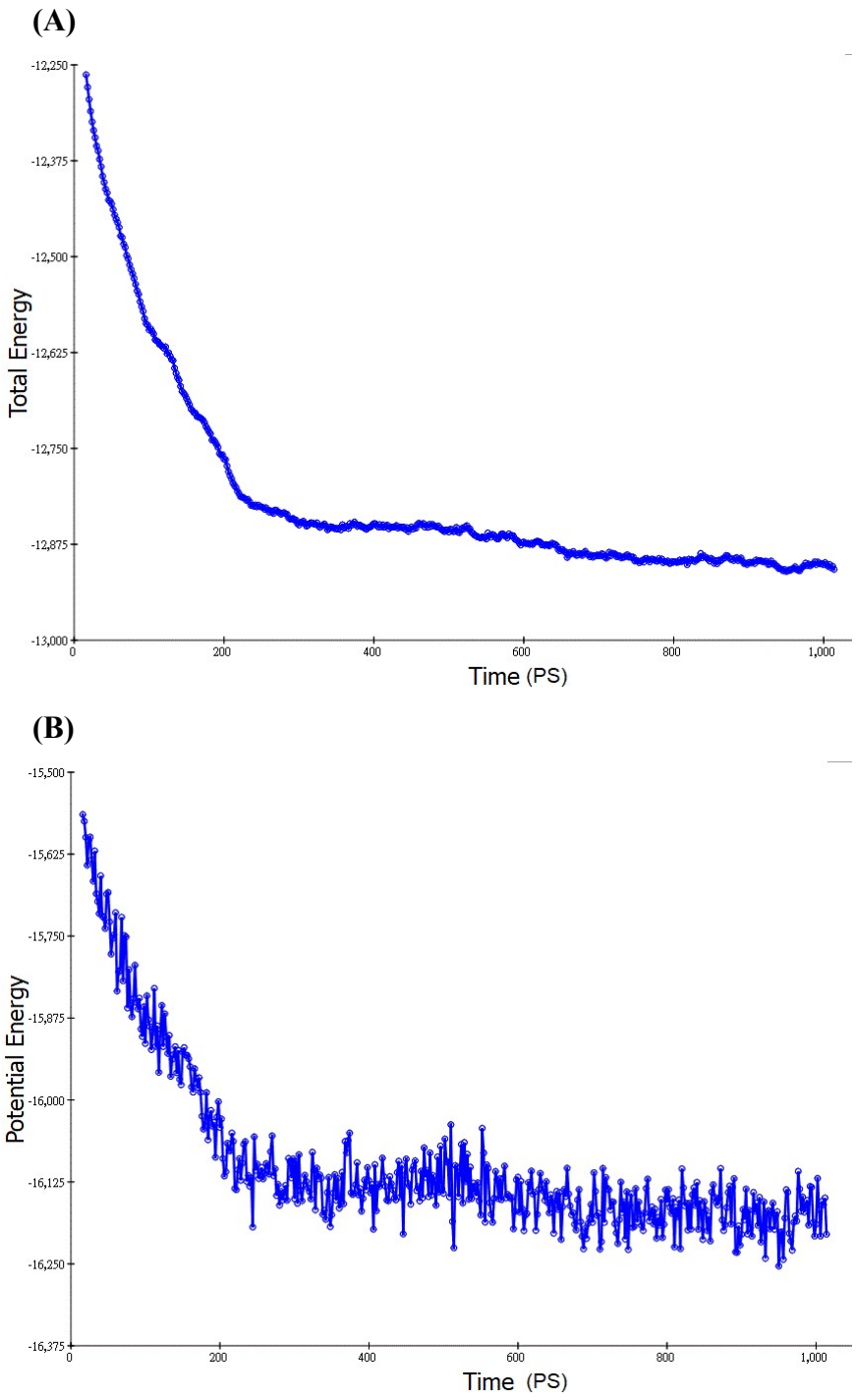

Figure S4. The molecular dynamics simulations of hMAGL-NP-2 complex.

(A) The total energy as a function of time. (B) The potential energy as a function of time.

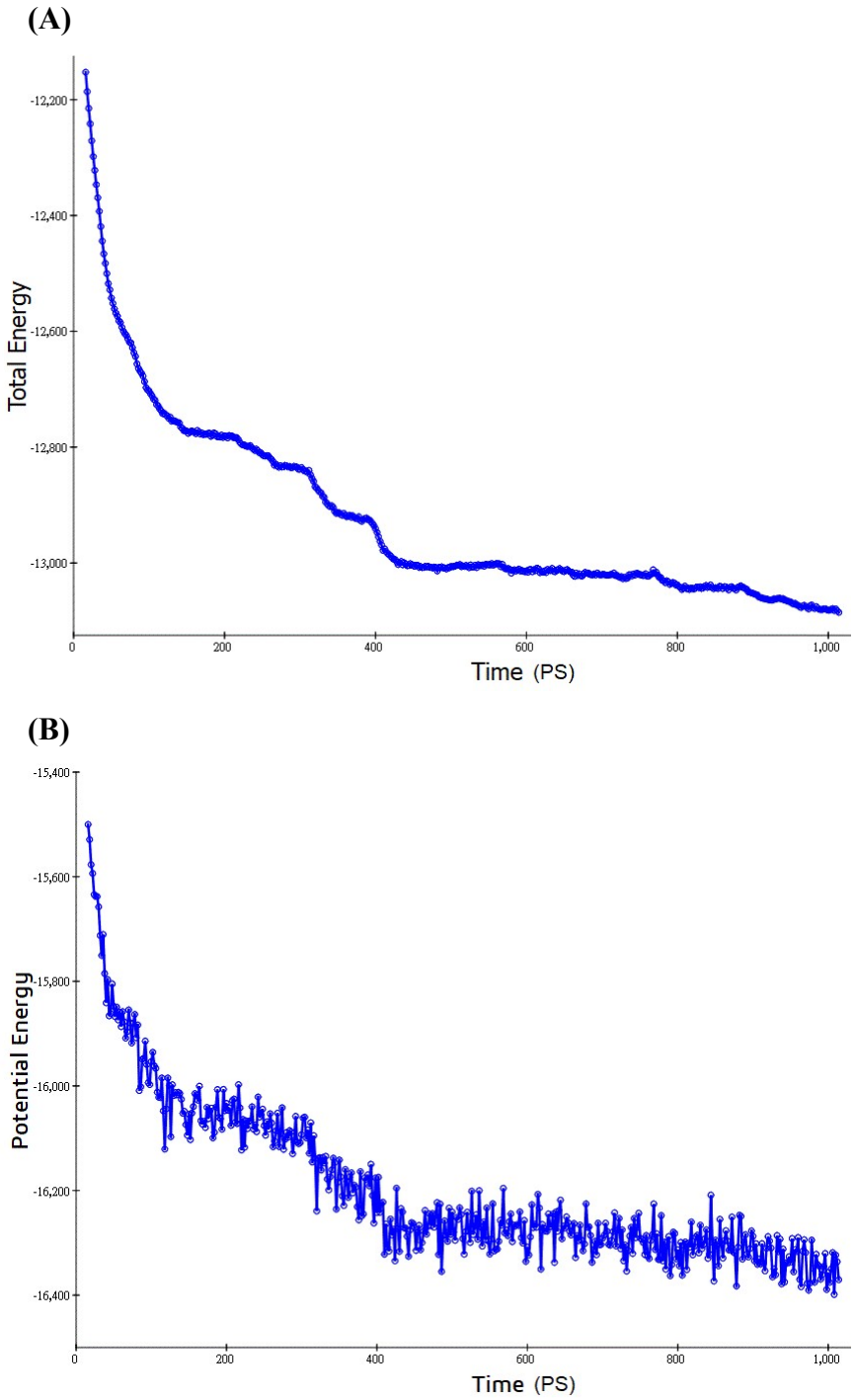

Figure S5. The molecular dynamics simulations of hMAGL-NP-3 complex.
(A) The total energy as a function of time. (B) The potential energy as a function of time.

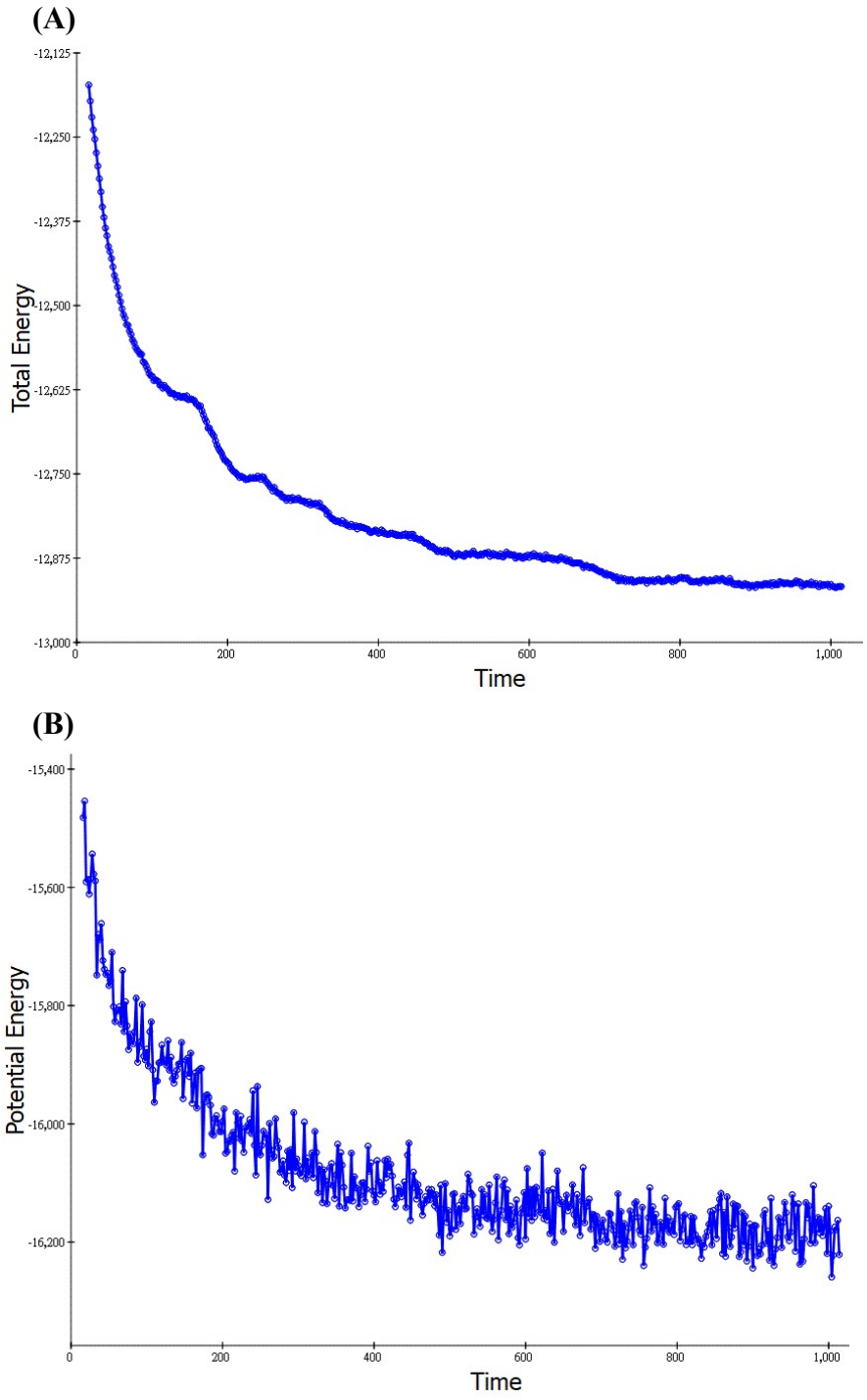

Figure S6. The molecular dynamics simulations of hMAGL-NP-4 complex.

(A) The total energy as a function of time. (B) The potential energy as a function of time.

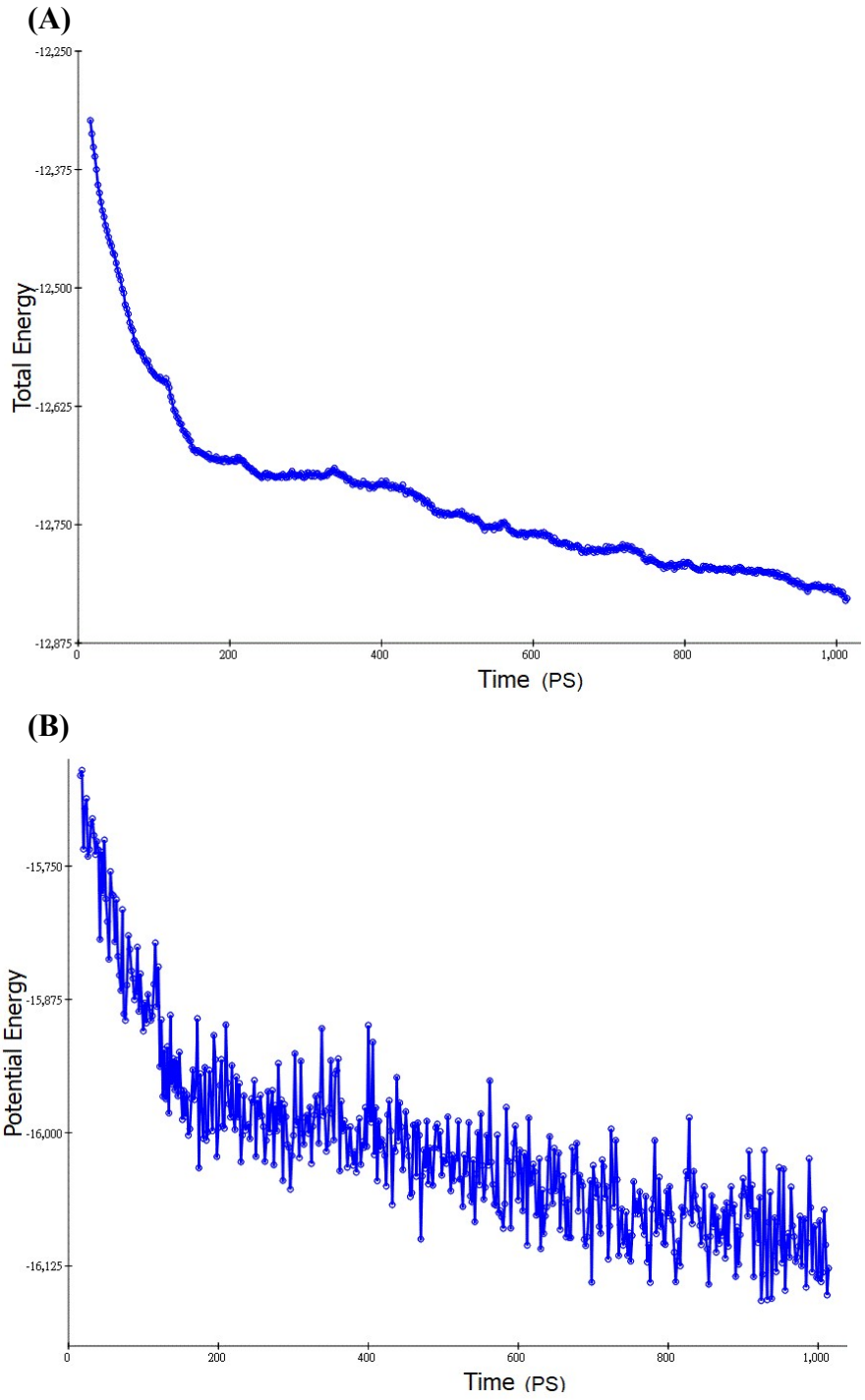

Figure S7. The molecular dynamics simulations of hMAGL-NP-5 complex.

(A) The total energy as a function of time. (B) The potential energy as a function of time.

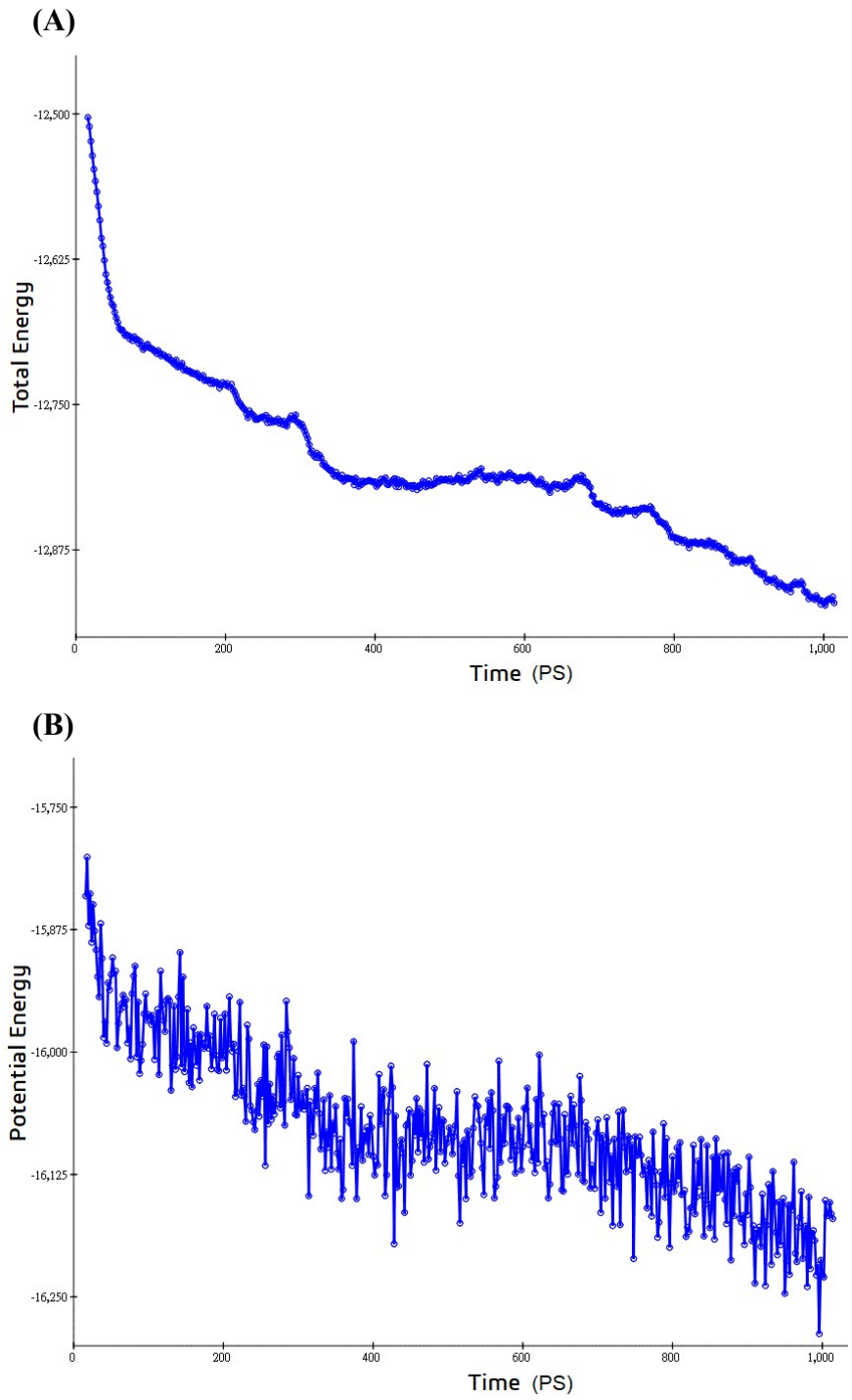

Figure S8. The molecular dynamics simulations of hMAGL-NP-6 complex.
(A) The total energy as a function of time. (B) The potential energy as a function of time.

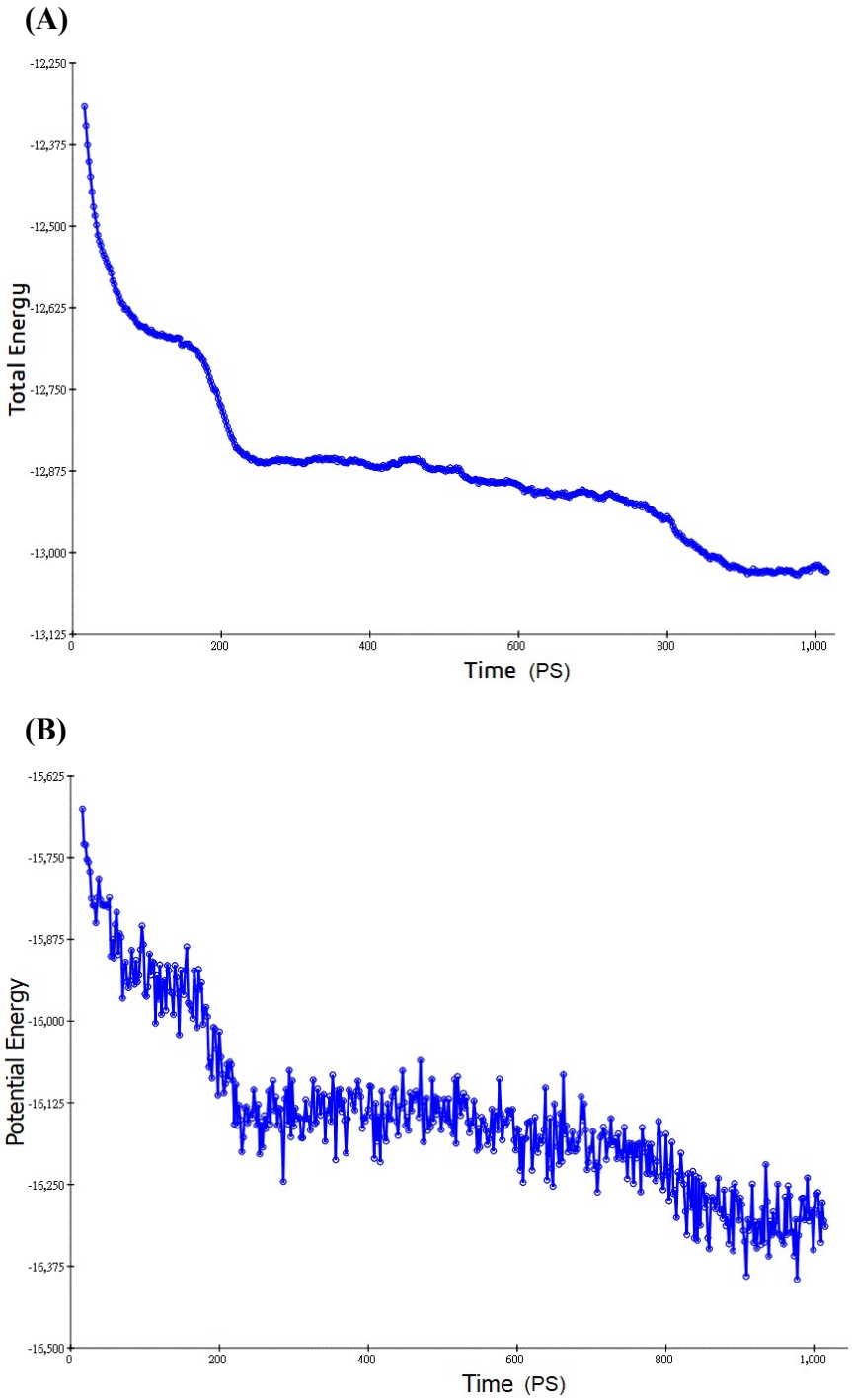

Figure S9. The molecular dynamics simulations of hMAGL-NP-7 complex.
(A) The total energy as a function of time. (B) The potential energy as a function of time.

Table S1. The result of protein-ligand interaction profiler of hMAGL-NP2 analyzing by PLIP web tool.

Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	51A	ALA	3.83	4373	530
2	179A	ILE	3.27	4365	2476
3	179A	ILE	3.72	4358	2473
4	205A	LEU	3.42	4360	2864
5	241A	LEU	3.99	4373	3454

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	51A	ALA	2.43	3.20	134.01	✓	×	526 [Nam]	4376 [O2]
2	122A	SER	1.80	2.56	134.73	×	✓	4375 [O2]	1631 [O3]
3	122A	SER	1.80	2.66	150.00	×	✓	4376 [O2]	1631 [O3]
4	123A	MET	3.01	4.00	167.76	✓	×	1635 [Nam]	4376 [O2]
5	177A	GLY	2.29	3.14	147.96	×	×	4380 [O2]	2448 [O2]
6	179A	ILE	2.33	3.27	155.54	✓	×	2463 [Nam]	4377 [O2]
7	194A	TYR	2.34	2.89	116.08	✓	✓	2715 [O3]	4374 [O2]
8	205A	LEU	2.84	3.65	139.05	✓	×	2860 [Nam]	4380 [O2]

Table S2. The result of protein-ligand interaction profiler of hMAGL-NP5 analyzing by PLIP web tool.

Hydrophobic Interactions .....

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	148A	LEU	3.02	4383	2000
2	176A	LEU	3.34	4372	2427
3	179A	ILE	3.10	4380	2469
4	179A	ILE	3.79	4367	2476
5	205A	LEU	3.33	4369	2873
6	241A	LEU	3.28	4383	3454

Hydrogen Bonds —

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	51A	ALA	2.77	3.30	113.34	✓	×	526 [Nam]	4387 [O2]
2	122A	SER	0.99	2.12	143.32	×	✓	4388 [O2]	1631 [O3]
3	122A	SER	2.19	3.22	139.63	×	✓	4387 [O2]	1631 [O3]
4	179A	ILE	2.02	2.99	163.34	✓	×	2463 [Nam]	4370 [O3]

Table S3. The result of protein-ligand interaction profiler of hMAGL-NP3 analyzing by PLIP web tool.

Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	51A	ALA	3.65	4370	530
2	123A	MET	3.98	4370	1639
3	148A	LEU	3.94	4368	2000
4	179A	ILE	3.42	4365	2469
5	213A	LEU	3.65	4368	3000
6	213A	LEU	3.90	4370	3004
7	241A	LEU	3.56	4373	3458

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	51A	ALA	1.86	2.83	163.68	✓	×	526 [Nam]	4375 [O2]
2	122A	SER	1.76	2.61	147.91	×	✓	4375 [O2]	1631 [O3]
3	123A	MET	2.02	2.88	142.84	✓	×	1635 [Nam]	4375 [O2]
4	152A	ASN	1.98	2.96	165.02	✓	×	2051 [Nam]	4376 [O2]
5	155A	SER	1.94	2.86	160.74	×	✓	4376 [O2]	2101 [O3]

Table S4. The result of protein-ligand interaction profiler of hMAGL-NP1 analyzing by PLIP web tool.

Hydrophobic Interactions .....

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	148A	LEU	3.82	4335	1996
2	184A	LEU	3.90	4362	2545
3	205A	LEU	2.86	4353	2873
4	213A	LEU	3.35	4342	3000
5	241A	LEU	2.90	4335	3425
6	241A	LEU	3.56	4340	3434
7	241A	LEU	3.98	4338	3430

Hydrogen Bonds —

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	152A	ASN	3.28	4.07	137.50	✔	✖	2051 [Nam]	4349 [O2]
2	241A	LEU	3.01	3.71	116.69	✖	✖	4349 [O2]	3421 [N3]
3	269A	HIS	2.19	2.99	127.24	✖	✔	4348 [O2]	3879 [Nar]

Table S5. The result of protein-ligand interaction profiler of hMAGL-NP4 analyzing by PLIP web tool.

Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	51A	ALA	3.97	4374	530
2	213A	LEU	3.97	4371	3000
3	241A	LEU	3.98	4370	3449

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	51A	ALA	2.74	3.53	136.51	✓	×	526 [Nam]	4378 [O2]
2	122A	SER	3.43	3.74	101.68	✓	✓	1631 [O3]	4377 [O2]
3	122A	SER	3.27	3.74	109.32	×	✓	4377 [O2]	1631 [O3]
4	122A	SER	1.69	2.50	139.40	×	✓	4378 [O2]	1631 [O3]
5	152A	ASN	2.36	3.17	137.79	✓	✓	2060 [Nam]	4375 [O2]
6	155A	SER	1.48	2.14	113.64	×	✓	4375 [O2]	2101 [O3]

Table S6. The result of protein-ligand interaction profiler of hMAGL-NP7 analyzing by PLIP web tool.

Hydrophobic Interactions .....

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	51A	ALA	3.95	4358	530
2	151A	ALA	3.66	4377	2045
3	176A	LEU	3.37	4379	2427
4	205A	LEU	3.43	4368	2873
5	213A	LEU	3.68	4362	3000
6	241A	LEU	3.90	4377	3449
7	241A	LEU	3.90	4359	3454

Table S7. The result of protein-ligand interaction profiler of hMAGL-NP6 analyzing by PLIP web tool.

Hydrophobic Interactions .....

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	148A	LEU	3.73	2184	1013
2	176A	LEU	3.82	2183	1217
3	179A	ILE	3.33	2175	1238
4	205A	LEU	3.92	2175	1435
5	213A	LEU	3.92	2184	1497
6	241A	LEU	3.88	2172	1716