Supplementary Table S1. List of natural compound libraries used for screening.

S.No.	Name of Libraries	No. of Compounds
1	AfroDb Natural Products	1008
2	AnalytiCon Discovery NP	20,000
3	Herbal Ingredients In-Vivo Metabolism	1465
4	Herbal Ingredients Targets	9862
5	IBScreen NP	68,000
6	Indofine Natural Products	20,000
7	Nubbe Natural Products	2147
8	Specs Natural Products	800
9	TCM Database @ Taiwan	20,000
10	NPACT Database	1574
11	AnalytiCon Discovery NP	
Total		**144,356**

Supplementary table S2. Table of binding energies for top 15 compounds.

S.No.	ZINC ID	Compound Name	[the energy of the lowest energy conformation]
1	ZINC00157548	Norpseudoephedrine hydrochloride	-6.39
2	ZINC95099135	7-hydroxycamphene	-6.18
3	ZINC00074836	Ephedrine	-6.01
4	ZINC00388198	Octopamine hydrochloride	-5.94
5	ZINC01597139	(±)-Carvomenthol	-5.86
6	ZINC59587245	4-Carene	-5.8
7	ZINC01081099	FENCHOL	-5.73
8	ZINC02034811	3-Pinanone	-5.73
9	ZINC00403588	Synephrine	-5.73
10	ZINC00968099	Borneol	-5.7
11	ZINC00968029	Darwinol	-5.7
12	ZINC02040990	Beta-terpineol	-5.69
13	ZINC00403588	Synephrine	-5.68
14	ZINC00967571	(+)-Fenchone	-5.68
15	ZINC03581377	L-Leucinamide hydrochloride	-5.68

Supplementary Table S3a. Agonist and antagonist probability prediction of top 15 compounds interaction with human Ffar2 homology model

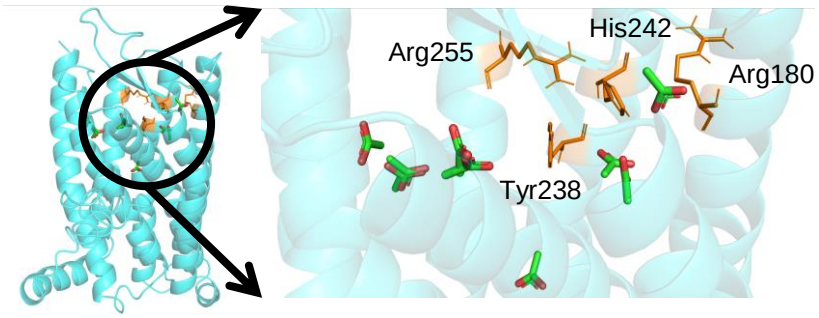
S. No.	Compounds	H-Bonding Residues Human_FFAR2	Probability as Agonist Ser86, Tyr90, His140, Ile145, Val179, Arg180, Leu183, Tyr238, His242, Arg255 Interaction with both Arg180 & Arg255 - Agonist	Probability as Antagonist Ser86, Tyr90, His140, Ile145, Val179, Arg180, Leu183, Tyr238, His242, Arg255 Interaction with either Arg180 or Arg255 - Antagonist
1	175 (Acetate)	**His242**, Tyr238	Potential Agonist	NA
2	ZINC00895132 (Butyrate)	Tyr238	Potential Agonist	NA
3	ZINC000118616157 (CatPB)	Gln166, Tyr238, **Arg255**, Lys65, Gln148, Ser86, Ser256	NA	Potential Antagonist
4	ZINC00157548 (Norpseudoephedrine hydrocholoride)	Tyr238, **His242**, Leu183, Gln148, Cys164, Glu166, Ser86, Thr85, Glu68	20%	0%
5	ZINC95099135 (7-Hydroxycamphene)	Thr85, Glu166, Ser86, Gln148, **Tyr238**, Glu68, **His242**	30%	0%
6	ZINC00074836 (Ephedrine)	Thr85, Gln148, Glu166, Ser86, Glu68, Cys164, **His242**	10%	0%
7	ZINC00388198 (Octopamine hydrocholride)	Leu183, **Tyr238**, His242, Asn239, Gln148, Cys164, Glu166, **Ser86**, Glu68, Thr85,	70%	0%
8	ZINC01597139 (Carvomenthol)	**Ser86**, Gln148, **Tyr238**, Glu166, Thr85, Glu68, **Arg255**	20%	60%
9	ZINC59587245 (4-Carene)	All Hydrophobic	0%	0%
10	ZINC01081099 (Fenchol)	Glu166, **Ser86**, **His242**, Gln148, **Tyr238**	50%	0%
11	ZINC02034811 (3-Pinanone)	**Ser86**, **Arg255**, Gln148	30%	70%
12	ZINC00403588 (Synephrine)	Leu183, Tyr238, **His242**, Gln148, Glu166, **Ser86**, Glu68, Thr85, **Tyr238**, **Arg255**	20%	70%
13	ZINC00968099 (Borneol)	**Ser86**, Glu166, Glu68, **Tyr238**, **Arg255**	10%	80%
14	ZINC00968029 (Darwinol)	Ser263, **Ser86**, Gln148, Glu166, Glu68, Cys164	20%	0%
15	ZINC02040990 (Beta-terpineol)	Cys184, Thr85, Cys164, **Tyr238**, Gln148, Glu166, **Arg255**, Glu68, **Ser86**	30%	60%
16	ZINC00967571 (Fenchone)	Gln148, **Tyr238**, Lys65	10%	0%
17	ZINC03581377 (Leucinamide hydrocholoride)	Ser263, Ile10, Lys65, Val259, Glu68, Gln148	0%	0%

Supplementary table S3b. Agonist and antagonist probability prediction of top 15 compounds interaction with Mice Ffar2 homology model

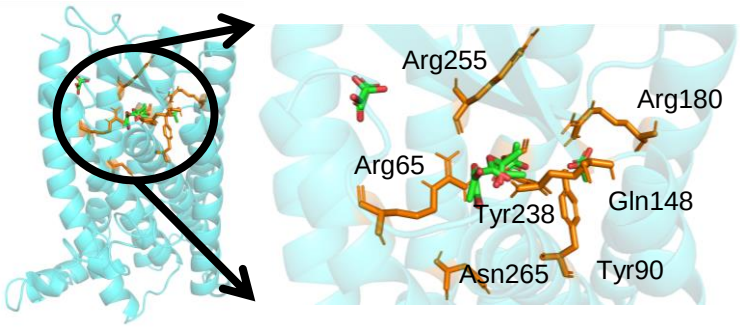
S.No.	Compounds	H-Bonding Residues Mice_FFAR2	Probability as Agonist Ser86, Tyr90, His140, Ile145, Val179, Arg180, Leu183, Tyr238, His242, Arg255 Interaction with both Arg180 & Arg255 - Agonist	Probability as Antagonist Ser86, Tyr90, His140, Ile145, Val179, Arg180, Leu183, Tyr238, His242, Arg255 Interaction with either Arg180 & Arg255 - Antagonist
1	175 (Acetate)	Tyr90, **Arg180**, Gln148, Asn265, Arg65, Gln148, Tyr238	Potential Agonist	NA
2	ZINC00895132 (Butyrate)	Tyr238, Arg65, **Arg180**, Tyr90, Gln170	Potential Agonist	NA
3	ZINC000118616157 (CatPB)	Asn151, Asn167, Arg255, Gln172, Pe168	NA	Potential Antagonist
4	ZINC00157548 (Norpseudoephedrine hydrocholoride)	Cys164, Val147, Asn167, Thr169, Arg65, Gln148, Val81, Thr85, **Arg255**, Leu60, Glu320	10%	60%
5	ZINC95099135 (7-Hydroxycamphene)	Thr85, Gln323, Gln170, Glu320, Thr169, Gln318	0%	70%
6	ZINC00074836 (Ephedrine)	**Arg255**, Val81, Thr85, Glu320, Ile146, Val147, Asn167	0%	70%
7	ZINC00388198 (Octopamine hydrocholride)	Glu68, Trp75, Glu166, Val147, Asn167, Thr169, Leu60, Thr85, Glu320, Gln323, Ala319, Ile146 Gln170, **Arg255**, Gln155, Leu60, Val81, Thr85	0%	70%
8	ZINC01597139 (Carvomenthol)	Arg255, Asn167, Thr169, Val81, Thr85, Leu60, Phe64	0%	60%
9	ZINC59587245 (4-Carene)	All hydrophobic	0%	0%
10	ZINC01081099 (Fenchol)	Glu320, Thr85	0%	0%
11	ZINC02034811 (3-Pinanone)	**Arg255**, Thr169, Gln170	0%	80%
12	ZINC00403588 (Synephrine)	Glu68, Trp75, Tyr90, Gln148, Cys164, Tyr238, Asn167, Phe168, Arg255, Ile146, Glu170, Val81, Thr85, Val147, Asn167, Thr169, Gln155	0%	80%
13	ZINC00968099 (Borneol)	Thr169, Gln170, Val81, Thr85, **Arg255**, Leu60, Glu320	0%	80%
14	ZINC00968029 (Darwinol)	Gln148, Ala319, Gln323, Glu320, Leu60, Val81, Thr85	0%	0%
15	ZINC02040990 (Beta-terpineol)	Glu166, Tyr90, Gln148, Tyr238, Val156, **Arg255**, Ile146, Val147	0%	60%
16	ZINC00967571 (Fenchone)	Arg255, Gln170	0%	50%
17	ZINC03581377 (Leucinamide hydrocholoride)	Arg65, Tyr90, Glu166, Val147, Asn167, Thr169, Gln170, Glu320, **Arg255**, Asn151	0%	50%

Supplementary Figure S1. In-silico Modeling and interaction data from human and mice Ffar2 homology modeling

Acetate interaction with human and mouse Ffar2 homology modeling

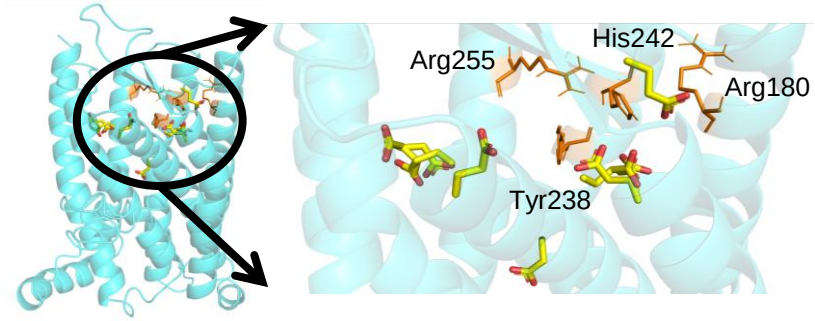


Acetate Interaction with human Ffar2

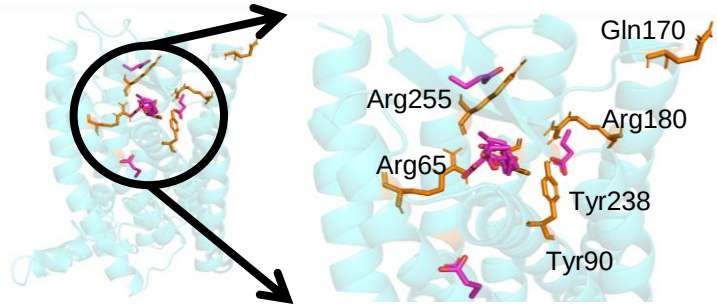


Acetate Interaction with mouse Ffar2

Butyrate interaction with human and mouse Ffar2 homology modeling

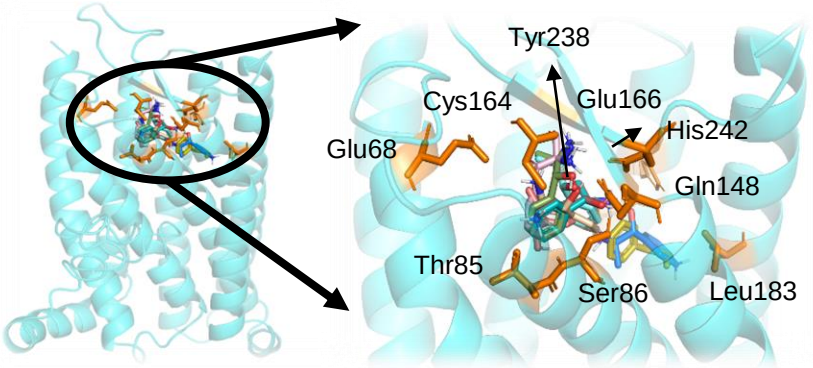


Butyrate Interaction with human Ffar2

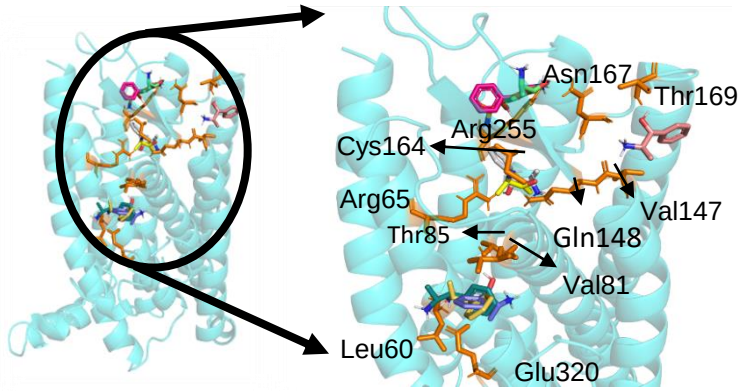


Butyrate Interaction with mouse Ffar2

Norpsedoephedrine hydrochloride (ZINC00157548) interaction with human and mouse Ffar2 homology modeling

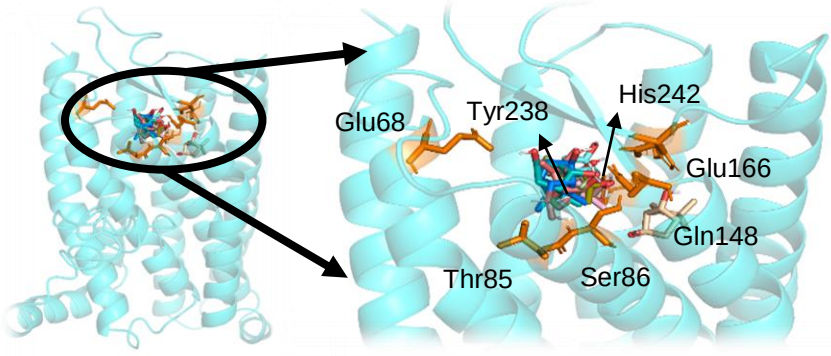


ZINC00157548 interaction with human Ffar2

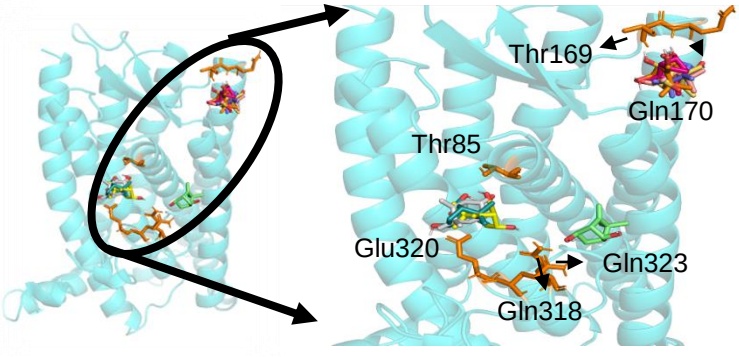


ZINC00157548 interaction with mouse Ffar2

7-Hydroxycamphene (ZINC95099135) interaction with human and mouse Ffar2 homology modeling

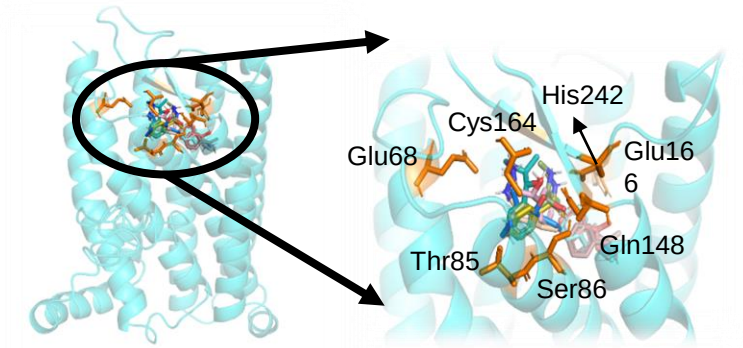


ZINC95099135 interaction with human Ffar2

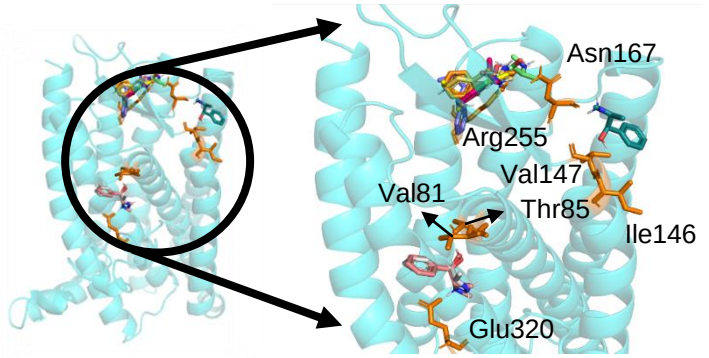


ZINC95099135 interaction with mouse Ffar2

Ephedrine (ZINC00074836) interaction with human and mouse Ffar2 homology modeling

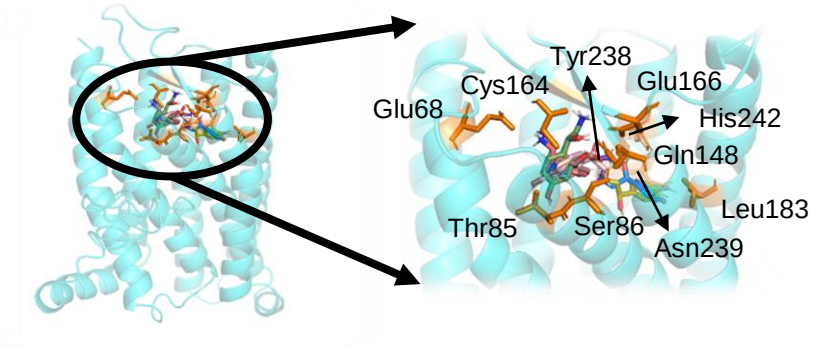


ZINC00074836 interaction with human Ffar2

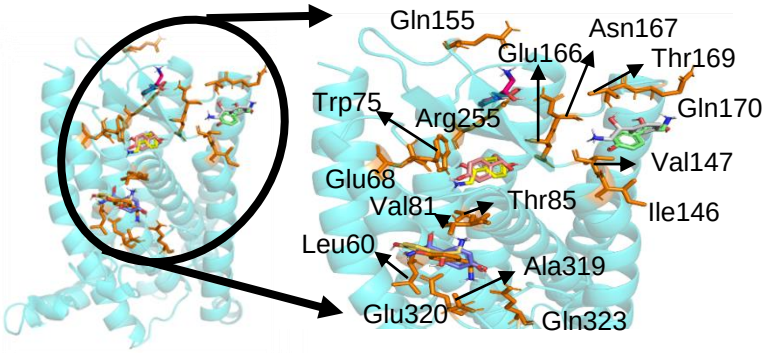


ZINC00074836 interaction with mouse Ffar2

Octopamine Hydrochloride (ZINC00388198) interaction with human and mouse Ffar2 homology modeling

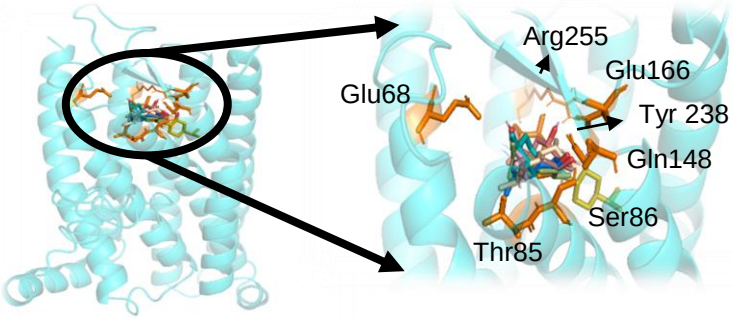


ZINC00388198 interaction with human Ffar2

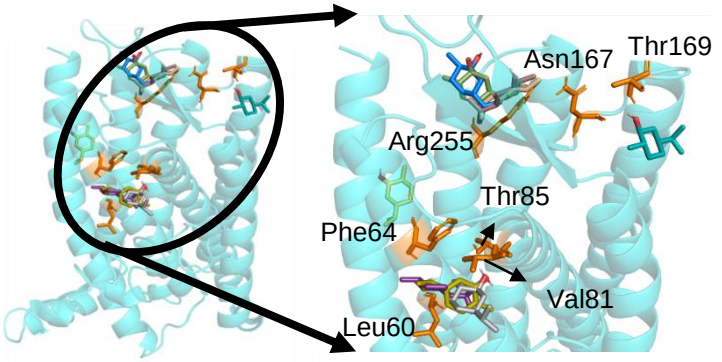


ZINC00388198 interaction with mouse Ffar2

Carvomenthol (ZINC01597139) interaction with human and mouse Ffar2 homology modeling

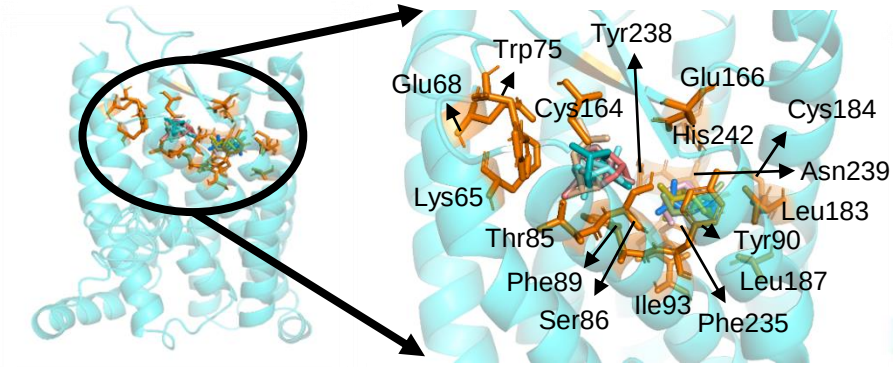


ZINC01597139 interaction with human Ffar2

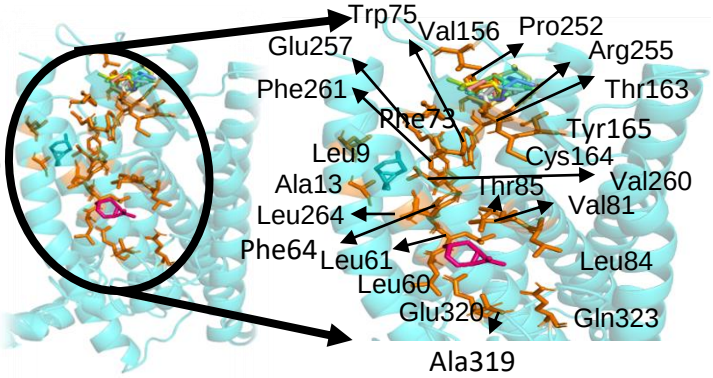


ZINC01597139 interaction with mouse Ffar2

4-Carene (ZINC59587245) interaction with human and mouse Ffar2 homology modeling

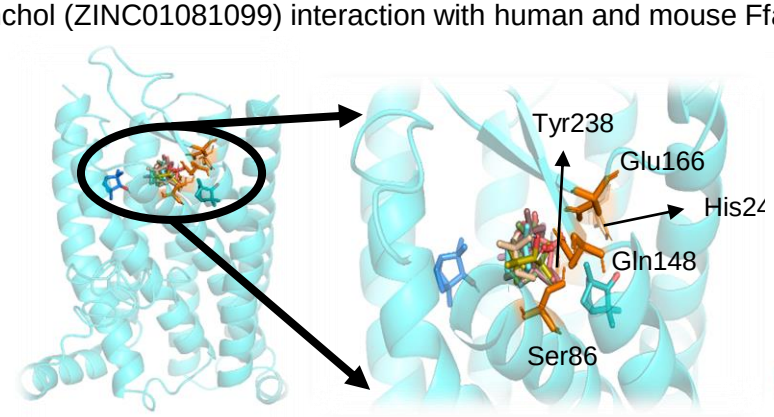


ZINC01597139 interaction with human Ffar2

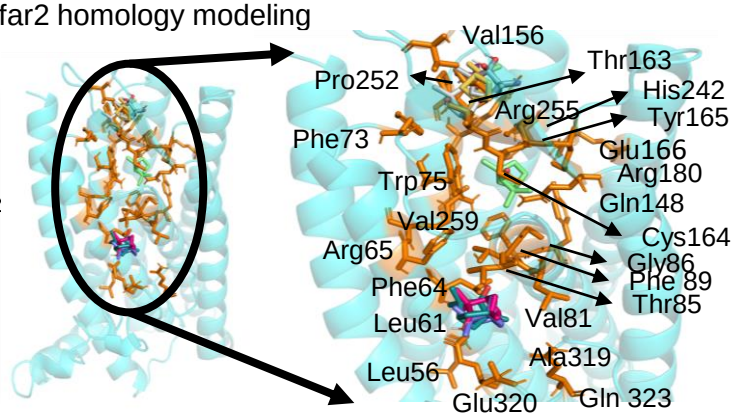


ZINC01597139 interaction with mouse Ffar2

Fenchol (ZINC01081099) interaction with human and mouse Ffar2 homology modeling

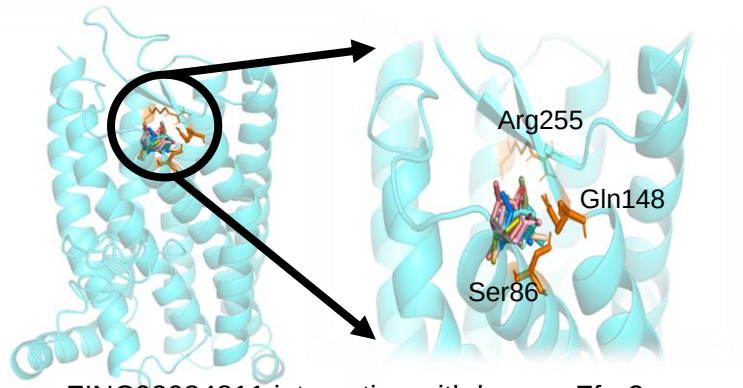


ZINC01081099 interaction with human Ffar2

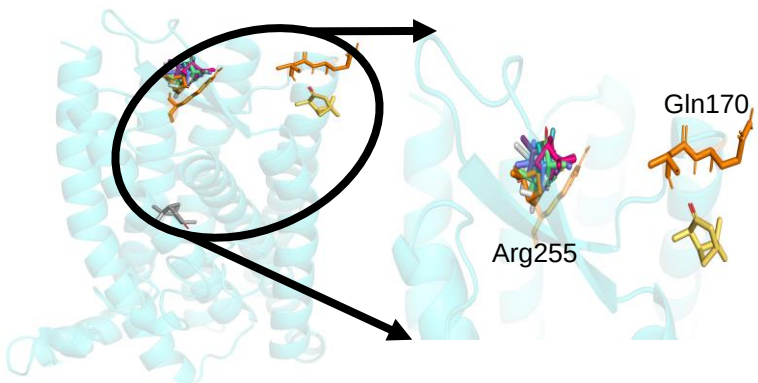


ZINC01081099 interaction with mouse Ffar2

3-Pinanone/3-Pentanone (ZINC02034811) interaction with human and mouse Ffar2 homology modeling

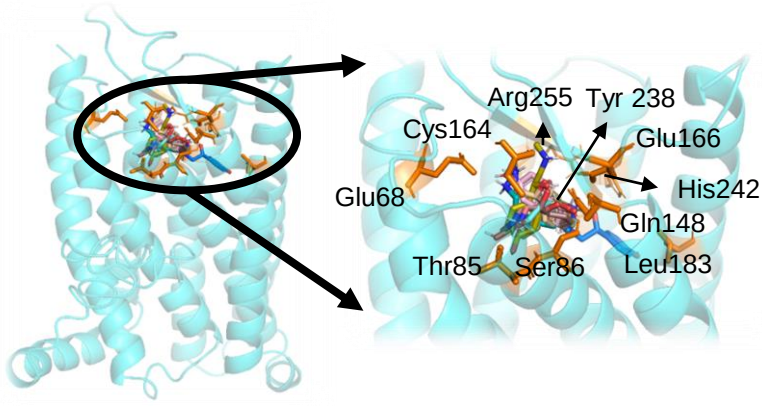


ZINC02034811 interaction with human Ffar2

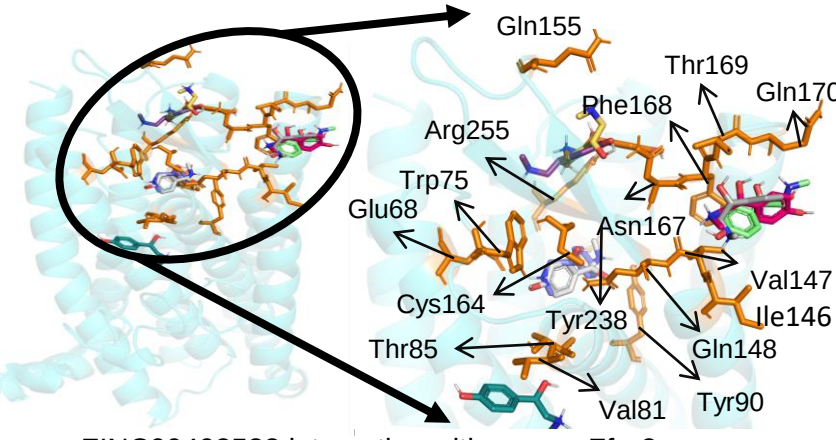


ZINC02034811 interaction with mouse Ffar2

Synephrine (ZINC00403588) interaction with human and mouse Ffar2 homology modeling

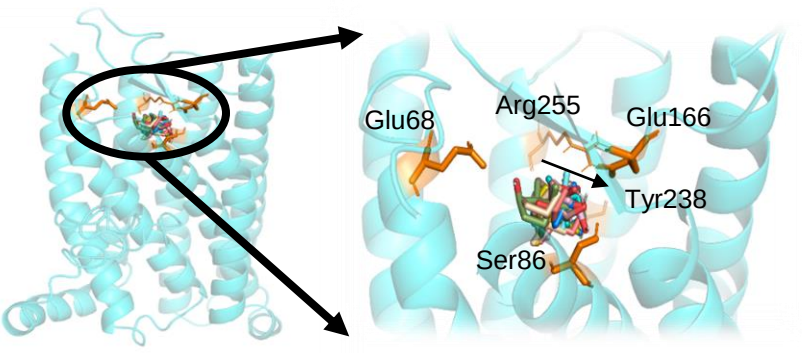


ZINC00403588 interaction with human Ffar2

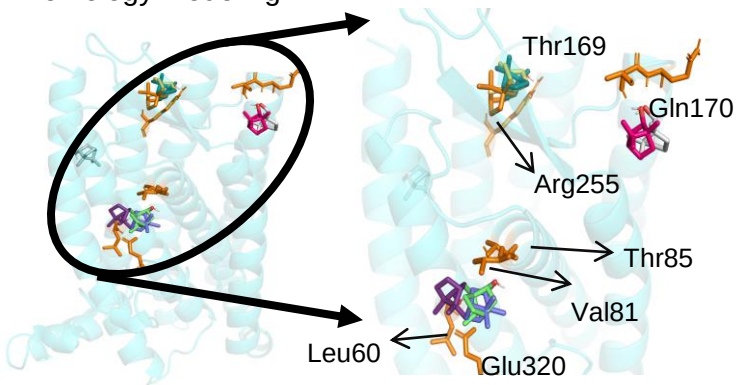


ZINC00403588 interaction with mouse Ffar2

Borneol (ZINC00968099) interaction with human and mouse Ffar2 homology modeling

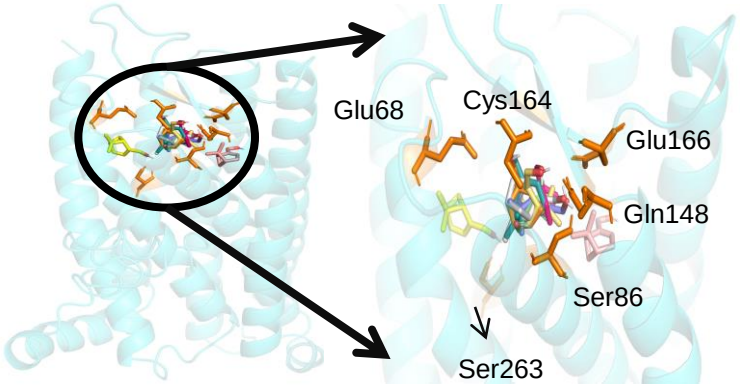


ZINC00968099 interaction with human Ffar2

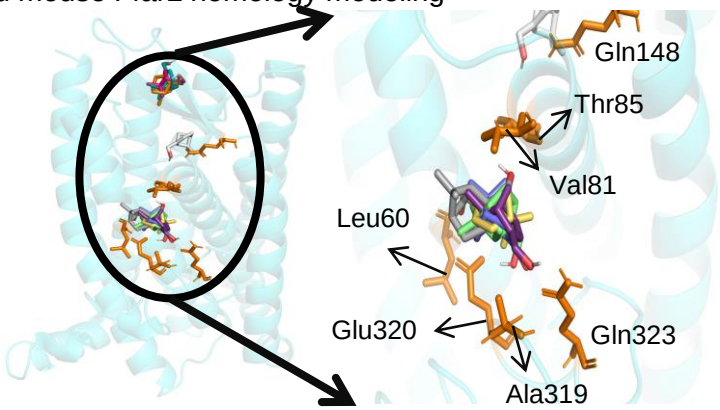


ZINC00968099 interaction with mouse Ffar2

Darwinol/ Myrtenol (ZINC000968029) interaction with human and mouse Ffar2 homology modeling

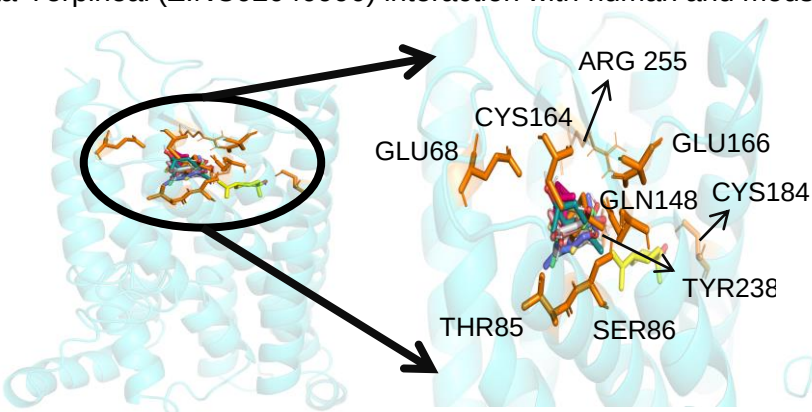


ZINC01081099 interaction with human Ffar2

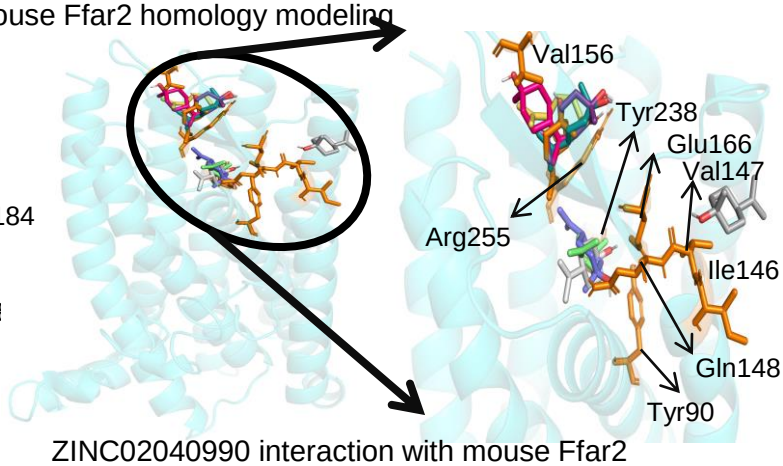


ZINC01081099 interaction with mouse Ffar2

Beta-Terpineal (ZINC02040990) interaction with human and mouse Ffar2 homology modeling

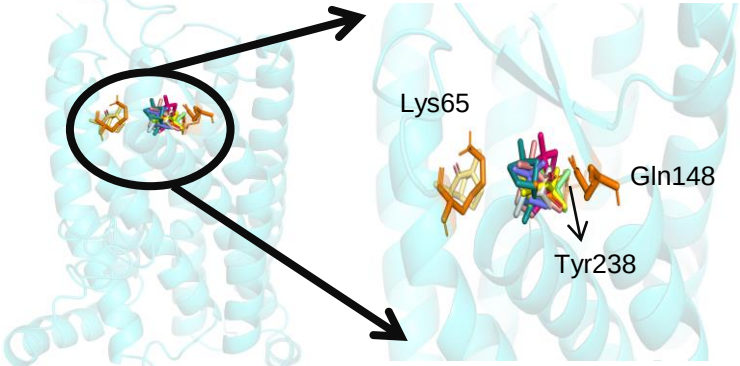


ZINC02040990 interaction with human Ffar2

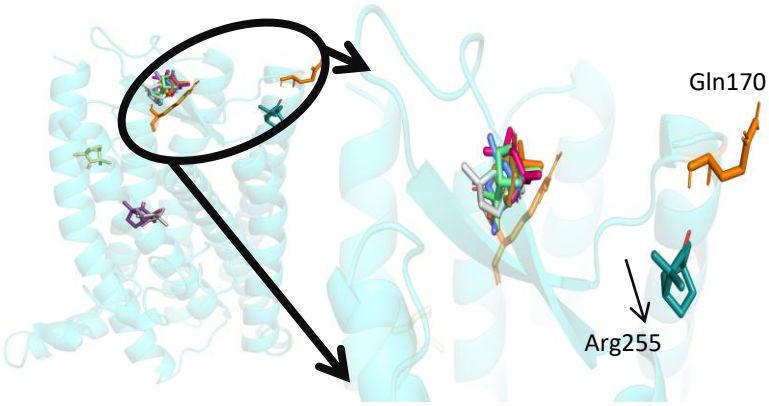


ZINC02040990 interaction with mouse Ffar2

Fenchone (ZINC00967571) interaction with human and mouse Ffar2 homology modeling

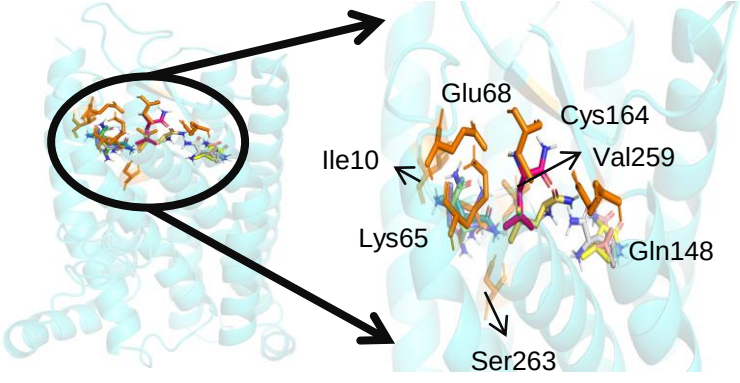


ZINC00967571 interaction with human Ffar2

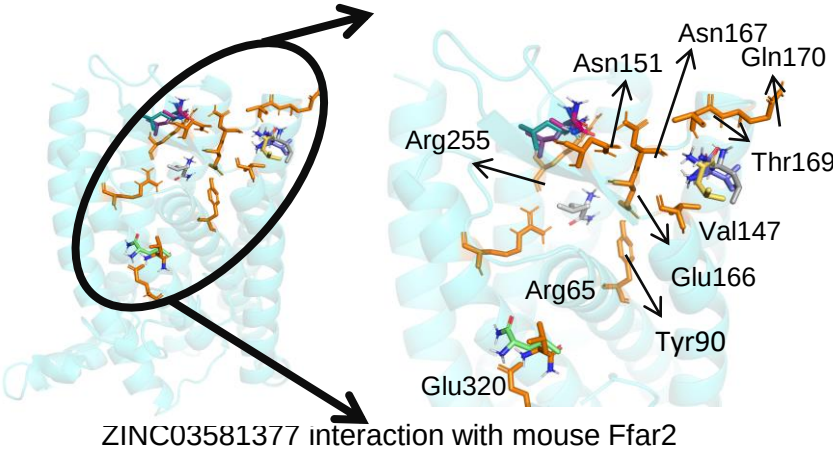


ZINC00967571 interaction with mouse Ffar2

L-Leucinamide hydrochloride (ZINC03581377) interaction with human and mouse Ffar2 homology modeling



ZINC03581377 interaction with human Ffar2



ZINC03581377 interaction with mouse Ffar2

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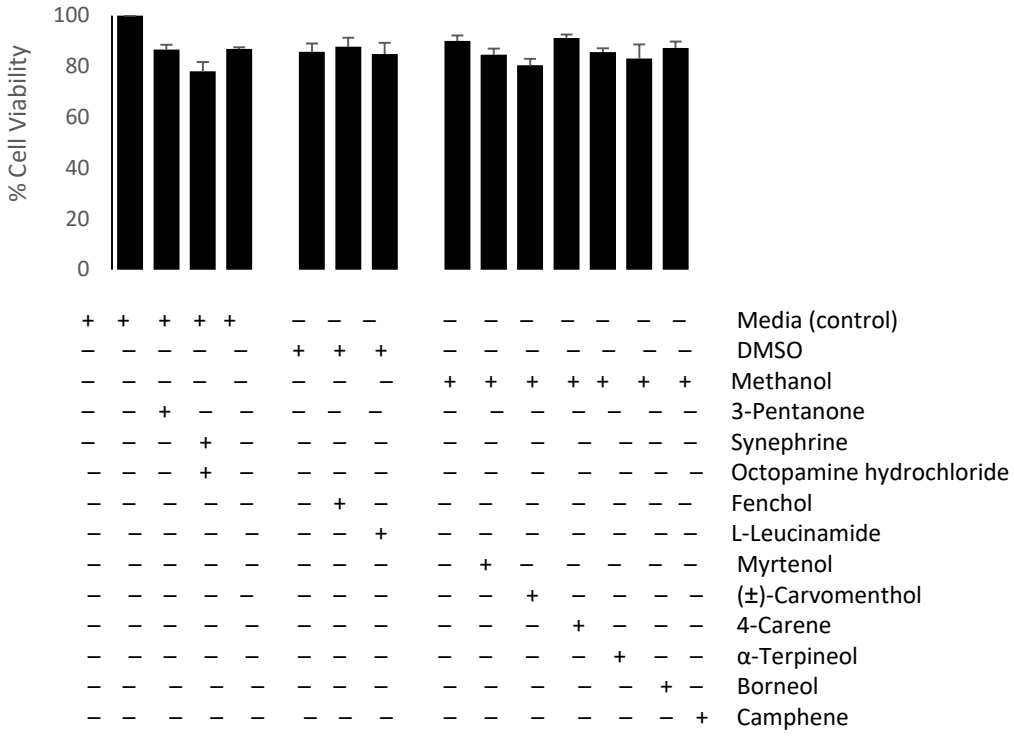

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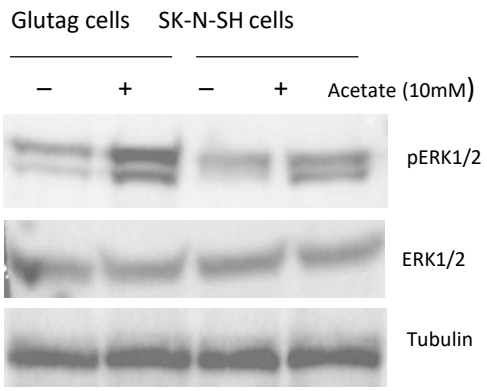

Figure S2. Effect of selected compounds on cell viability of neural cell. a) SK-N-SH cell lines were treated with 10μM of each compounds at 37 °C for 24 h**.** b) Expression of phpsphoERK1/2 protein in Glutag and SK-N-SH cells. Both cell lines were treated with 10mM acetate at 37 °C for 30 min.