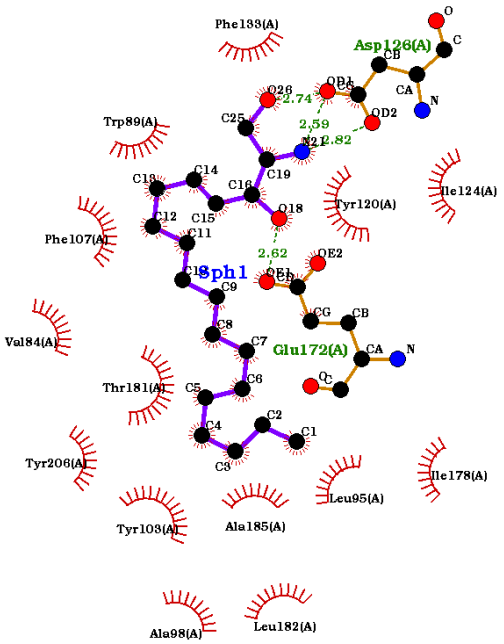
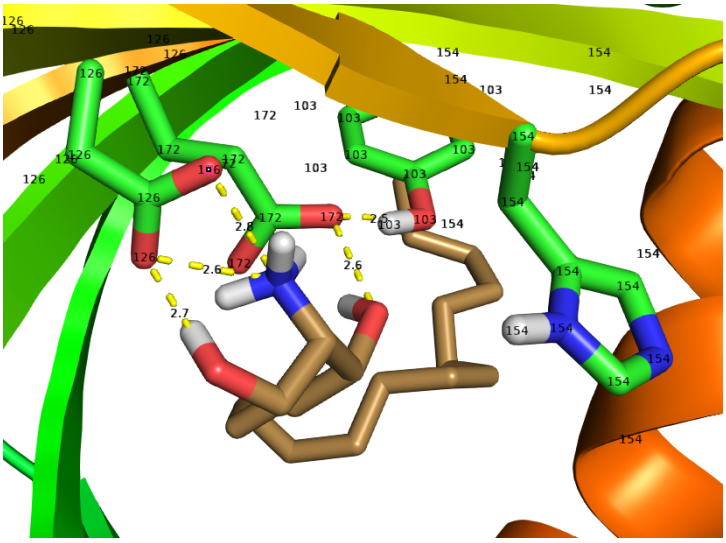
SUPPLEMENTAL TABLES AND ASSOCIATED DOCKED STRUCTURES

Table S1A.

Sphingosine (SPH) 6DJZ S1R (first docking run).

```
_____|____________|_____|____________|_____|________________________________________
     |            |     |            |     |
Clus | Lowest     | Run | Mean       | Num | Histogram
-ter | Binding    |     | Binding    | in  |
Rank | Energy     |     | Energy     | Clus|    5    10   15   20   25   30   35
_____|____________|_____|____________|_____|____:____|____:____|____:____|____:___
   1 |    -10.15  |  14 |     -8.73  |  23 |########################
   2 |     -9.29  |   5 |     -9.29  |   1 |#
   3 |     -8.70  |  13 |     -8.16  |   3 |###
   4 |     -8.54  |  17 |     -8.51  |   2 |##
   5 |     -8.44  |  24 |     -8.44  |   1 |#
_____|____________|_____|____________|_____|________________________________________
MODEL        16
MODEL        14
USER    Run = 14
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 23
USER
USER    RMSD from reference structure       = 1.900 A
USER
USER    Estimated Free Energy of Binding    =  -10.15 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =   36.60 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -13.91 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -10.93 kcal/mol
USER        Electrostatic Energy            =   -2.98 kcal/mol
USER    (2) Final Total Internal Energy     =   -2.36 kcal/mol
USER    (3) Torsional Free Energy           =   +5.37 kcal/mol
USER    (4) Unbound System's Energy         =   -0.75 kcal/mol
USER
USER
USER
USER    DPF = SPN1_molA_6djz_recep_min.dpf
USER    NEWDPF move    SPH1.pdbqt
USER    NEWDPF about   11.049500 38.264500 -36.382800
USER    NEWDPF tran0   10.282394 36.294722 -37.057911
```





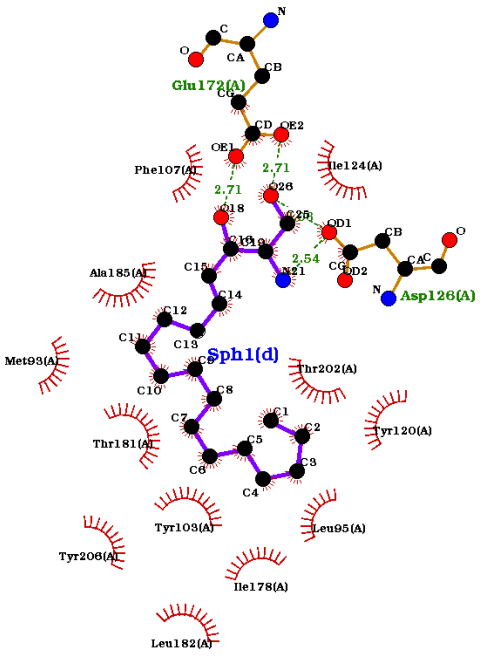
molA-6djz-recep-min_SPH1_1

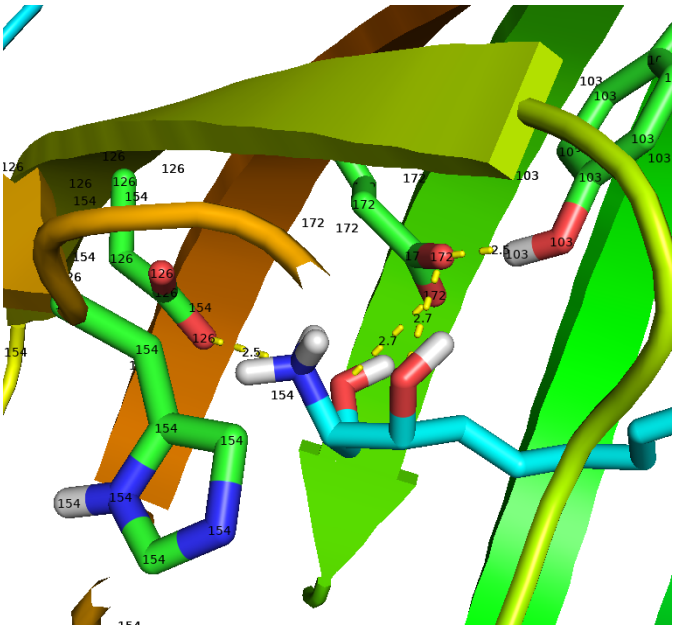
Table S1B.

Sphingosine (SPH) 6DJZ S1R (second docking run).

Clus-ter Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram 5 10 15 20 25 30 35
1	-10.11	22	-8.93	22	######################
2	-9.20	30	-8.41	3	###
3	-9.11	13	-8.31	3	###
4	-8.77	2	-8.74	2	##

```
MODEL        22
USER    Run = 22
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 22
USER
USER    RMSD from reference structure       = 1.498 A
USER
USER    Estimated Free Energy of Binding    =  -10.11 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =   38.68 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -13.28 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -10.58 kcal/mol
USER        Electrostatic Energy            =   -2.70 kcal/mol
USER    (2) Final Total Internal Energy     =   -2.97 kcal/mol
USER    (3) Torsional Free Energy           =   +5.37 kcal/mol
USER    (4) Unbound System's Energy         =   -0.76 kcal/mol
USER
USER
USER
USER    DPF = SPN21_molA_6djz_recep_min.dpf
USER    NEWDPF move    SPH21.pdbqt
USER    NEWDPF about  11.871500 37.560000 -35.771600
```



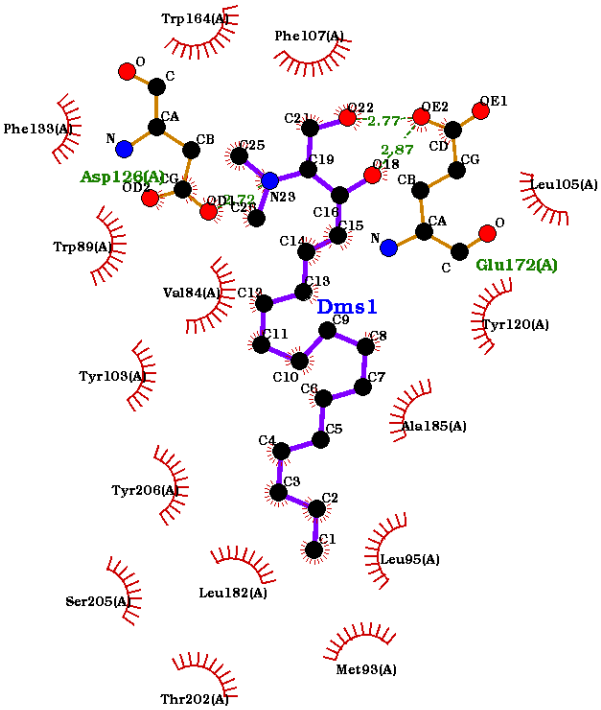


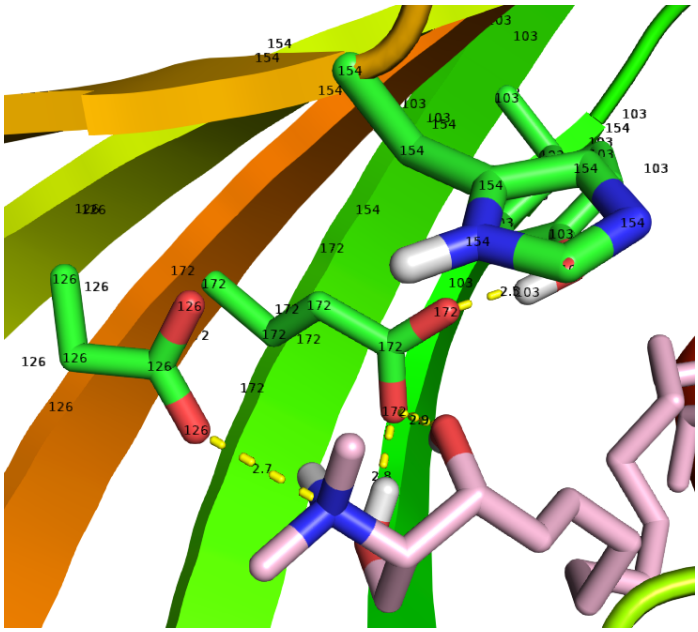
molA-6djz-recep-min_SPH21_1

Table S2A.

N,N′ Dimethylsphingosine (DMS) 6djz S1R (first docking run).

```
_____|____________|_____|____________|_____|________________________________________
     |            |     |            |     |
Clus | Lowest     | Run | Mean       | Num | Histogram
-ter | Binding    |     | Binding    | in  |
Rank | Energy     |     | Energy     | Clus|    5    10   15   20   25   30   35
_____|____________|_____|____________|_____|___:____|___:____|____:____|____:____|___:___
   1 |      -9.43 |  16 |      -8.56 |  15 |###############
   2 |      -9.39 |  13 |      -8.56 |   6 |######
   3 |      -8.46 |   8 |      -8.46 |   1 |#
   4 |      -7.98 |  11 |      -7.27 |   7 |#######
   5 |      -4.45 |  18 |      -4.45 |   1 |#
_____|____________|_____|____________|_____|________________________________________
MODEL        16
USER    Run = 16
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 15
USER
USER    RMSD from reference structure       = 1.776 A
USER
USER    Estimated Free Energy of Binding    =   -9.43 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =  122.41 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -12.31 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -10.44 kcal/mol
USER        Electrostatic Energy            =   -1.87 kcal/mol
USER    (2) Final Total Internal Energy     =   -3.31 kcal/mol
USER    (3) Torsional Free Energy           =   +5.37 kcal/mol
USER    (4) Unbound System's Energy         =   -0.81 kcal/mol
USER
USER
USER
USER    DPF = DMS1_molA_6djz_recep_min.dpf
USER    NEWDPF move    DMS1.pdbqt
USER    NEWDPF about  11.259200 37.279700 -35.935300
```





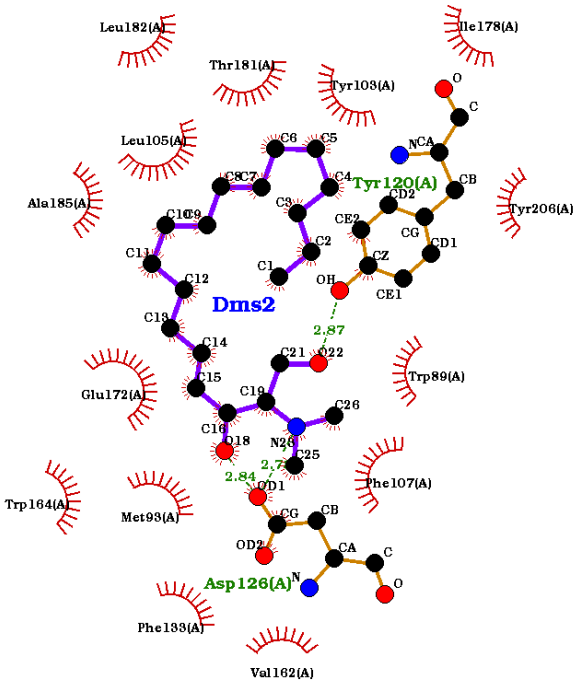
molA-6djz-recep-min_DMS1_1

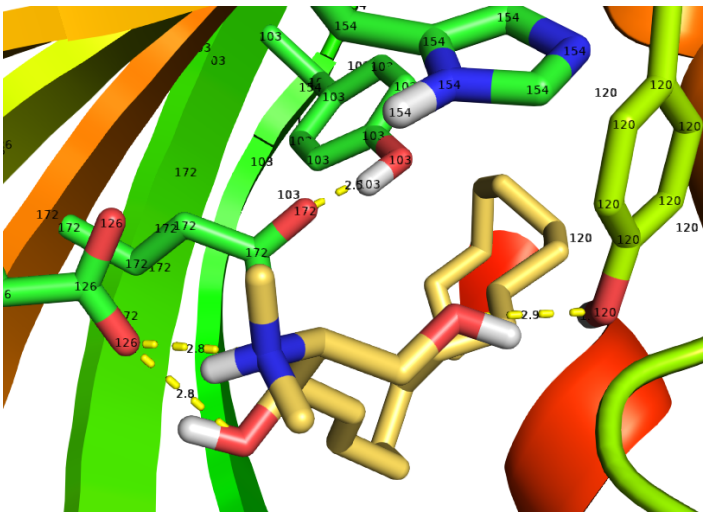
Table S2B.

N,N Dimethylsphingosine (DMS) 6djz S1R (second docking run).

Clus-ter Rank	Lowest Binding Energy	Run	Mean Binding Energy	Num in Clus	Histogram 5 10 15 20 25 30 35
1	-9.43	14	-8.15	21	#####################
2	-8.23	27	-7.97	2	##
3	-7.81	4	-7.10	4	####
4	-7.39	13	-7.39	1	#
5	-6.88	29	-6.88	1	#
6	-4.69	22	-4.69	1	#

```
MODEL        14
USER    Run = 14
USER    Cluster Rank = 1
USER    Number of conformations in this cluster = 21
USER
USER    RMSD from reference structure       = 1.756 A
USER
USER    Estimated Free Energy of Binding    =   -9.43 kcal/mol  [=(1)+(2)+(3)-(4)]
USER    Estimated Inhibition Constant, Ki   =  122.88 nM (nanomolar)  [Temperature = 298.15 K]
USER
USER    (1) Final Intermolecular Energy     =  -13.53 kcal/mol
USER        vdW + Hbond + desolv Energy     =  -11.46 kcal/mol
USER        Electrostatic Energy            =   -2.07 kcal/mol
USER    (2) Final Total Internal Energy     =   -2.07 kcal/mol
USER    (3) Torsional Free Energy           =   +5.37 kcal/mol
USER    (4) Unbound System's Energy         =   -0.81 kcal/mol
USER
USER
USER
USER    DPF = DMS2_molA_6djz_recep_min.dpf
USER    NEWDPF move    DMS2.pdbqt
USER    NEWDPF about   11.555000 37.443300 -36.209500
USER    NEWDPF tran0   11.567927 34.841621 -36.325919
```

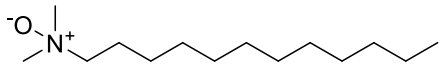




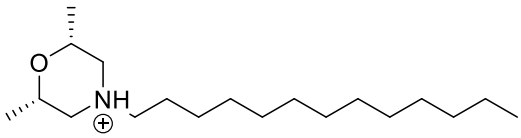
molA-6djz-recep-min_DMS2_1

SUPPLEMENTAL FIGURE-1

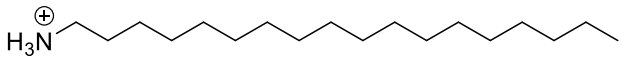
A.



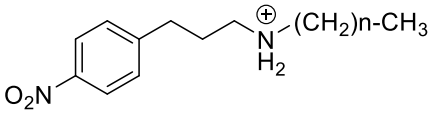
Lauryldimethylamine oxide



tridemorph



stearylamine

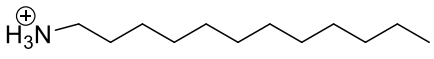


n = 3, N-3-(4-nitrophenylpropyl)tetrane-1-amine

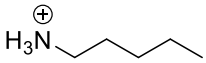
n = 6, N-3-(4-nitrophenylpropyl)heptane-1-amine

n = 11, N-3-(4-nitrophenylpropyl)dodecane-1-amine

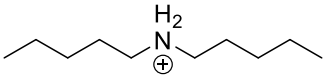
n = 17, N-3-(4-nitrophenylpropyl)octadecane-1-amine



dodecylamine

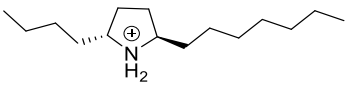


pentylamine

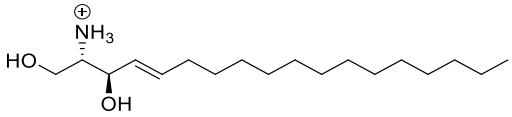


dipentylamine

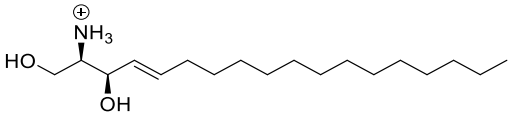
B.



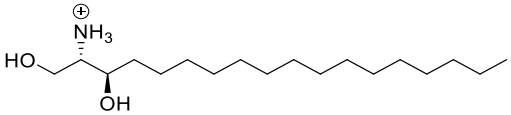
(2R-trans)-2-butyl-5-heptyl-pyrrolidine



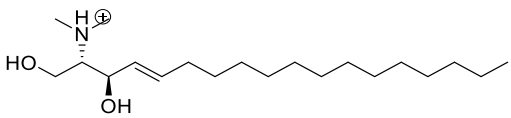
D-erythrosphingosine



L-threosphingosine



D-erythrosphinganine



D-erythro-N,N Dimethylsphingosine

Figure S1. Exogenous and endogenous amines that bind to the S1R.

A. Exogenous amines including N-substituted compounds such as lauryldimethylamine oxide (LDAO) [Ramachandran, S., Doctoral Dissertation, UW Madison, 2008], tridemorph [51,110], dodecylamine, stearylamine [51, 55], pentylamine, dipentylamine [51] and similar compounds [52, 53] plus a series of N-3-(4-nitrophenylpropyl)-alkyl-1-amines [51, 54].

B. An endogenous amine and SPH derivatives that bind to the S1R include (2R-trans)-2-butyl-5-heptylpyrolidine [111], (SPH), L-threosphingosine, D-erythrosphinganine and D-erythro-N,N-dimethylsphingosine (DMS) [55]. With a pKa between 8-9.5 these compounds will generally be positively charged at neutral pH as ammonium salts but the charge will depend on the intracellular environment of the cell and the lipid bilayer.