Supplemental Files

LASSO-ing Potential Nuclear Receptor Agonists and Antagonists: A New Computational Method For Database Screening

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Running Head: Models for Nuclear Receptor Agonists and Antagonists

Supplemental Table 1. LASSO 23 Surface Point Types with description.

Number	Surface Point Type	Description
1	Metal	positively charged metal ion interaction point
2	Charged_Hplus	positively charged hydrogen bond donor, e.g. Arginine
3	Primary_Amine_Hlp	primary amine hydrogen/lone-pair, e.g. $-NH_3^+$ or $-NH_2$
4	Hdonor	strong hydrogen bond donor H (polar-atom-H)
5	Weak_Hdonor	weak (secondary) hydrogen bond donor H (polarized C-H)
6	Charged_Lonepair	lone pair of negatively charged group, e.g. PO_3
7	Acid_Lonepair	lone pair of an acidic functional group, e.g. carboxolate
8	Lonepair strong	(primary) hydrogen bond acceptor lone pair
9	Weak_Lonepair	weak (secondary) hydrogen bond acceptor lone pair
10	Ambivalent_Hlp	donor H or acceptor Lp depending on protonation state
11	Rotatable_H	rotatable-hydroxy donor H
12	Rotatable_Lp	rotatable-hydroxy acceptor Lp
13	Hydrophob	H on Sp^3 hydrophobic carbon
14	H_Arom_Edge	H on hydrophobic carbon in aromatic ring (non-polarized)
15	Ws_Lipo	H on weak secondary hydrophobic atom (e.g. carbon next to polar)
16	Neutral	H/Lp on neutral atom (no recognized activity)
17	Pi_Aromatic	π electron of an aromatic ring
18	Pi_Reson_Polar	π electron on polar atom (N/O) in resonance chain, e.g. amide
19	Pi_Reson_Carbon	π electron on carbon atom in resonance chain, e.g. amide
20	Pi_Sp2_Polar	π electron on sp^2 polar atom (N/O)(non-resonating, nonaromatic)
21	Pi_Sp2_Carbon	π electron on sp^2 carbon atom (non-resonating, non-aromatic)
22	Halogen	lone electron pair of a halogen atom (F,Cl,I,Br)
23	Sulfur	lone electron pair of a sulfur atom

Supplemental Table 2

Model building details for PXR.

#Actives/ from position	1st position	9th position	17th position	33rd position	64th position
8 actives	Model 8 from 1	Model 8 from 9	Model 8 from 17	Model 8 from 33	Model 8 from 64
16 actives	Model 16 from 1	Model 16 from 9	Model 16 from 17	Model 16 from 33	Model 16 from 64
32 actives	Model 32 from 1	Model 32 from 9	Model 32 from 17	Model 32 from 33	Model 32 from 64
64 actives	Model 64 from 1	Model 64 from 9	Model 64 from 17	Model 64 from 33	Model 64 from 64
128 actives	Model 128 from 1	Model 128 from 9	Model 128 from 17	Model 128 from 33	Model 128 from 64

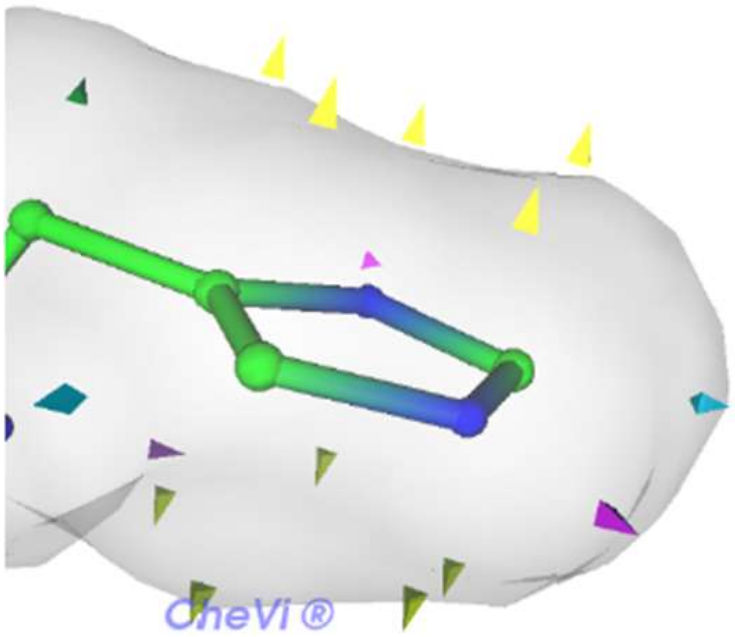
Supplemental Table 3

LASSO 6.1 surface point types with Mibolerone's values:

ID	Count	Name	Description
1	0	Metal	positively charged metal ion point
2	0	Charged_Hplus	positively charged hydrogen, e.g. Argini
3	0	Primary_Amine_Hlp	primary amine hydrogen/lone-pair, e.g.
4	0	Hdonor	strong (primary) hydrogen bond donor H
5	0	Weak_Hdonor	weak (secondary) hydrogen bond dono
6	0	Charged_Lonepair	lone pair of negatively charged group, e
7	0	Acid_Lonepair	lone pair of an acid group, e.g. carboxo
8	**2**	**Lonepair strong**	**strong (primary) hydrogen bond acc**
9	0	Weak_Lonepair	weak (secondary) hydrogen bond accep
10	0	Ambivalent_Hlp	donor H OR acceptor Lp depending on
11	1	Rotatable_H	rotatable-hydroxy donor H
12	**2**	**Rotatable_Lp**	**rotatable-hydroxy acceptor Lp**
13	**28**	**Hydrophob**	**H on aliphatic (chain) hydrophobic c**
14	0	H_Arom_Edge	H on hydrophobic carbon in aromatic ri
15	0	Ws_Lipo	H on weak secondary hydrophobic aton
16	1	Neutral	H/Lp on neutral atom (no recognised ac
17	0	Pi_Aromatic	Pi electron of an aromatic ring
18	0	Pi_Reson_Polar	Pi electron on polar atom (N/O) in reson
19	1	Pi_Reson_Carbon	Pi electron on carbon atom in resonanc
20	1	Pi_Sp2_Polar	Pi electron on sp2 polar atom (N/O) (no
21	**2**	**Pi_Sp2_Carbon**	**Pi electron on sp2 carbon atom (non**
22	0	Halogen	lone electron pair of a halogen atom (F,
23	0	Sulfur	lone electron pair of a sulfur atom
24	0	misc	

Supplemental Figure 1

Histidine-like fragment of a molecules showing the surface point types as different colored triangles.



Supplemental Figure 2

Mibolerone displayed in SimBioSys' CheVi 3D desktop visualization tool, showing the 3D structure, color-coded interaction surface of the molecule, and the surface points (triangles colored according to interaction types).