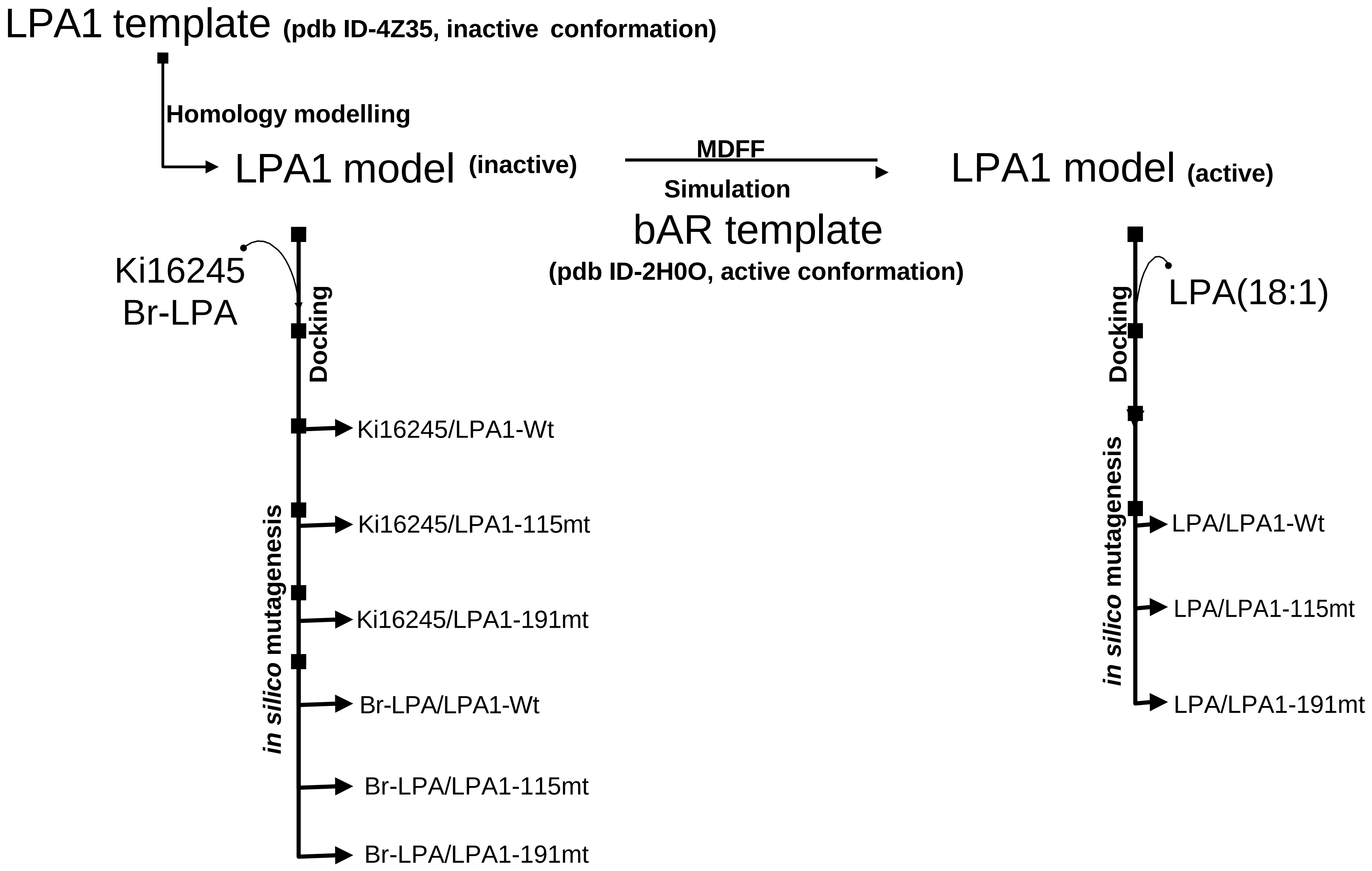
Electronic Supplementary Material (ESI) for RSC Advances.

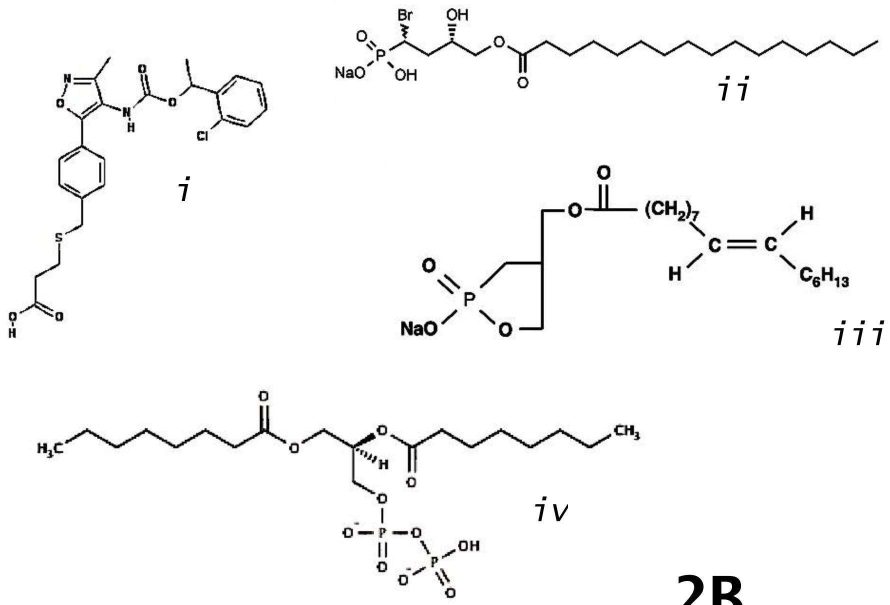
Supplementary figures: (1A) Schematic representation of modeling, and simulation workflow. (1B) Library of antagonists tested in this study. (2A) Sequence alignment of V_2R, LPA_1, LPA_2, LPA_3, and LPA_5 (all human) showing positive charged residues are conserved in similar or proximal residues in EL1 (black bar). (2B) Superimposed 3D structures depicting similar orientation of positively charged amino acid.

1A

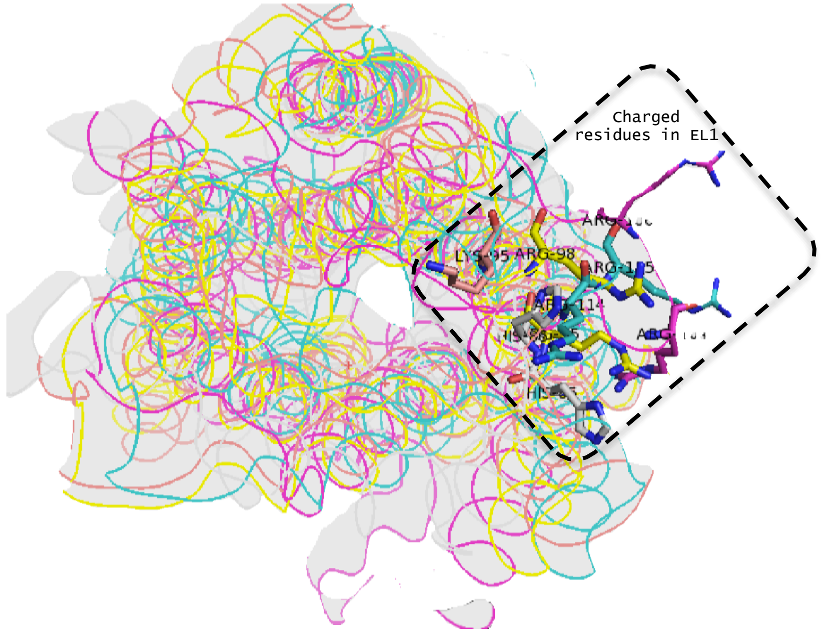

LPA1 template (pdb ID-4Z35, inactive conformation)
Homology modelling
LPA1 model (inactive)
MDFF
Simulation
LPA1 model (active)
bAR template
(pdb ID-2H0O, active conformation)
Ki16245
Br-LPA
Docking
in silico mutagenesis
Ki16245/LPA1-Wt
Ki16245/LPA1-115mt
Ki16245/LPA1-191mt
Br-LPA/LPA1-Wt
Br-LPA/LPA1-115mt
Br-LPA/LPA1-191mt
LPA(18:1)
Docking
in silico mutagenesis
LPA/LPA1-Wt
LPA/LPA1-115mt
LPA/LPA1-191mt

Supplementary

1B



2B



2A

```
MLMASTTSAVPGHP--------------SLPSLPSNSSQERPL----D---TRDPLLARA
MAAISTSIPVISQPQFTAMNEPQCFYNESIAFFYNRSGKHLAT----EWN-TVSKLV---
---------------MVIMG--QCYYNETIGFFYNNSGKELSS----HWR-PKDVVV---
------------------MN--ECHYDKHMDFFYNRSNTDTVD----DWTGTKLVIV---
-------------------------------MLANSSSTNSSVLPCPDYR-PTHRLH---

ELALLSIVFVAVALSNGLVLAALARRGRRGHWAPIHVFIGHLCLADLAVALFQVLPQLAW
-MGLGITVCIFIMLANLLVMVAIYVN--RRFHFPIYYLMANLAAADFFAGLAYFY--LMF
-VALGLTVSVLVLLTNLLVIAAIASN--RRFHQPIYYLLGNLAAADLFAGVAYLF--LMF
-LCVGTFFCLFIFFSNSLVIAAVIKN--RKFHFPFYYLLANLAAADFFAGIAYVF--LMF
-LVVYSLVLAAGLPLNALALWVFLRA--LRVHSVVSVYMCNLAASDLLFTLSLPV-RLSY

KATDRFRGPDALCRAVK-YLQMVGMYASSYM-----ILAMTLDRHRAICRPMLAYRHGSG
NT-----GPNTRRLTVSTWLLRQGLIDTSLTASVANLLAIAIERHITVFR-MQLHTRMSN
HT-----GPRTARLSLEGWFLRQGLLDTSLTASVATLLAIAVERHRSVMA-VQLHSRLPR
NT-----GPVSKTLTVNRWFLRQGLLDSSLTASLTNLLVIAVERHMSIMR-MRVHSNLTK
YALHHWPFPDLLCQTTG-AIFQMNMYGSCIF-----LMLINVDRYAAIVH-PLRLRHLRR

AHWNRPV-LVAWAFSLLLS-LPQLFIFAQRNVEGGSGVTDCWAC-FAE--------PWGR
RRVVVVI-VVIWTMAIVMGAIPSV----------------GWNC-ICDIENCSNMAPLYS
GRVVMLI-VGVWVAALGLGLLPAH----------------SWHC-LCALDRCSRMAPLLS
KRVTLLI-LLVWAIAIFMGAVPTL----------------GWNC-LCNISACSSLAPIYS
PRVARLLCLGVWALILVFA-VPAA------RVHR------PSRCRYRDLEVRLCFESFSD

RTYVT-WIALMVFVAPTLGIAACQVLIFREIHASLVPGPSERPGGRRRGRRTGSPGEGAH
DSYLVFWAIFNLVTFVVMVVLYAHIFGYVRQRTMRM---SRHSSGPRRNRDT--------
RSYLAVWALSSLLVFLLMVAVYTRIFFYVRRRVQRM---AEHVSCHPRYRET--------
RSYLVFWTVSNLMAFLIMVVVYLRIYVYVKRKTNVL---SPHTSGSISRRRT--------
ELWKGRLLPLVLLAEALGFLLPLAAVVYSSGRVFWT---LARPDATQSQRRR--------

VSAAVAKTVRMTLVIVVVYVLCWAP--------FFLVQLWA--AWDPEAPLEGAPFVLLM
----MMSLLKTVVIVLGAFIICWTP--------GLVLLLLD-VCCPQCDVLAYEKF--FL
----TLSLVKTVVIILGAFVVCWTP--------GQVVLLLDGLGCESCNVLAVEKY--FL
----PMKLMKTVMTVLGAFVVCWTP--------GLVVLLLDGLNCRQCGVQHVKRW--FL
------KTVRLLLANLVIFLLCFVPYNSTLAVYGLLRSKLVAASVPARDRVRGVLMV-MV

LLASLNSCTNPWIYASFSSSVSSELRSLLCCARGRTPPS---------LGPQDESCTTAS
LLAEFNSAMNPIIYSYRDKEMSATFRQILCC---QRSEN-----PTGPTEGSDRSASSLN
LLAEANSLVNAAVYSCRDAEMRRTFRRLLCCACLRQSTR-----ESVHYTSSAQGGASTR
LLALLNSVVNPIIYSYKDEDMYGTMKKMICCFSQENPERRPSRIPSTVLSRSDTGSQYIE
LLAGANCVLDPLVYYFSAEGFRNTLRGLGTPHRARTSAT--NG-TRAALAQSERSAVTTD

------------------SSLAKDTSS------  V2R
   -----------------HTILAGVHSNDHSVV  LPA1
   -----------------IMLPENGHPLMDSTL  LPA2
   -----------------DSISQGAVCNKSTS-  LPA3
   ATRPDAASQGLLRPSDSHSLSSFTQCPQDSAL  LPA5
```