

## Supplementary

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1                                     60
TBA_PIG      MRECISSIHVG QAGVIQIGNAC WELYCLEHGI QPDGQMPSDK TIGGGDDSSFN TFFSETGAGK
TBA1_BOVIN  MRECISSVHVG QAGVIQMGNNAC WELYCLEHGI QPDGQMPSDK TIGGGDDSSFT TFFCETGAGK
TBA1_ARATH  MREISSIHIG QAGTIQVGNSC WELYCLEHGI QPDGTMPSSDS TVGAACHDAFN TFFSETSSGQ
TBA_PLAFK   MREVISSIHVG QAGTIQVGNSC WELFCLEHGI QPDGQMPSDK ASRAANDDAFN TFFSETGAGK

61                                     120
TBA_PIG      HVPRAVFVDL EPTVIDEVRT GTYRQLFHPE QLITTGKEDAA NNYIARGHYTI GKEIIDLVLD
TBA1_BOVIN  HVPRAVFVDL EPTVIDEIRN GPYRQLFHPE QLITTGKEDAA NNYIARGHYTI GKEIIDPVLD
TBA1_ARATH  HVPRAVFLDL EPTVIDEVRT GTYRQLFHPE QLISSGKEDAA NNFARGHYTV GREIVDTCLE
TBA_PLAFK   HVPRCVFVDL EPTVVDEVRT GTYRQLFHPE QLISSGKEDAA NNFARGHYTI GKEVIDVCLD

121                                     180
TBA_PIG      RIRKLADQCT GLQGFSSVFHS FGGGTGSGFT SLLMMERTSSVD YGKKSLEFS IYPAPQVSTA
TBA1_BOVIN  RIRKLSDQCT GLQGFLVFHS FGGGTGSGFT SLLMMERTSSVD YGKKSLEFS IYPAPQVSTA
TBA1_ARATH  RLRKLADNCT GLQGFLVFNA VGGGTGSGLG SLLLLERTSSVD FGKKSLEGFT IYPSQVSTA
TBA_PLAFK   RIRKLADNCT GLQGFLMFS AVGGGTGSGFG CLMLERTSSVD YGKKSLENF CWPSQVSTA

181                                     240
TBA_PIG      VVEPYNSILT THTTLEHSDC AFMVDNEAIY DICRRNLDIE RPTYTNLNRL IGQIVSSITA
TBA1_BOVIN  VVEPYNSILT THTTLEHSDC AFMVDNEAIY DICRRNLDIE RPTYTNLNRL ISQIVSSITA
TBA1_ARATH  VVEPYNSVLS THSLLEHTDV VVLLDNEAIY DICRRSLDIE RPTYSNLNRL ISQTISSLTT
TBA_PLAFK   VVEPYNSVLS THSLLEHTDV AIMLDNEAIY DICRRNLDIE RPTYTNLNRL IAQVISSLTA

241                                     300
TBA_PIG      SLRFDGALNV DLTEFQTNLV PYPRAHFPLA TYAPVISAEK AYHEQLSVAE ITNACFEFAN
TBA1_BOVIN  SLRFDGALNV DLTEFQTNLV PYPRIHFPLA TYAPVISAEK AYHEQLSVAE ITNACFEFAN
TBA1_ARATH  SLRFDGAINV DITEFQTNLV PYPRIHFMLS SYAPVISSAK AYHEQFSVPE ITTSVFEPN
TBA_PLAFK   SLRFDGALNV DVTEFQTNLV PYPRIHFMLS SYAPVVSAEK AYHEQLSVSE ITNSAFEFAN

301                                     360
TBA_PIG      QMVKCDPRHG KYMACCLLYR GDVVPKDVNA AIATIKTKRT IQFVDWCPTG FKVGINYEP
TBA1_BOVIN  QMVKCDPRHG KYMACCLLYR GDVVPKDVNA AIAAIKTKRS IQFVDWCPTG FKVGINYQPP
TBA1_ARATH  MAAKCDPRHG KYMACCLMYR GDVVPKDVNT AVAAIAKAKRT IQFVDWCPTG FKCGINYQPP
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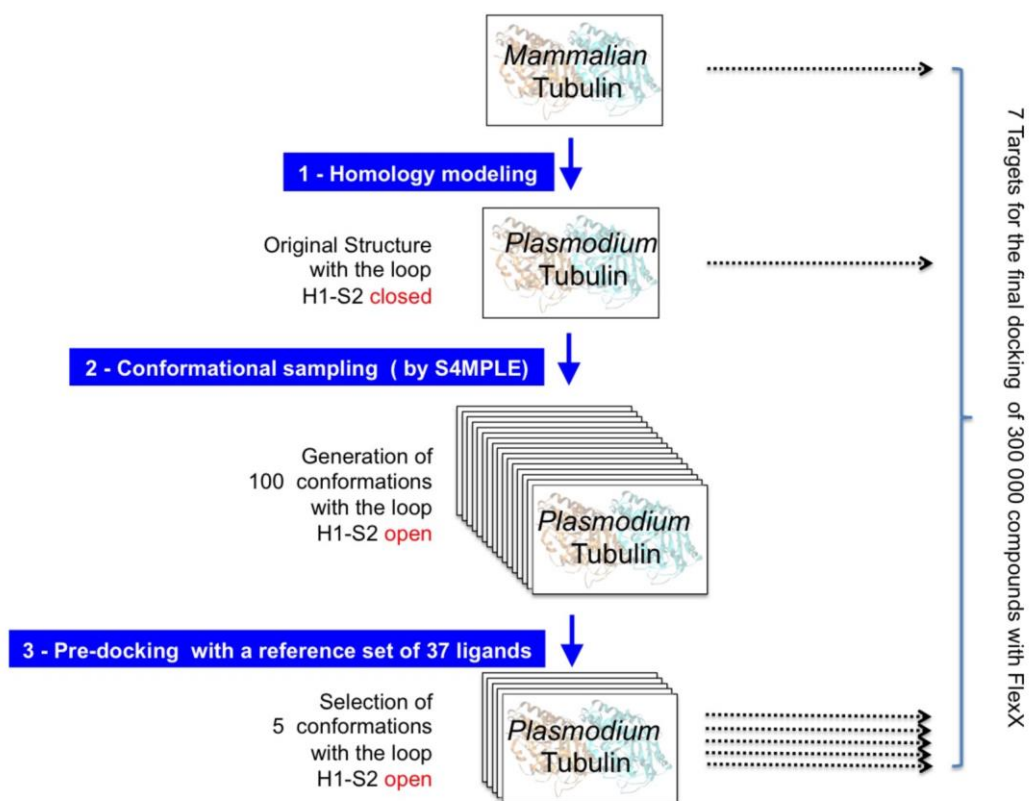
361                                     420
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TBA1_ARATH  SVVPGDLAK VQRAVCMISN NTAVAEVFSR IDHKFDLMYS KRAFVHWYVG EGMEEGEFSE
TBA_PLAFK   TVVPGDLAK VMRAVCMISN STAIAEVFSR MDQKFDLMYA KRAFVHWYVG EGMEEGEFSE

421                                     453
TBA_PIG      AREDMAALEK DYEEVGVDSV EGEEEEGEE Y
TBA1_BOVIN  AREDMAALEK DYEEVGIDSY EDE--DEGEE
TBA1_ARATH  AREDLAALEK DYEEVGGEGA E-DDDEGEDE Y
TBA_PLAFK   AREDLAALEK DYEEVGIESN EAEGEEDEGEY ADY

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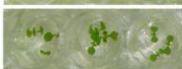






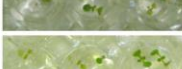



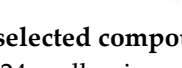
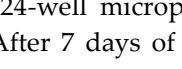


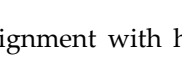
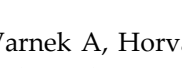










## Supplementary Figure 1

**Supplementary Figure 1: Alignment of the sequences of *Bos taurus*, *Sus scrofa*, *Arabidopsis thaliana* and *Plasmodium falciparum*  $\alpha$ -tubulin.** Alignments have been performed using Multalin software with default options [1]. Highly conserved residues appear in red, weakly conserved in blue and divergent residues in black. High consensus regions predominate low ones indicating that  $\alpha$ -tubulin is a highly conserved protein. Some plant/mammal differences (framed residues) are also detected in *P. falciparum*  $\alpha$ -tubulin. The residues Ser6, Ile235 or Leu167 used in docking as criteria for the selection of ligands are highlighted in white on red background.



**Supplementary Figure 2**

**Supplementary Figure 2 Strategy for the selection of potential 3D structures of plasmodium tubulin to be used as targets for a virtual screen of compounds with FlexX.** First, the *Plasmodium* tubulin 3D structure has been predicted by homology with the *Mammalian* tubulin. This original structure has a loop (H1-S2 loop) that locks the dinitroaniline binding site. Using S4MPLE [2], a conformational sampler software, 100 **open** conformations of this loop were generated. A set of 37 molecules (10 known to bind to the dinitroaniline binding site and 27 not having been described to bind tubulin) was docked against the dinitroaniline binding site of these 100 conformations. The 5 conformations which best discriminated the active molecules from the inactive ones were selected. These 5 conformations, the mammalian tubulin and the original *Plasmodium* tubulin conformations were the final targets for the docking of 300 000 compounds with FlexX in the dinitroaniline binding site.

Compound ID	DMSO	50 $\mu$ M	100 $\mu$ M	Growth	Chlorosis
CM539				+	-
CM571				-	+
CM903				+	-
CM094				-	-
CM406				+	-
CM973				+	-
CM694				+	-
CM272				+	-
CM505				+	-
CM901				+	-
CM852				-	+

### Supplementary Figure 3

#### Supplementary Figure 3: Effect of the selected compounds on *Arabidopsis thaliana* growth

Arabidopsis seedlings were sown on 24-well microplates containing an agar-based solid medium containing compounds, as indicated. After 7 days of incubation in a growth chamber, growth was monitored.

#### Supplementary references

1. Corpet F: Multiple sequence alignment with hierarchical clustering. *Nucleic Acids Res.* 1988, 16:10881–90.
2. Hoffer L, Chira C, Marcou G, Varnek A, Horvath D: S4MPLE--Sampler for Multiple Protein-Ligand Entities: Methodology and Rigid-Site Docking Benchmarking.. *Molecules* 2015, 20:8997–9028.