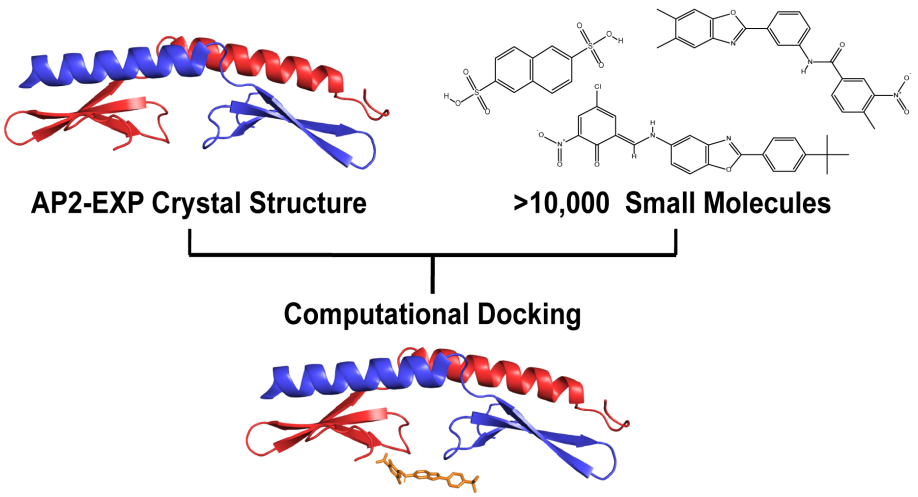
## SI Figures

**A**




**B**

| Letter Code | Compound Used Originally for *in silico* Docking | Compound Name Used for Purchase | PubChem ID of Compound used in this study |
|---|---|---|---|
| A | GSK-like (TCMDC-124220) | CB5768506* | CID1365835 |
| B | GSK (TCMDC-123924) | CB5842949 | CID1365471 |
| C | GSK-like (TCMDC-124220) | ChemDiv-8002-1285* | CID5750730 |
| D | GSK-like (TCMDC-124220) | ChemDiv-8004-0752* | CID4541005 |
| E | Drug Bank (DB00562) | Benzathiazide | CID2343 |
| F | Drug Bank (DB04409) | Napthalene Trisulfonate | CID4437 |
| G | Drug Bank (DB04640) | 2,6 Napthalene Sulfonate | CID11390 |
| H | Drug Bank (DB01219) | Dantrolene | CID6914273 |
| I | Drug Bank (DB02633) | Procion Blue | CID25863 |

**Figure S1. Putative AP2-EXP competitors were identified using computational docking**

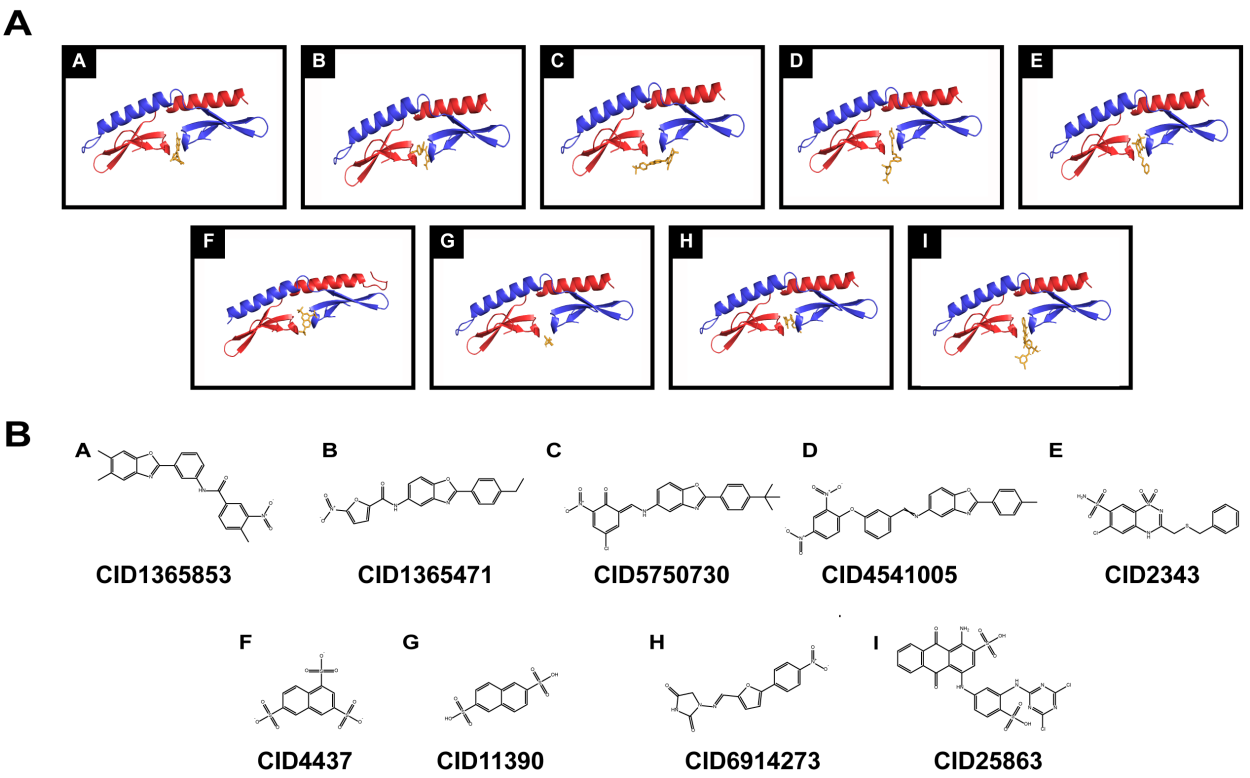



**Figure S2. Docking conformations for Compounds A-I**

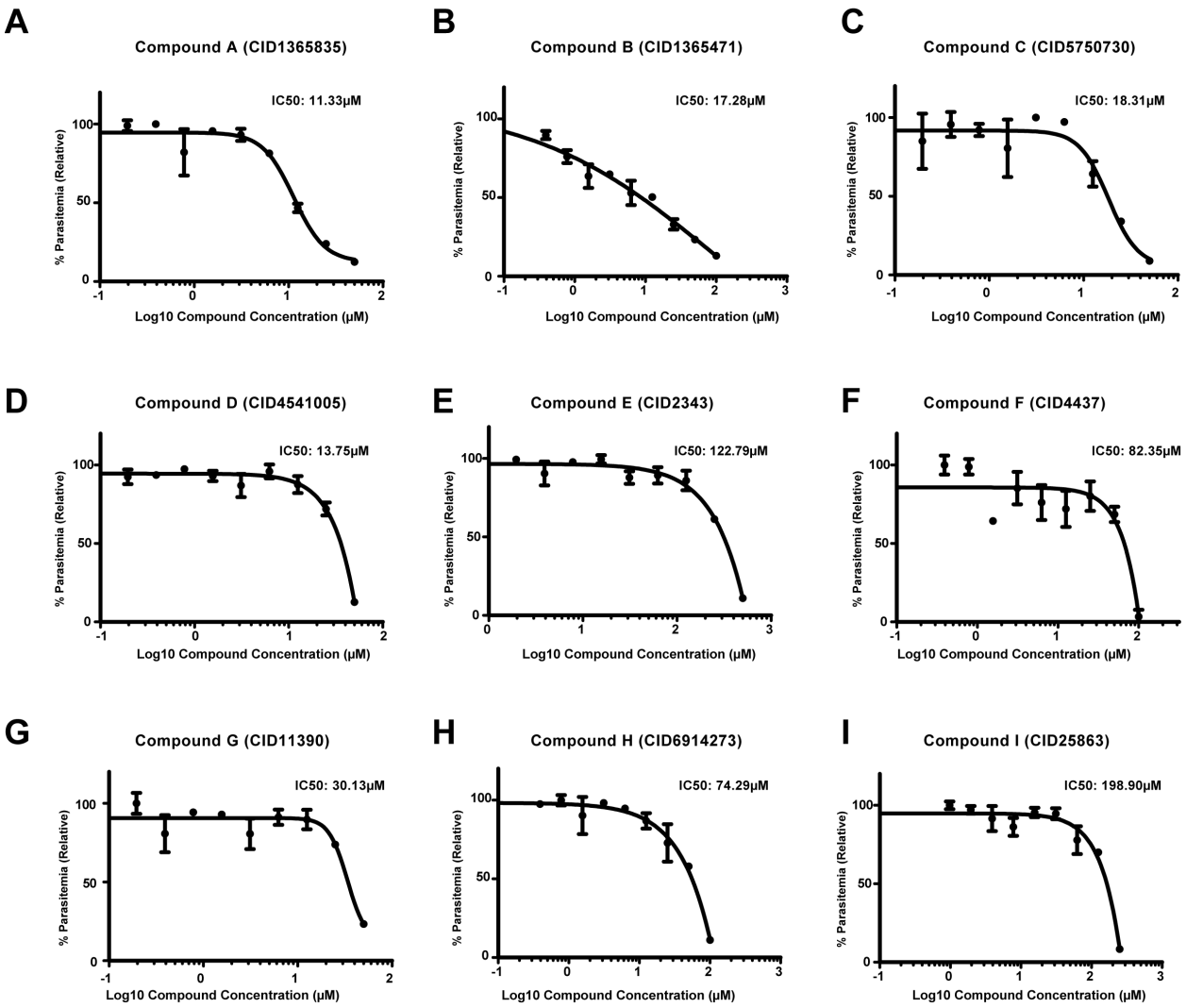



**Figure S3. IC50 assays for Compounds A-I**

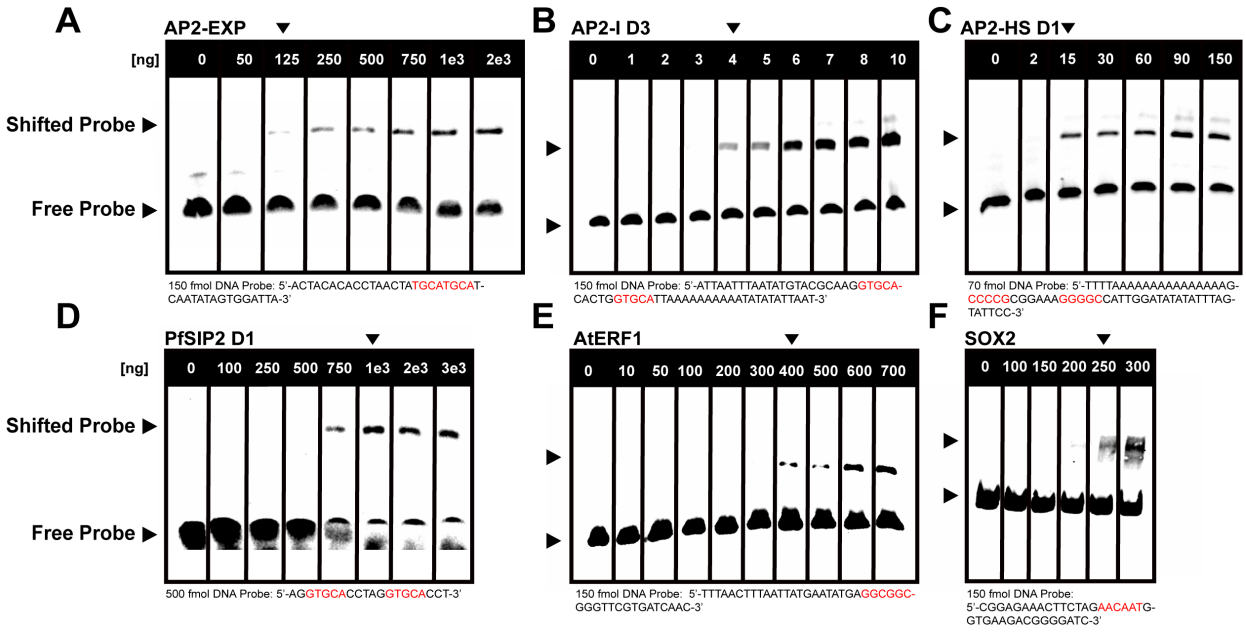



**Figure S4. Titration of recombinant DNA binding domains to optimize competition electrophoretic mobility shift (EMSA) assays**

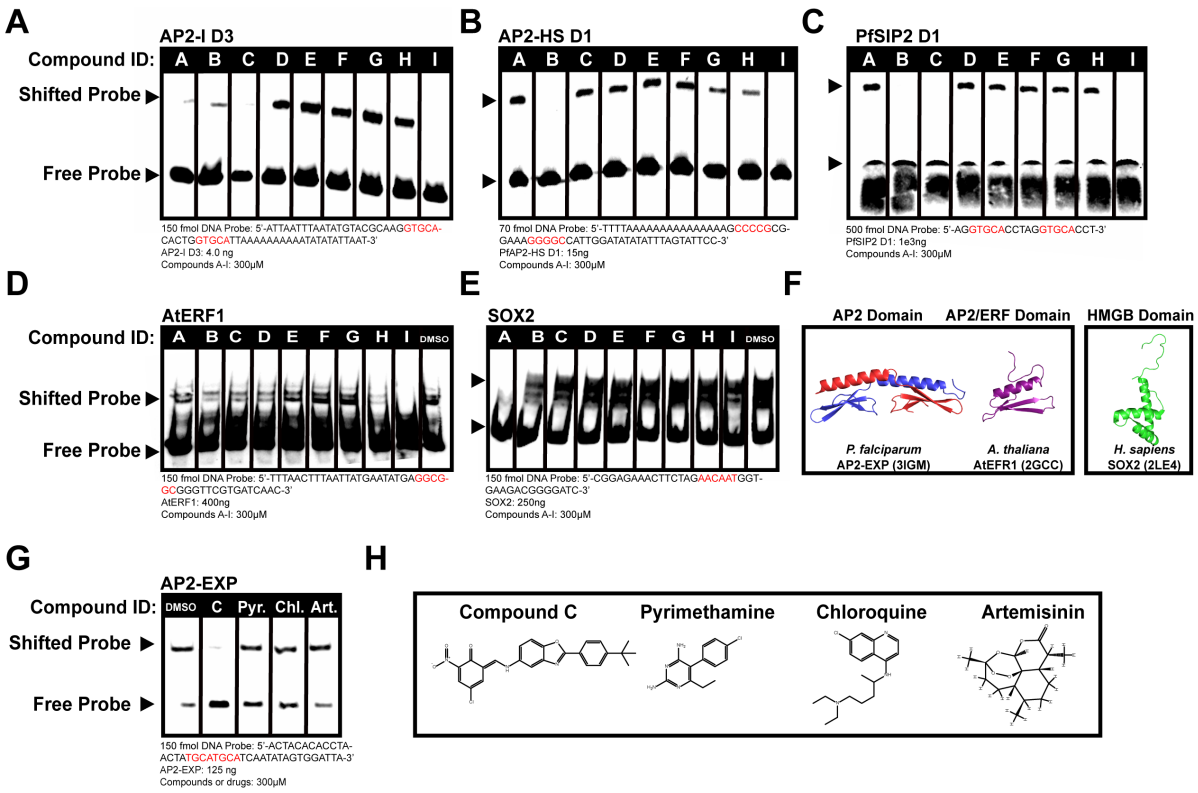



**Figure S5. Putative ApiAP2 competitor compounds were tested against additional proteins in a competitive EMSA**

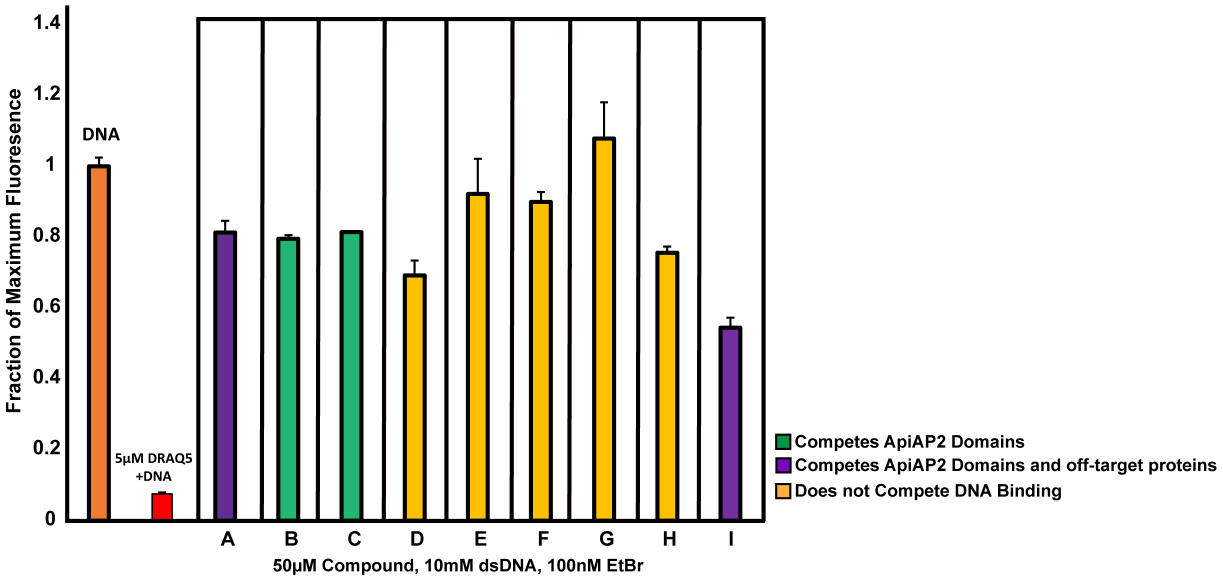



**Figure S6. Compounds A-I were tested for DNA intercalation in an ethidium bromide exclusion assay**

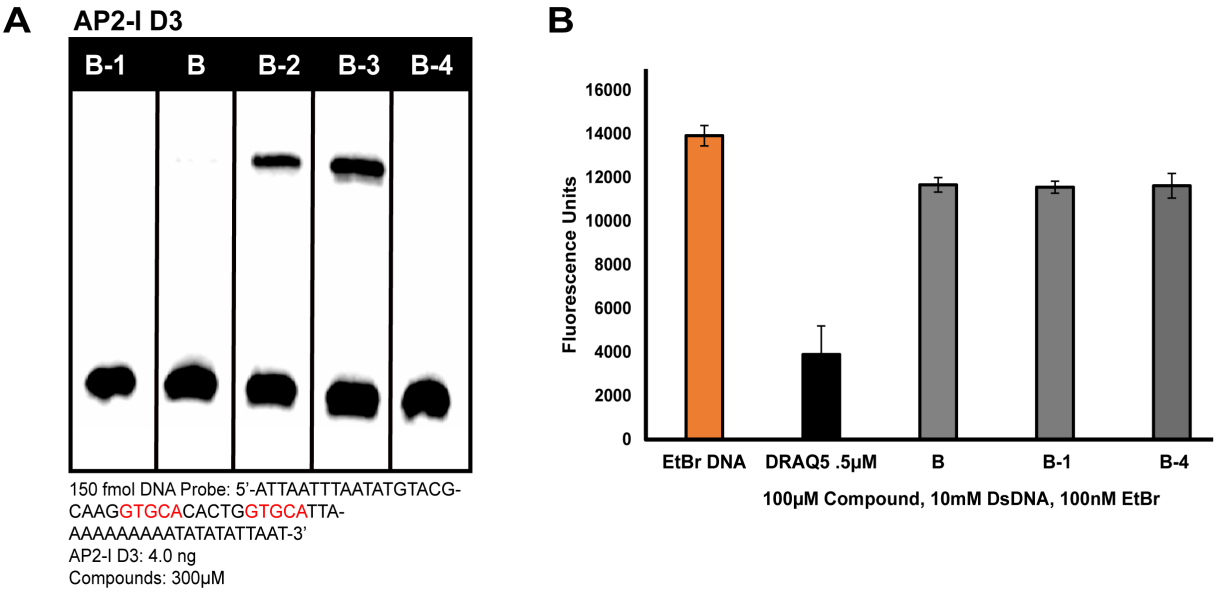



**Figure S7. Compound B analogues were tested against AP2-I D3 in a competitive EMSA and checked for DNA intercalation ability**

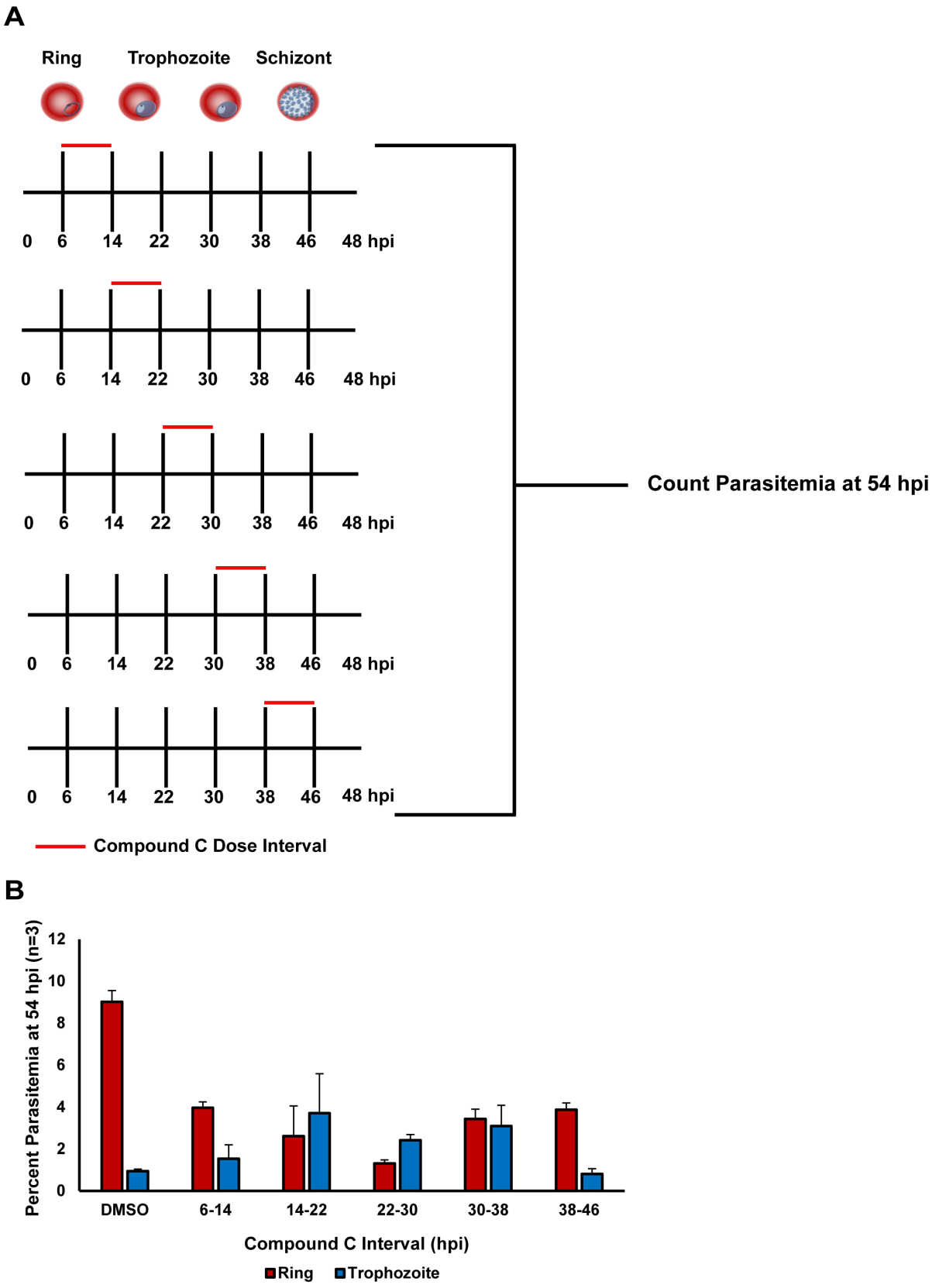



**Figure S8. A fixed interval Compound C dosage assay to determine the timing of antimalarial action**

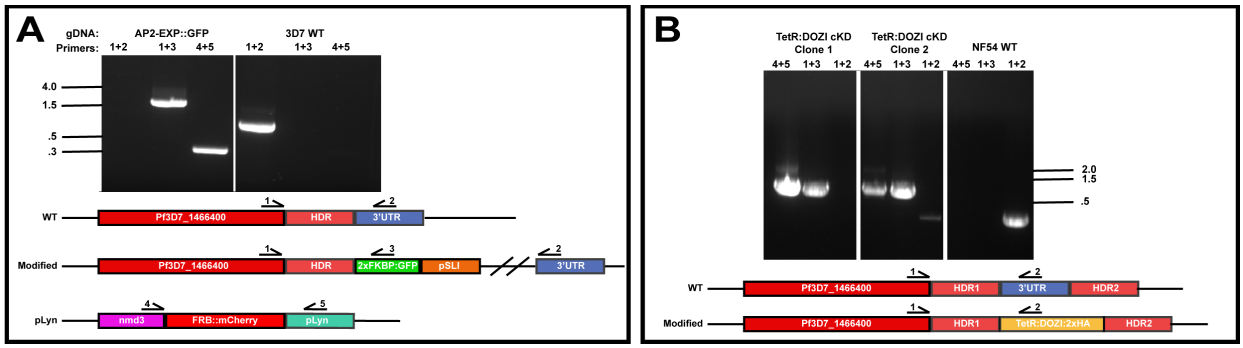



**Figure S9. Creation of endogenously tagged parasite lines AP2-EXP::GFP and AP2-EXP::HA**

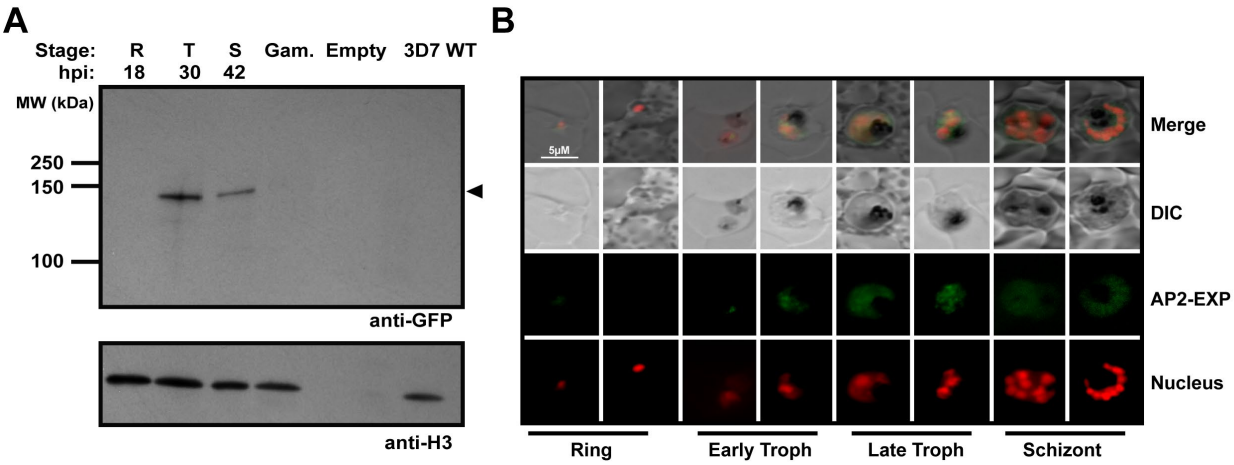



**Figure S10. AP2-EXP protein expression in the AP2-EXP::GFP endogenously tagged parasite line (related to figure 3A)**

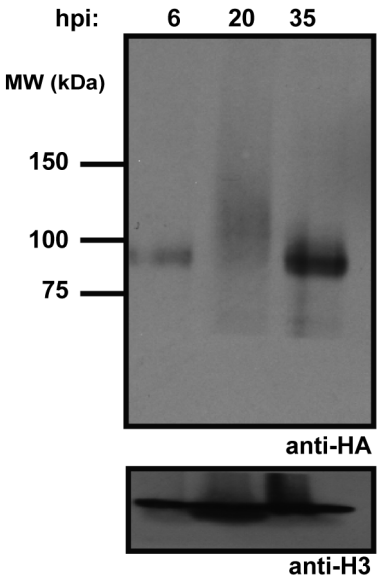



**Figure S11. AP2-EXP protein expression in the AP2-EXP::HA endogenously tagged parasite line**

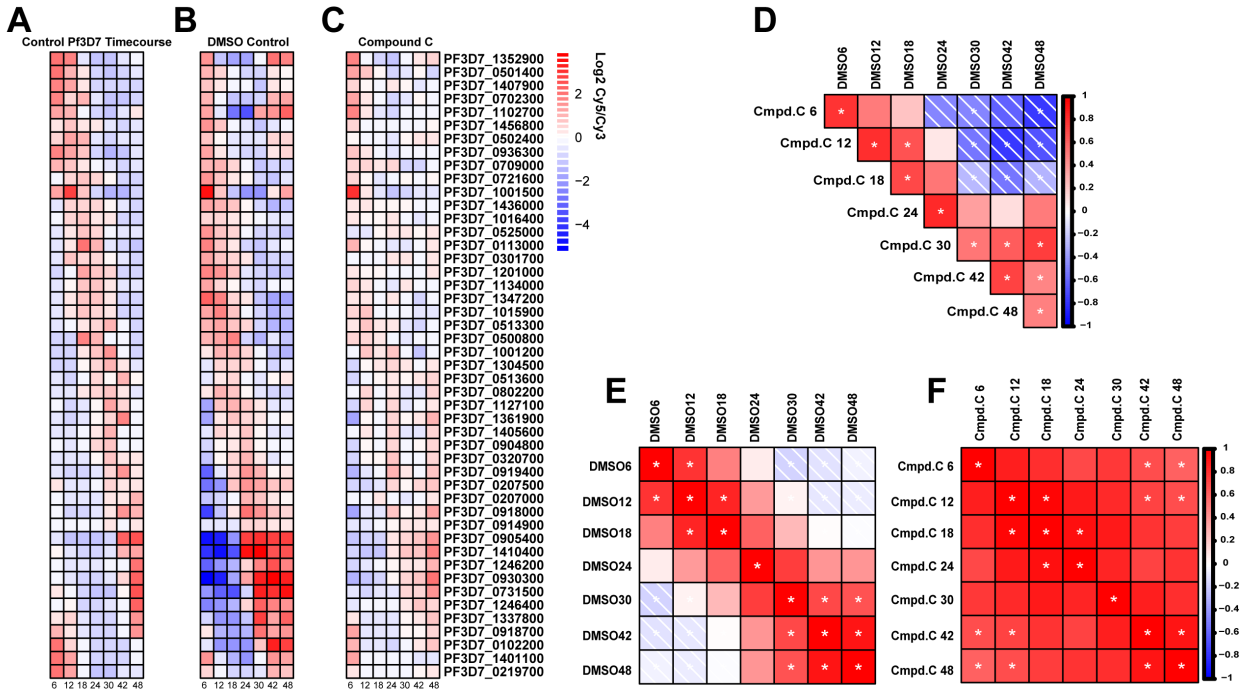



**Figure S12. Quality control of DNA microarray data for DMSO vehicle control and Compound C parasites, related to figure 4**

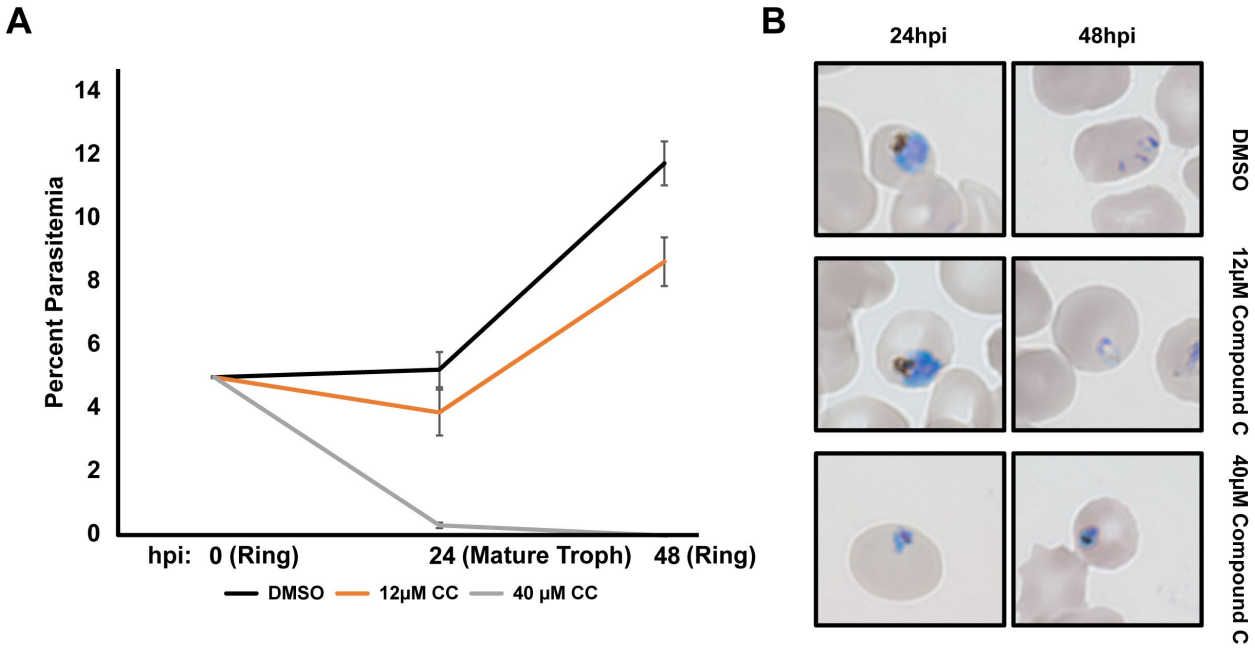



**Figure S13. A 48-hour time course to determine the phenotype for 12μM Compound C, related to Figure 4A**

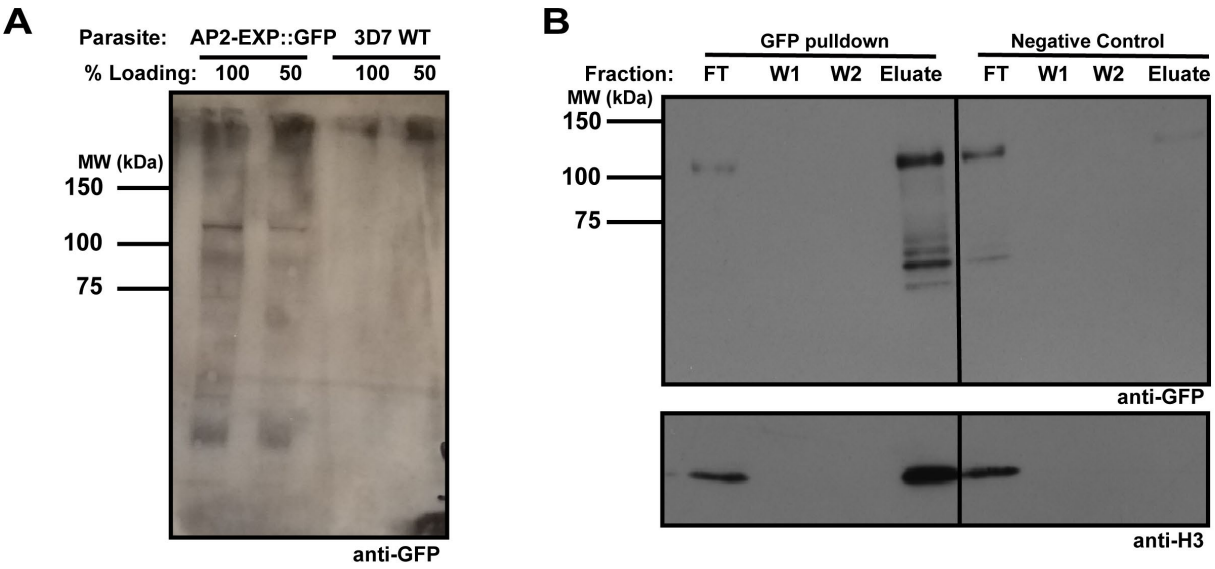



**Figure S14. ChIP-seq protein quality control, related to figure 4B**

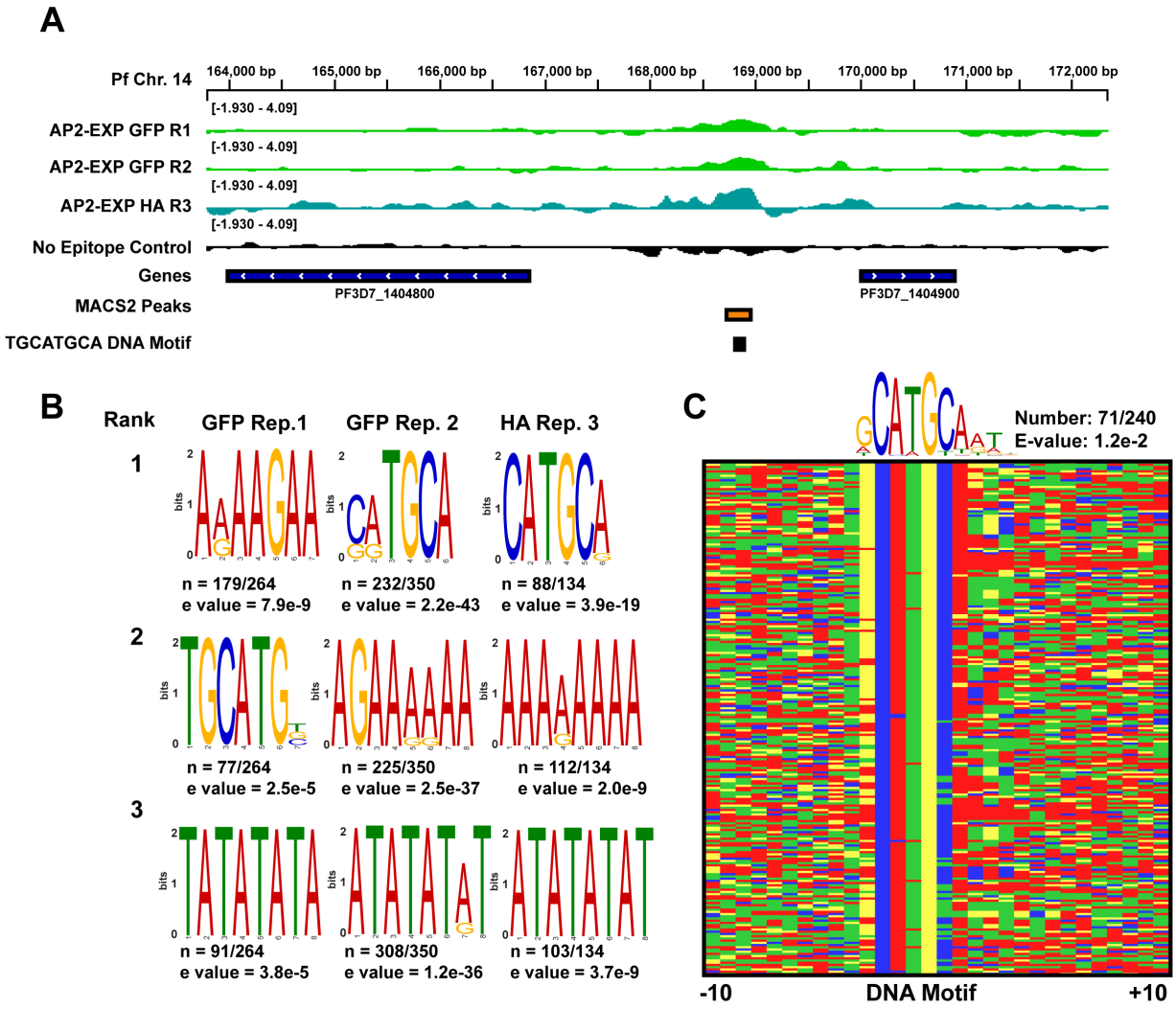



**Figure S15. ChIP-seq extended data**

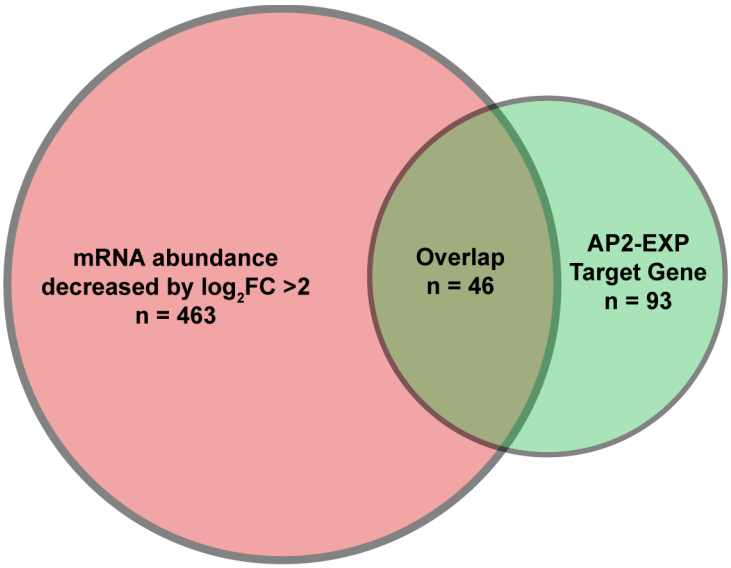



**Figure S16. Comparison of AP2-EXP target genes with Compound C induced changes in transcript abundance**

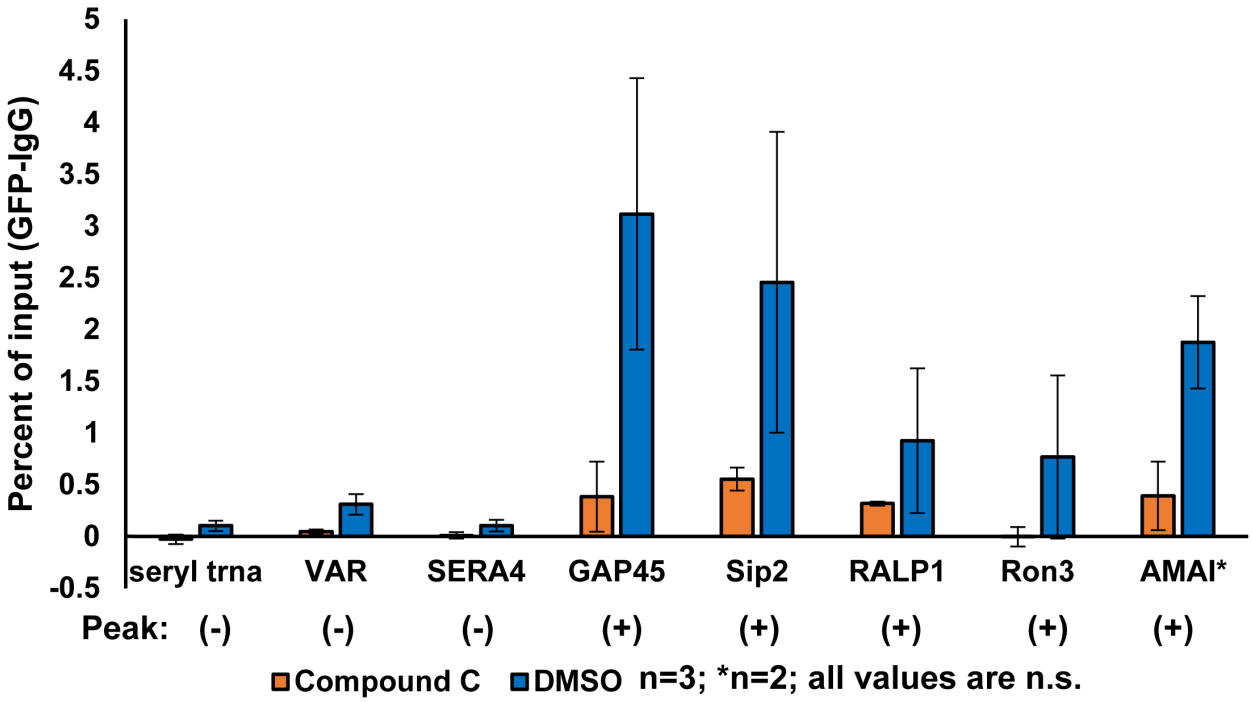



**Figure S17. ChIP-Quantitative PCR to assess Compound C impact on AP2-EXP genomic occupancy**

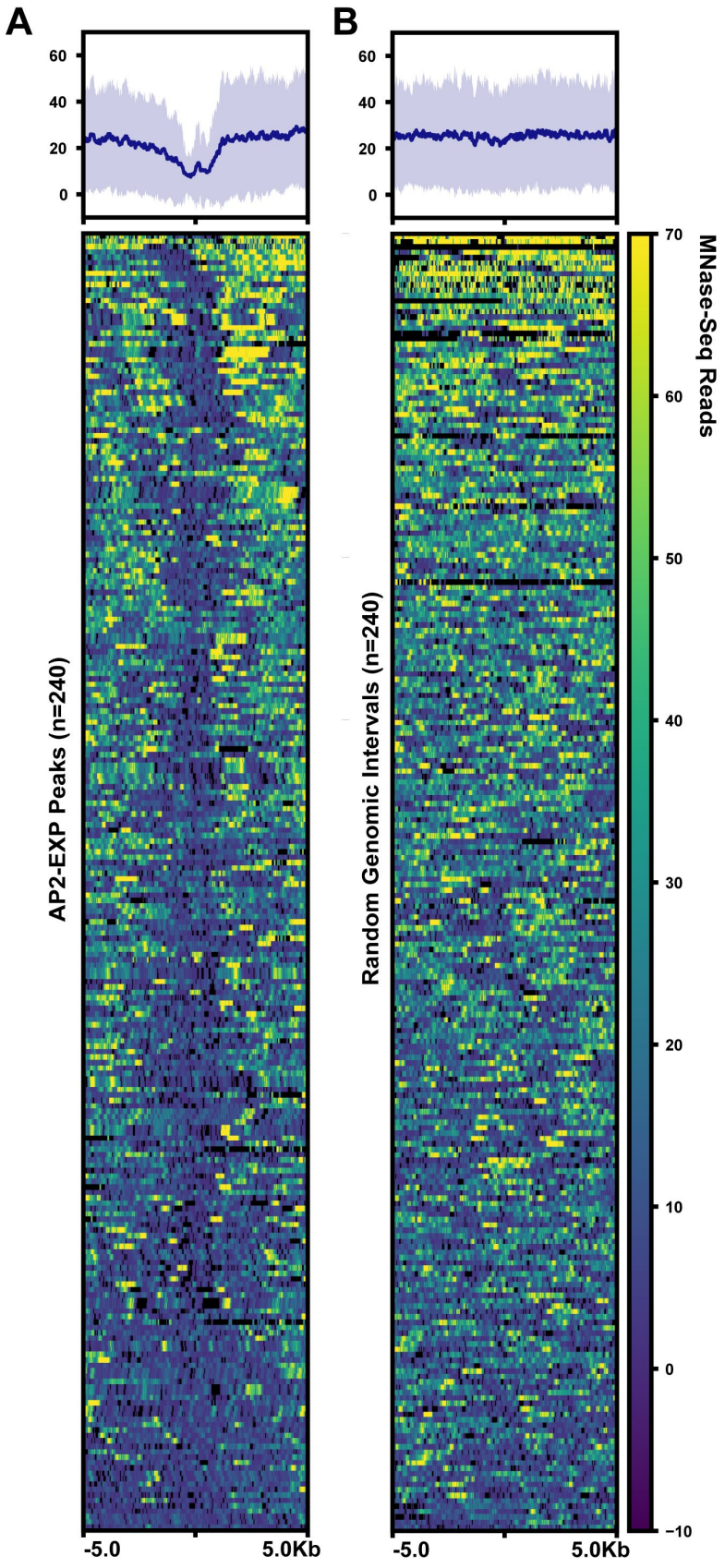



**Figure S18. Nucleosome occupancy is depleted at AP2-EXP DNA binding sites**

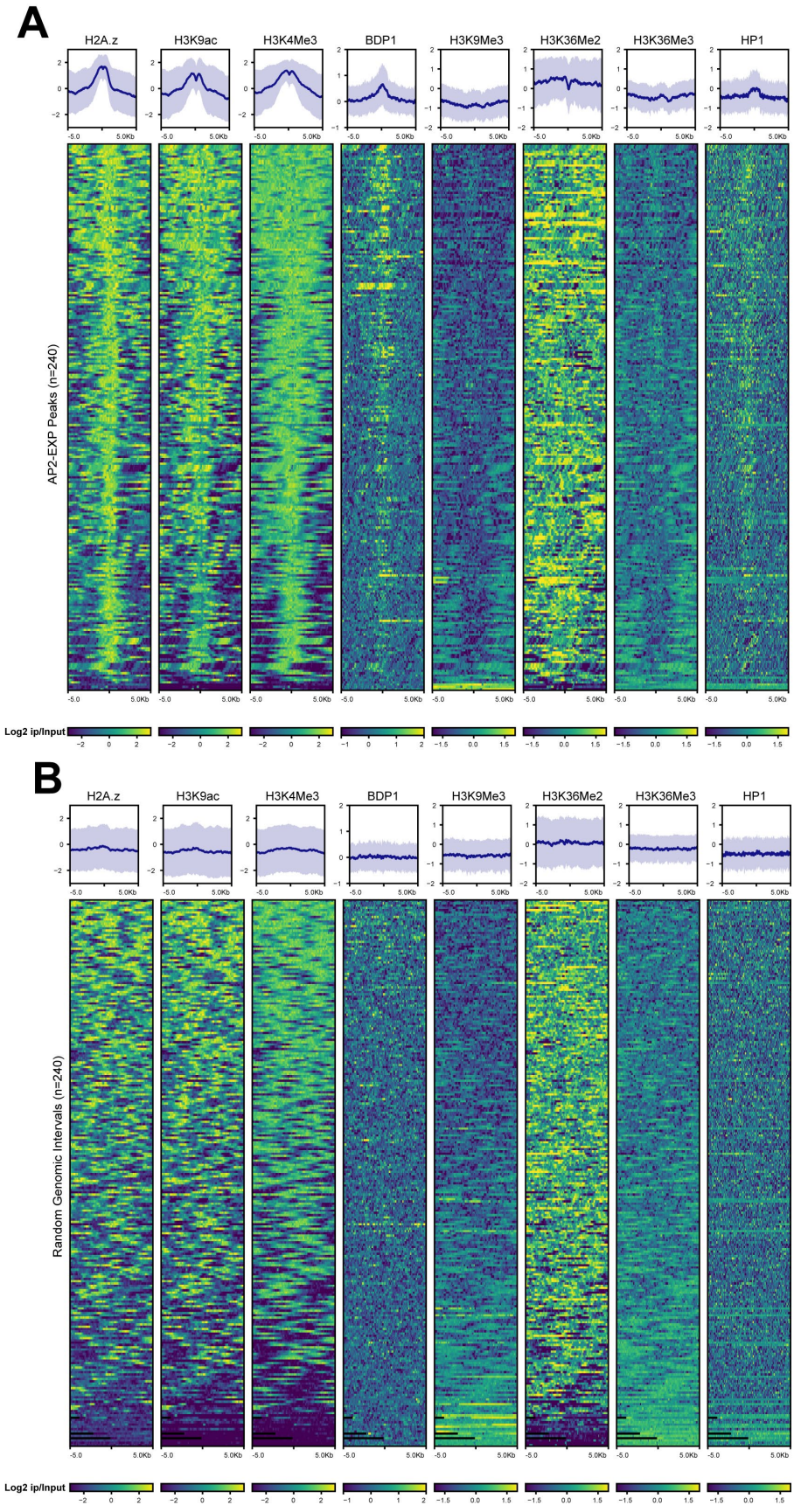



**Figure S19. Histone post translational modifications and chromatin reader occupancy at AP2-EXP peaks**

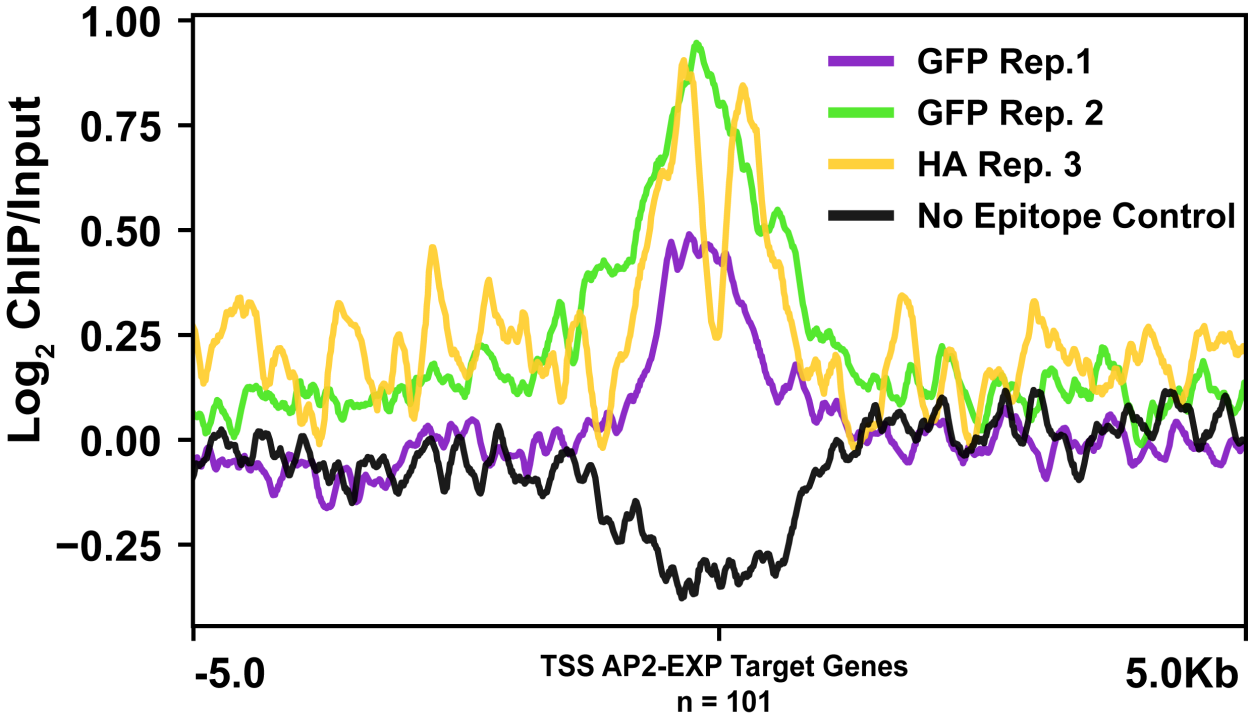



**Figure S20. AP2-EXP DNA occupancy with respect to the Transcription Start Site (TSS) of target genes**

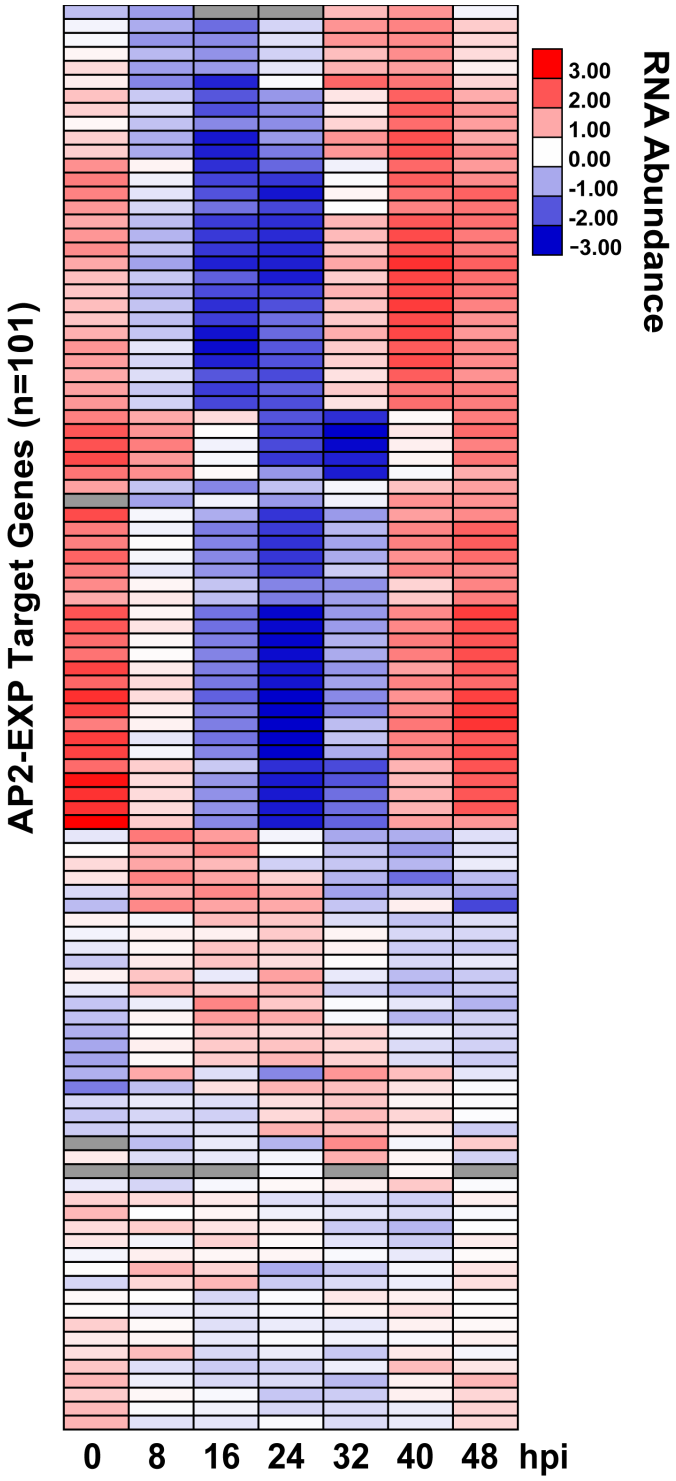



**Figure S21. Normal Transcript Abundance of AP2-EXP Target Genes**

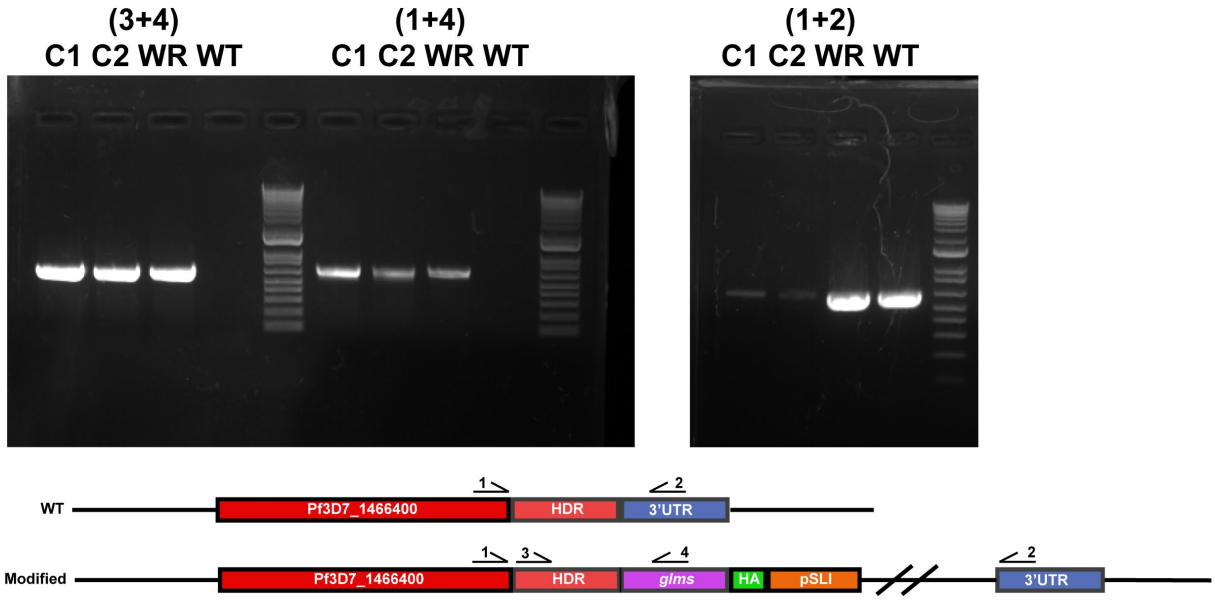



**Figure S22. Creation of a *glms* ribozyme based knockdown line for AP2-EXP**

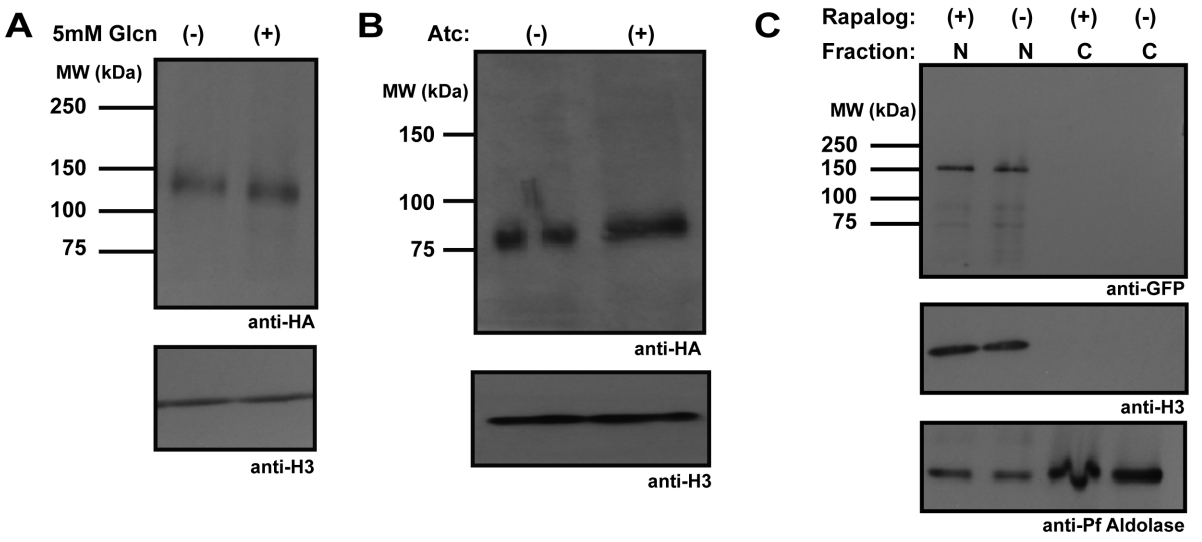



**Figure S23. Western blot phenotyping of attempts to genetically knockdown AP2-EXP**

```
AP2-EXP   58 --SNNKVIKKEEKVSTSSSGYPGVSWNKRMCAWLAFFYDGASRRSRTFHPKHFNMDKEKA
PbAP2-Sp  60 ATSANKIVKKEEKASTSSSGYPGVSWNKRMCAWLAFFYDGASRRSRTFHPKHFNMNKDQA
                * **::*****.**************************************:*::*

AP2-EXP   RLAAVEFMKTVENNGRKKSGKGKGGRSKSKQLND 92
PbAP2-Sp  RLAAVEFMKSLENHGRKKSTKIKGGKNKIKQM-- 92
          *********::**:***** * ***:.* **:
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**Figure S24. Sequence alignment between the AP2-EXP and PbAP2-Sp AP2 domains**

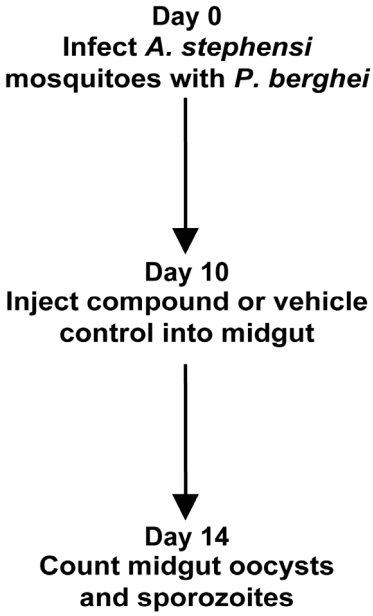


**Figure S25. Mosquito stage *P. berghei* inhibition assay schematic**