

Supplementary Materials

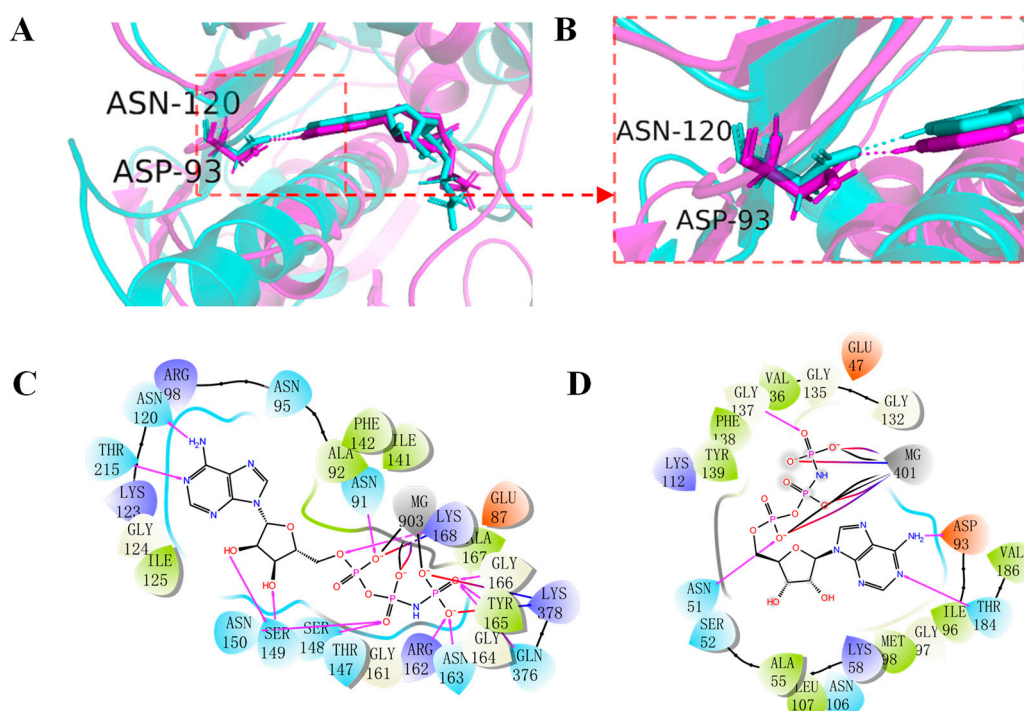
# Discovery of Quinacrine as a Potent Topo II and Hsp90 Dual-target Inhibitor Repurposing for Cancer Therapy

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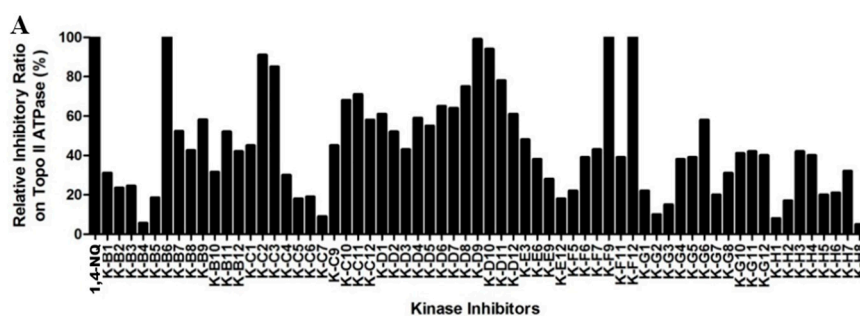
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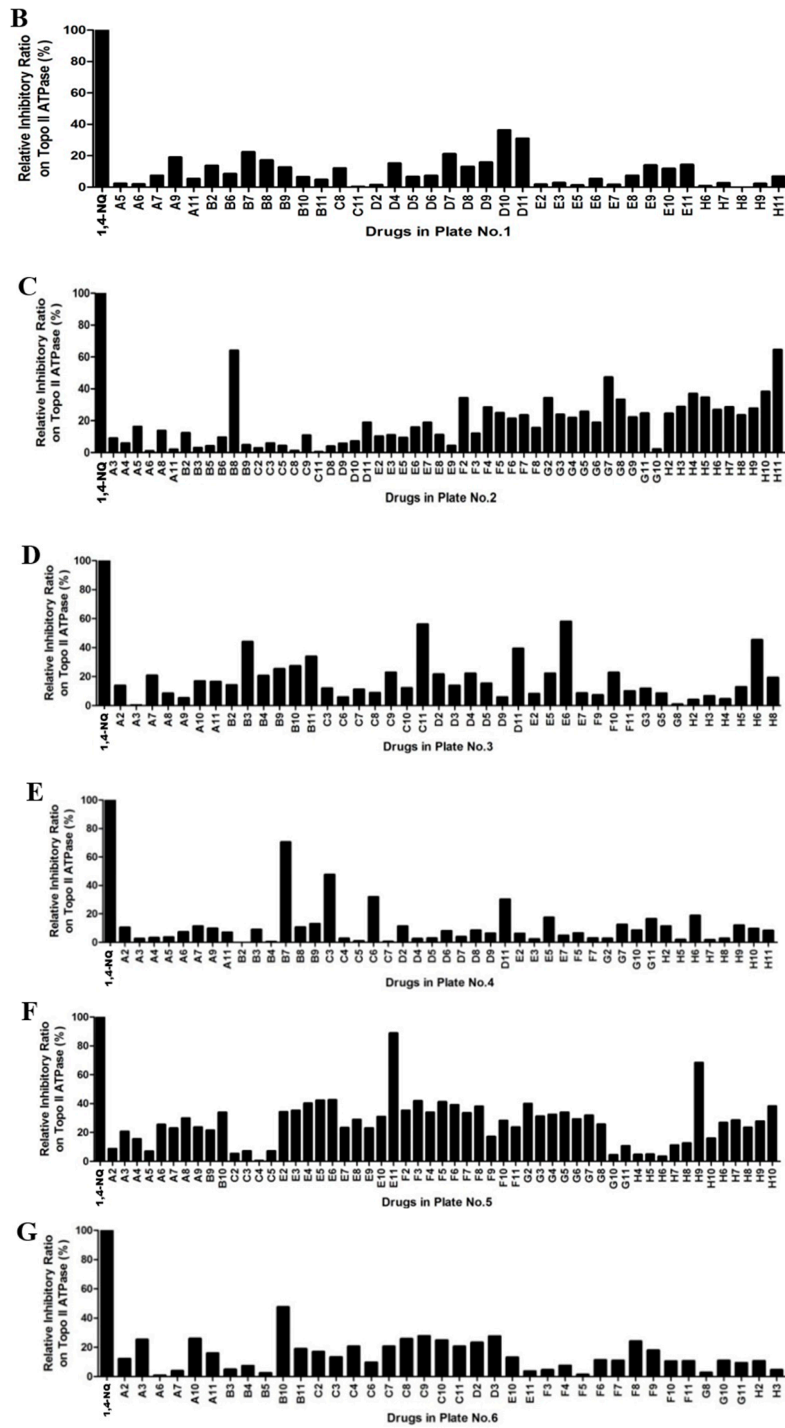
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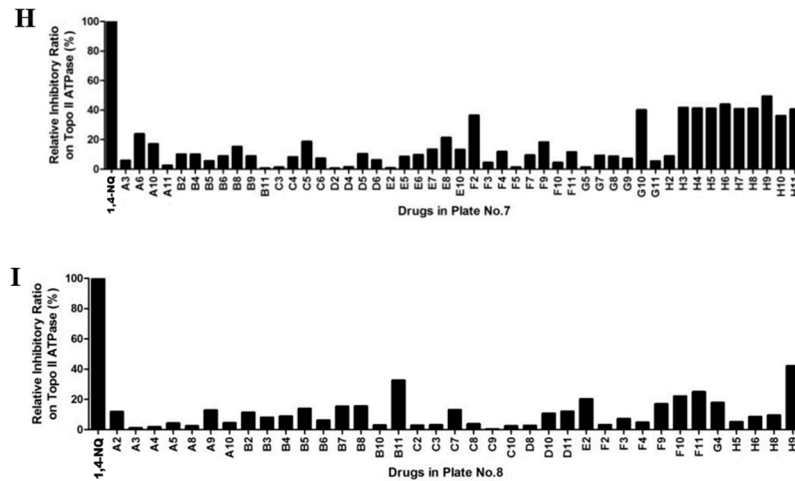
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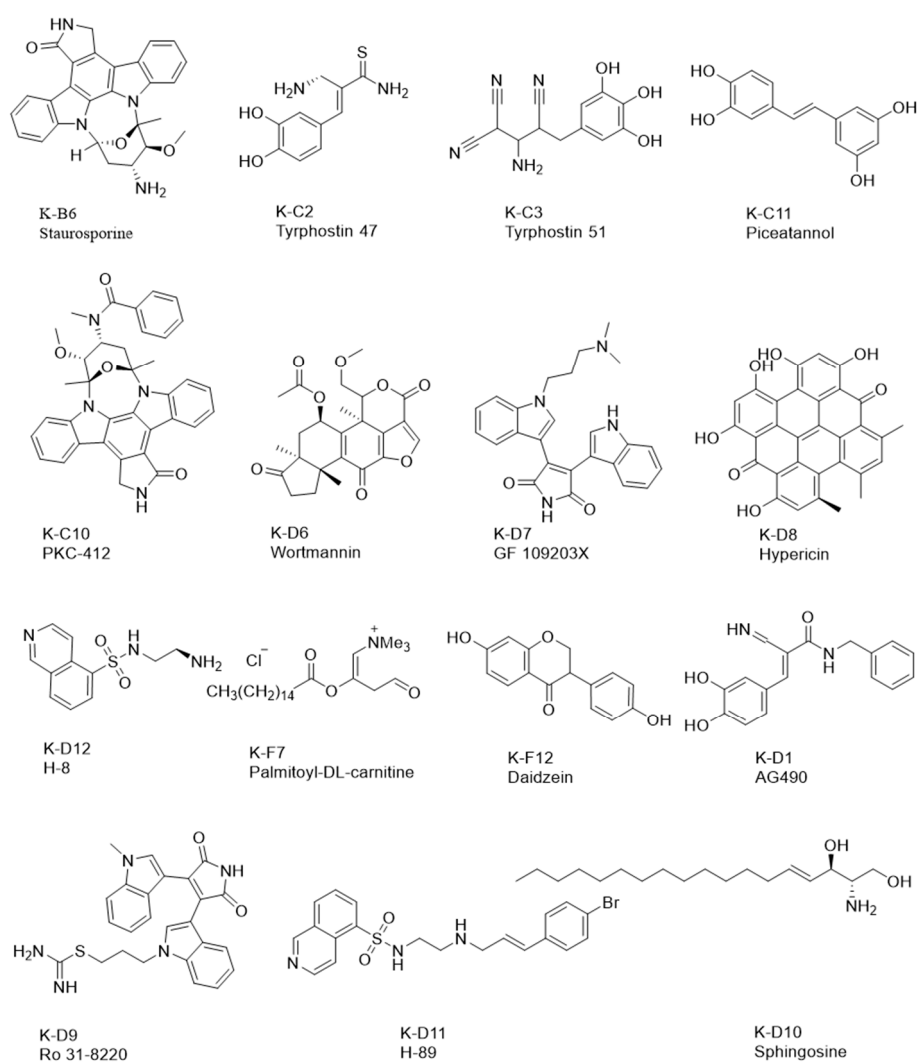
**Figure S1.** Structural alignment of Topo IIα ATPase and Hsp90 N-ATPase. (A–B) Structural alignment of the ATPase domains of Topo IIα (purple) and Hsp90α (blue). The hydrogen bonds between QA and ASN120 (Topo IIα ATPase) and ASP93 (Hsp90 N-ATPase) are indicated by dotted lines. (C) Binding mode of ANP with Topo II (PDB: 1ZXN). (D) Binding mode of ANP with Hsp90 (PDB: 3T1K).



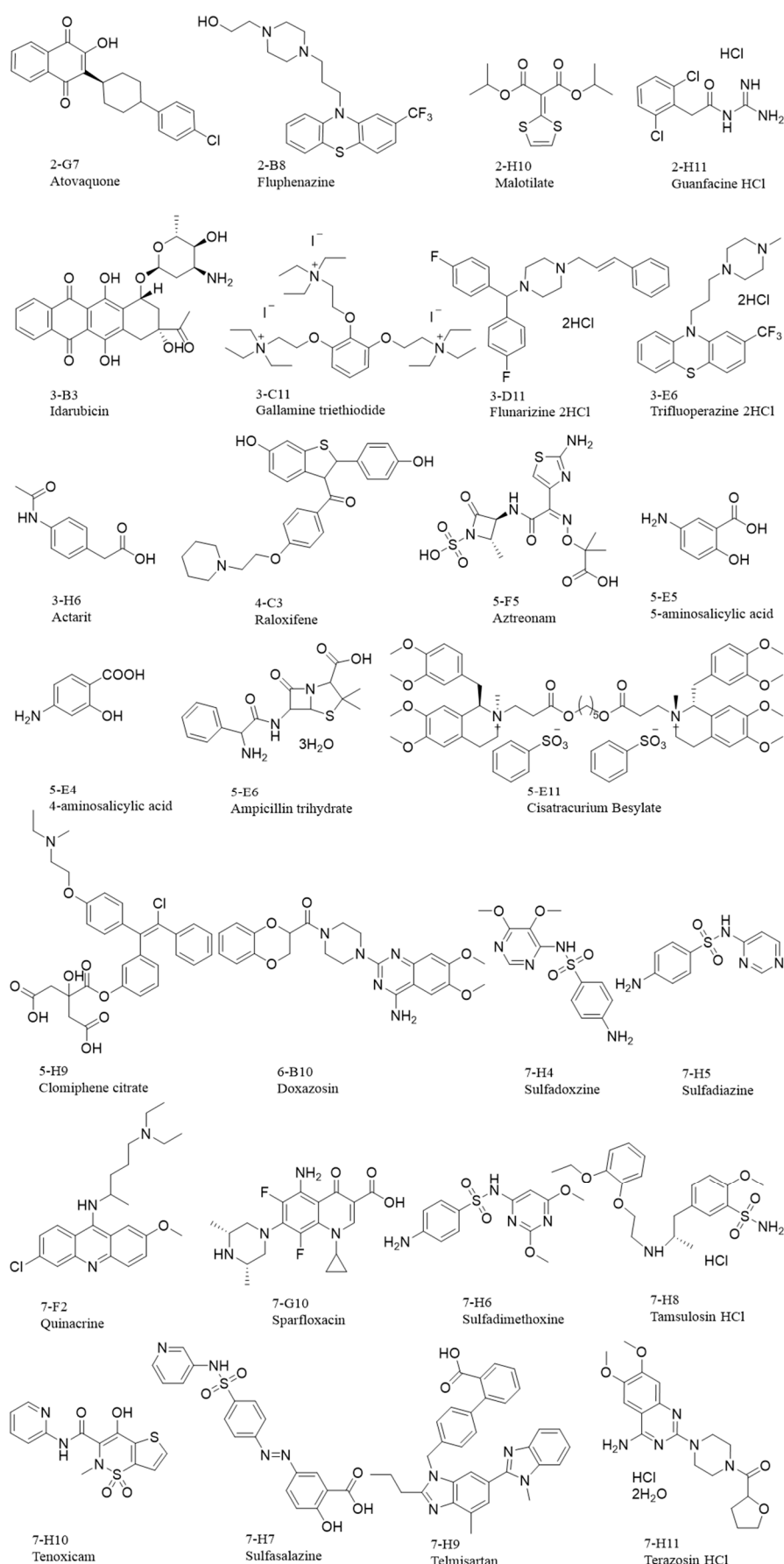




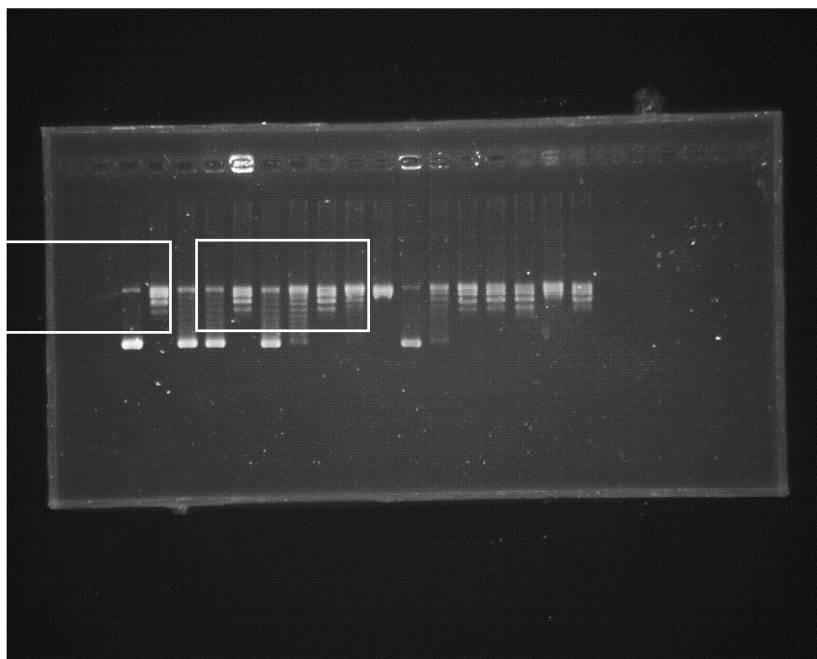
**Figure S2.** Results of preliminary screening of Topo II $\alpha$  inhibitors in the existing drug library by the malachite green phosphate assay (Due to space limitations, the results for compounds with an inhibition rate below 0 are not shown in the Figure). (A) Relative inhibitory ratio of kinase inhibitors on ATPase. (B-I) Inhibitory effect of FDA-approved drugs on Topo II ATPase activity. Topo II ATPase activity at 100  $\mu$ M of compounds and 200  $\mu$ M of 1,4-NQ as positive control were tested by the malachite green phosphate assay. After 45 min, the reaction was stopped and the OD620 value measured(A-I).



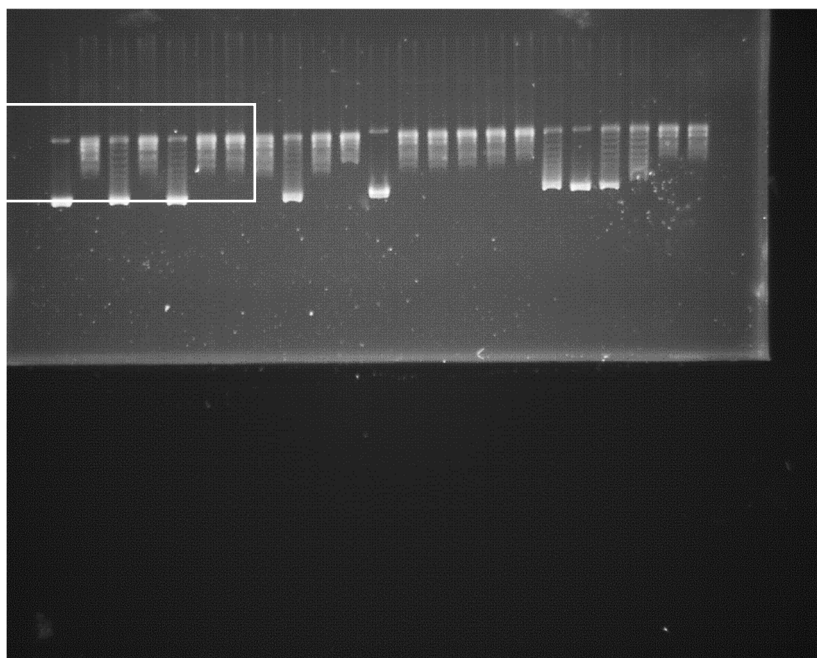
**Figure S3.** Chemical structure of kinase inhibitors with inhibition on Topo II ATPase.



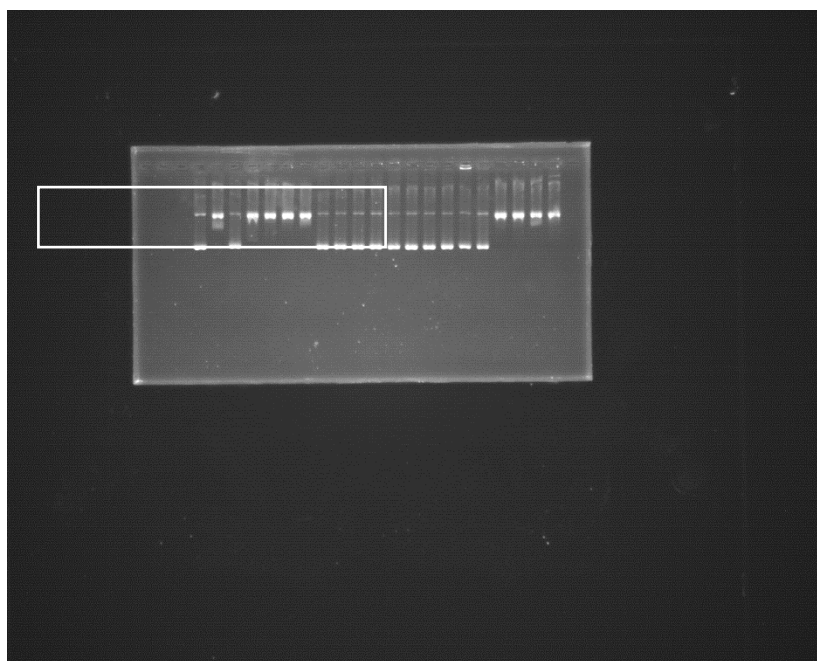
**Figure S4.** Structures of drugs with inhibitory effect on Topo II ATPase.



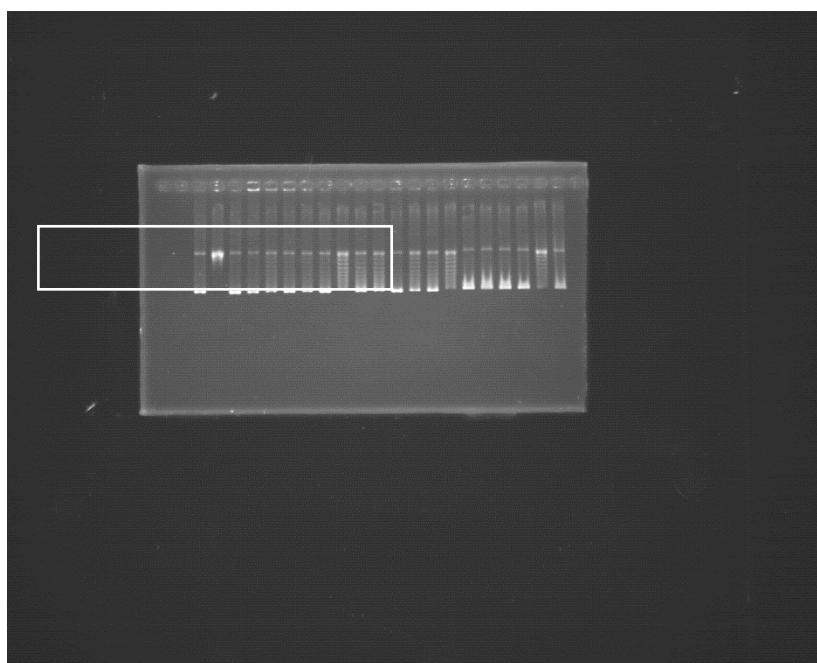
**Figure S5.** Original full-length gels of Figure 1A (in white boxes) in the article.



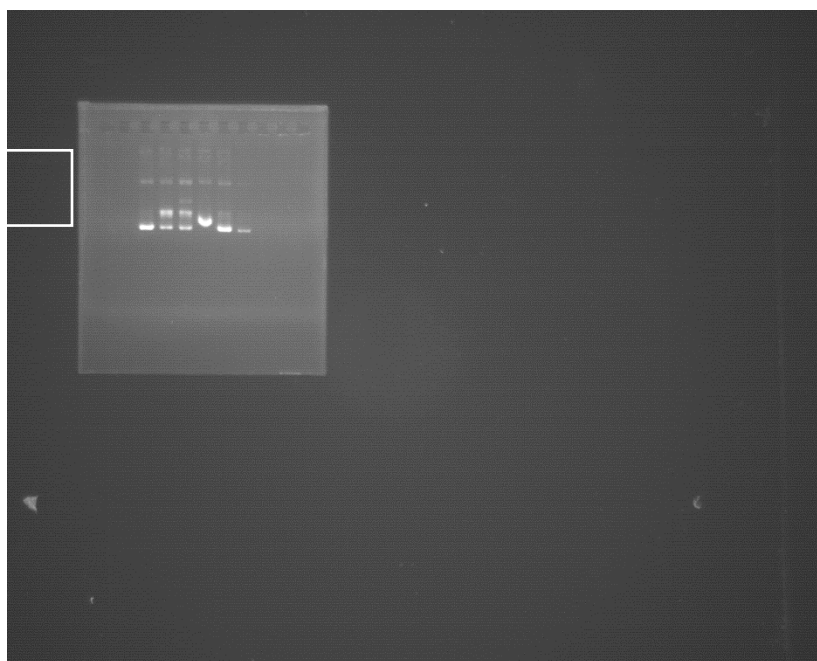
**Figure S6.** Original full-length gels of Figure 1B (in white boxes) in the article.



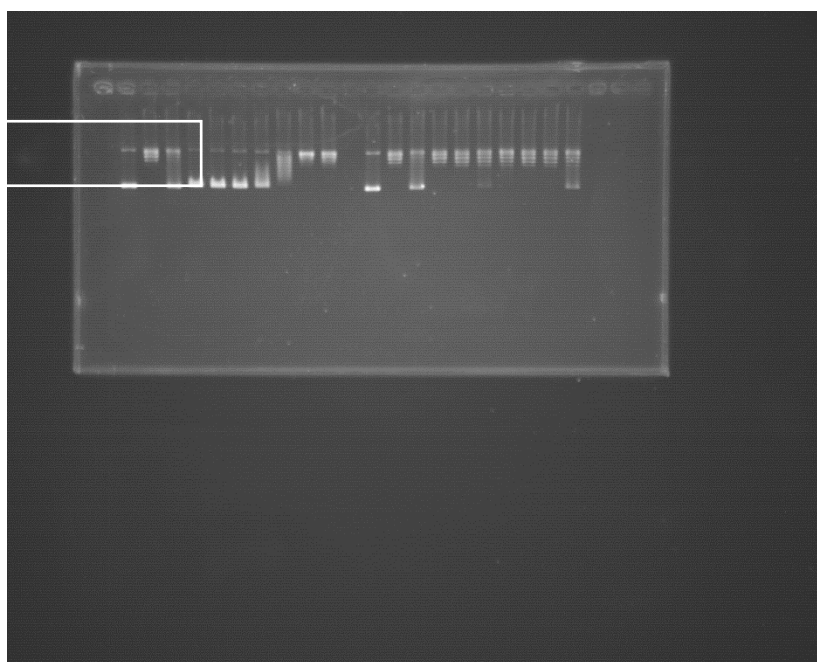
**Figure S7.** Original full-length gels of Figure1C (in white boxes) in the article.



**Figure S8.** Original full-length gels of Figure1D (in white boxes) in the article.

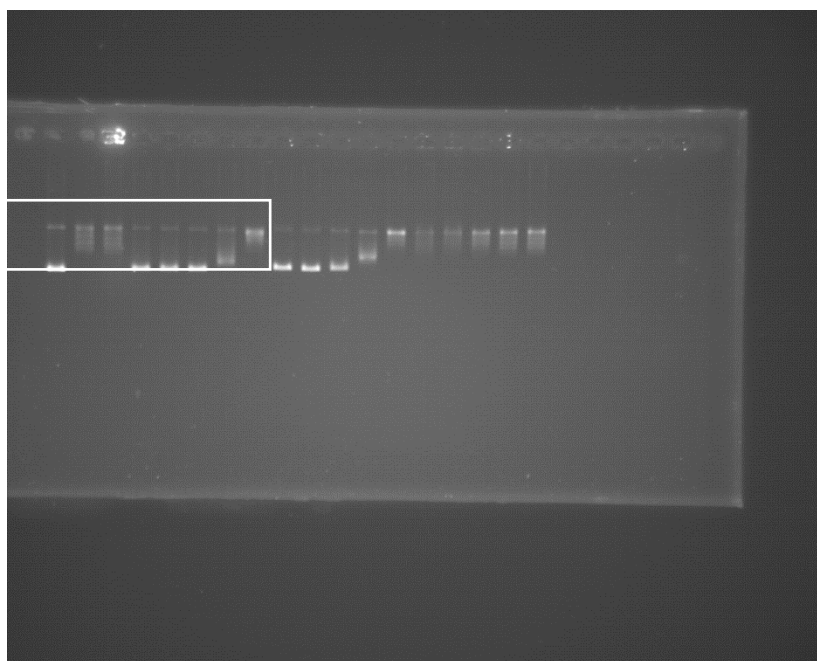


**Figure S9.** Original full-length gels of Figure2A (in white boxes) in the article.

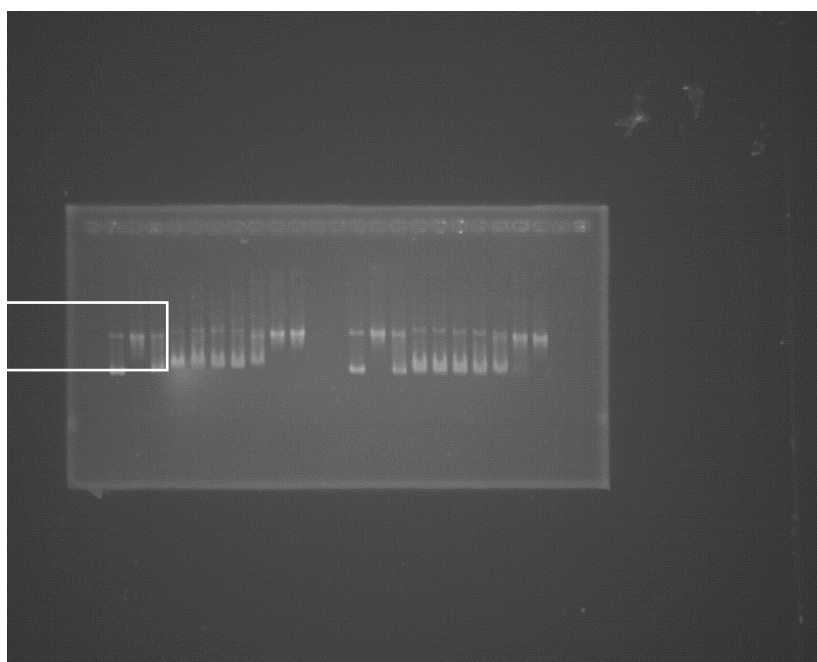


**Figure S10.** Original full-length gels of Figure 2B (in white boxes) in the article.





**Figure S11.** Original full-length gels of Figure 2C (in white boxes) in the article.



**Figure S12.** Original full-length gels of Figure2D (in white boxes) in the article.