TopoGEN

Products and Services for **Cancer Research.**

Contract R&D To Identify Drugs that Target Human Top1, Top2, Bacterial Top4 and DNA Gyrase.

Experience. Rapid Turn-Around. Publication Quality.

Our group has >20 yrs. experience in the area as a **Contract Research Organization** and we stand behind our results. We guarantee clear, cosmetic data and unambiguous interpretations. You will receive a publication quality product. We are seasoned veterans in the arena of in vitro testing. More importantly, we can help you develop a tractable strategy for analysis of drug mechanisms in the context of the tumor cell. We can evaluate potential genotoxicity independently from topo effects without extra charge. Finally, all our topo enzymes are homogeneously pure. We do not screen using extracts. Controls with specific drugs (e.g., etoposide vs. Topo IIa) guarantee specificity in all assays and validate even negative results with unknowns.

We save our clients considerable time and labor by offering services that are designed as a multi-tier approach to testing. For example, a limited scope screen (3-5 concentration inputs) is reasonable to quickly assess potential targeting. If the results are clearly negative, there is no need for follow-up. If we obtain a hit/lead, we will work closely with you to design next logical steps in a tier -2 testing strategy.

We find and validate valuable hits and optimize hit to lead results. Our strength is our experience with a wide variety of prokaryotic and eukaryotic topos and related pathway proteins. Competitive pricing and publication quality results, guaranteed.

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In all cases, we will craft a strategy with you to move ahead or not. Our screens are designed to reveal catalytic inhibition; however, because of the way the screens are set up, we can detect IFP action, if present (since some agents are dual mode). Because we cross reference our findings with topo drugs as positive and negative as controls, we obtain highly significant mechanistic details on drug action. For example as internal proof, we typically QC test topo II with both CPT and VP16 to show that IFP is specific to the former.

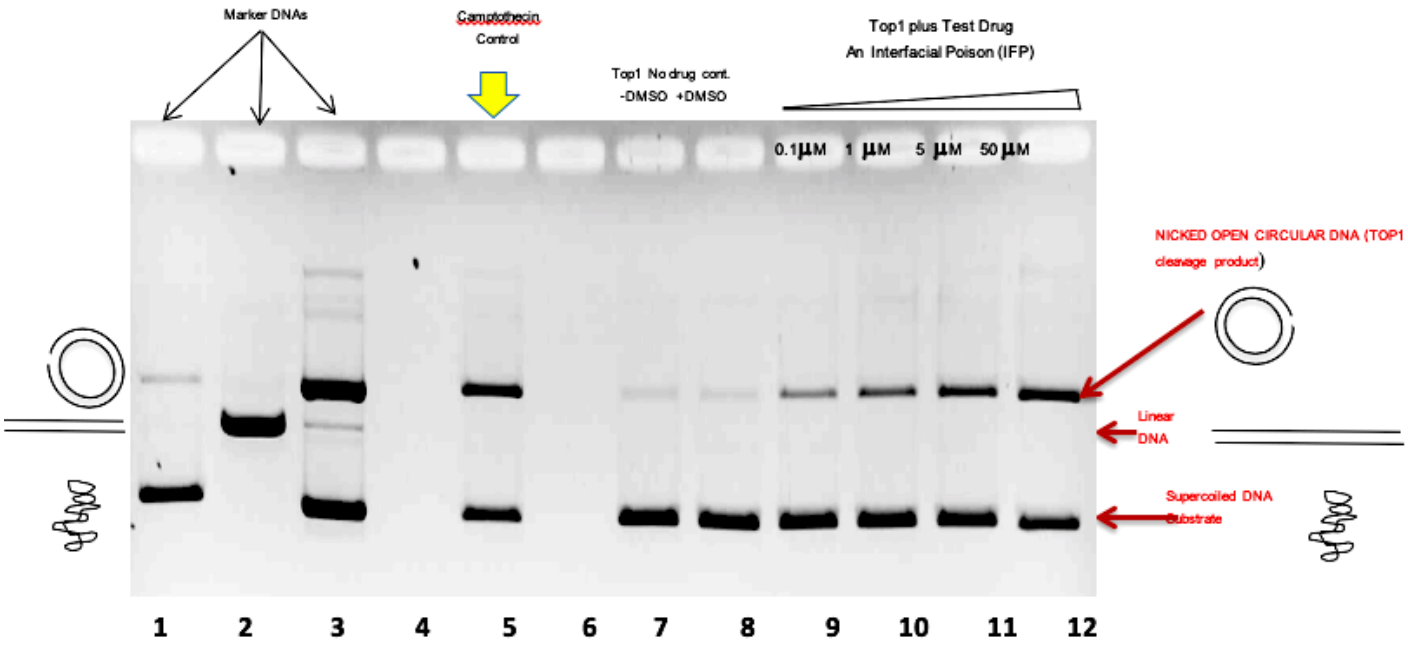
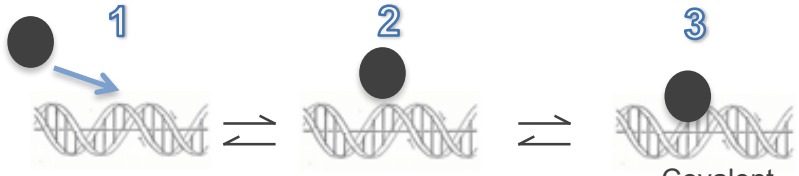


Figure 1 Detecting a Topoisomerase I Interfacial Poison (IFP)

This is an example of the use of TopoGEN's proprietary gel system to identify novel IFP activities (small molecules, synthetics, bio-effectors). A type I IFP targets Topoisomerase I by disrupting the cycle of breaking/resealing of the DNA substrate. The 'resealing' step (or re-ligation) is inhibited leading to an arrested complex containing denatured enzyme and nicked DNA in a covalent protein-DNA structure. This covalent structure is difficult to detect in the absence of a bona fide IFP. The assay simply detects the nicked DNA intermediate (nicked open circular DNA, see above on right side of gel). In this titration experiment, the formation of the nicked DNA is clearly increased with higher input concentrations of the test drug. Controls and markers are included to allow unambiguous interpretation of the data.

Contact us to learn how we can further your research goals!



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