The discovery and optimisation of selective small-molecule inhibitors of human 5’-tyrosyl DNA phosphodiesterase 2 (Tdp2)

• Tdp2 plays a central role in maintaining normal DNA topology in cells, through repairing topo-mediated DNA damage
• Cellular depletion of Tdp2 is reported to result in an increased susceptibility and sensitivity to topo II-induced DNA double strand breaks
• Selective pharmacological inhibition of Tdp2 may be a novel approach to overcome intrinsic or acquired resistance to topo II targeted drug therapy

Toxoflavin derivatives display strong assay interference potential and should be treated with extreme caution

Deazaflavin derivatives potential tools to explore the pharmacology of Tdp2 in cancer using A549 cell lysates.