Evaluation of SHP inhibitor NSC87877 using a protein tyrosine phosphatase (PTP) microarray

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Study Design
Known SHP inhibitor NSC87877 was evaluated with two PTPs on the new PTP microarray. The enzymes used were the inhibitor’s target SHP2, and LAR which is known to have a low affinity for the inhibitor. A concentration series used during spotting of the microarray provides different substrate concentrations allowing calculation of $K_m$ and $v_{max}$. By applying different inhibitor concentrations, $K_i$ may be determined as well.

Key Findings
Inhibition of target PTP SHP2 was dependent on concentrations of substrate and inhibitor as expected. A $K_i$ was calculated from the resulting data which correlated well with published inhibitor potency data. The non-target PTP LAR indeed showed no significant inhibition by NSC87877.

“Author Quote”
The parallel nature of the new microarray is a distinct advantage over non-microarray formats, allowing rapid profiling of substrate specificity, inhibitor potency and enzymological parameters.

Background
Unlocking the undoubted potential of phosphatases as a drug target has been held back by a lack of suitable high-throughput assays such as are available for kinases. Because of the higher homology amongst phosphatases compared to the kinase family, gauging selectivity of potential inhibitor drugs is even more essential. The new PTP microarray setup allows rapid evaluation of different inhibitors against different combinations of enzymes and substrates. This is in fact borne out by the published observation that NSC87877 inhibits both homologous SHP1 and SHP2 as well as to a slightly lesser extent more distantly related PTP1B.

Conclusion
The new protein tyrosine phosphatase (PTP) microarray can be used to study activity and selectivity of potential PTP inhibitor drugs. It produced reliable data on known SHP inhibitor NSC87877.