



same day selectivity and potency data against hundreds of kinases

Sense Proteomic’s arrays of functional human kinases can determine the selectivity and specificity of small molecule inhibitors by assaying against a set of more than 300 arrayed kinases in parallel. Of these 300 kinases, more than 160 kinases are assayable in a single experiment using our proprietary labelled ligands. Label-free kinase inhibitors compete with the fluorescent Broad Spectrum Ligand (BSL) for binding to the immobilized kinases and differences in fluorescence are observed (figure 1).

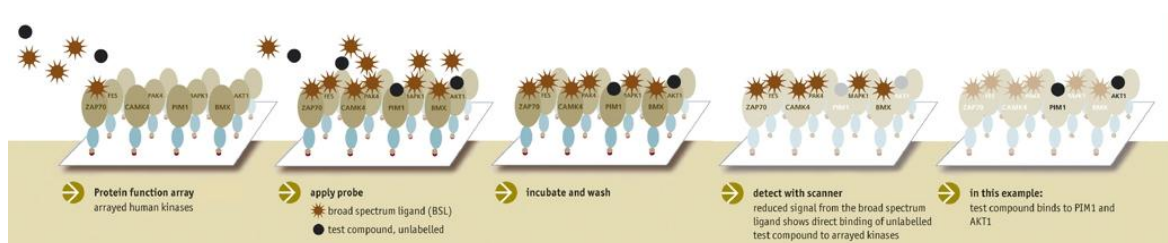


figure 1: This assay format can be applied to compound profiling to generate data on hundreds of kinases with same-day results.

screen against more kinases in your program

With the Sense Proteomic kinome 2.0^{plus} compound profiling kit, it is possible to measure the selectivity of compounds across over 160 kinases in one experiment. Using the labeled-BSL, Sense Proteomic has identified assayable kinases by measuring dissociation constants (K_d) for the binding of broad specificity ligands to each kinase on the array. The coverage of the fluorescent ligands for the kinases families on the array are shown in figure 2. As there is excellent coverage of the kinome, there is no need for additional protein expression saving you months of work and assay development time.

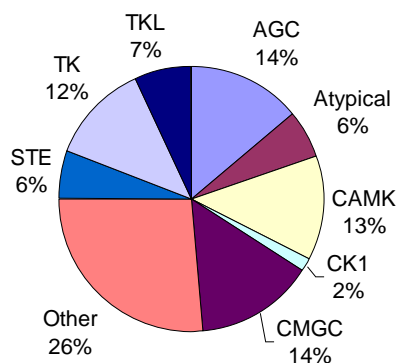


figure 2: Illustrates the binding of the BSL2-Cy3B and BSL3-Cy3 ligands across kinase families as defined by Park *et al* (1).



measure the selectivity of your kinase inhibitor

Measure the selectivity of inhibitors across and within kinase families in one experiment in less than a day! Comparison of a control array to a separate array probed with both BSL and the test compound provides selectivity across more than 160 kinases in a few hours. Simply enter the raw data into the provided Kinome 2.0 Selectivity Analysis Workbook to generate a list of target kinases for your compound. This quick study provides instant information about the selectivity of compounds that can be used in the secondary screening process for SAR studies.

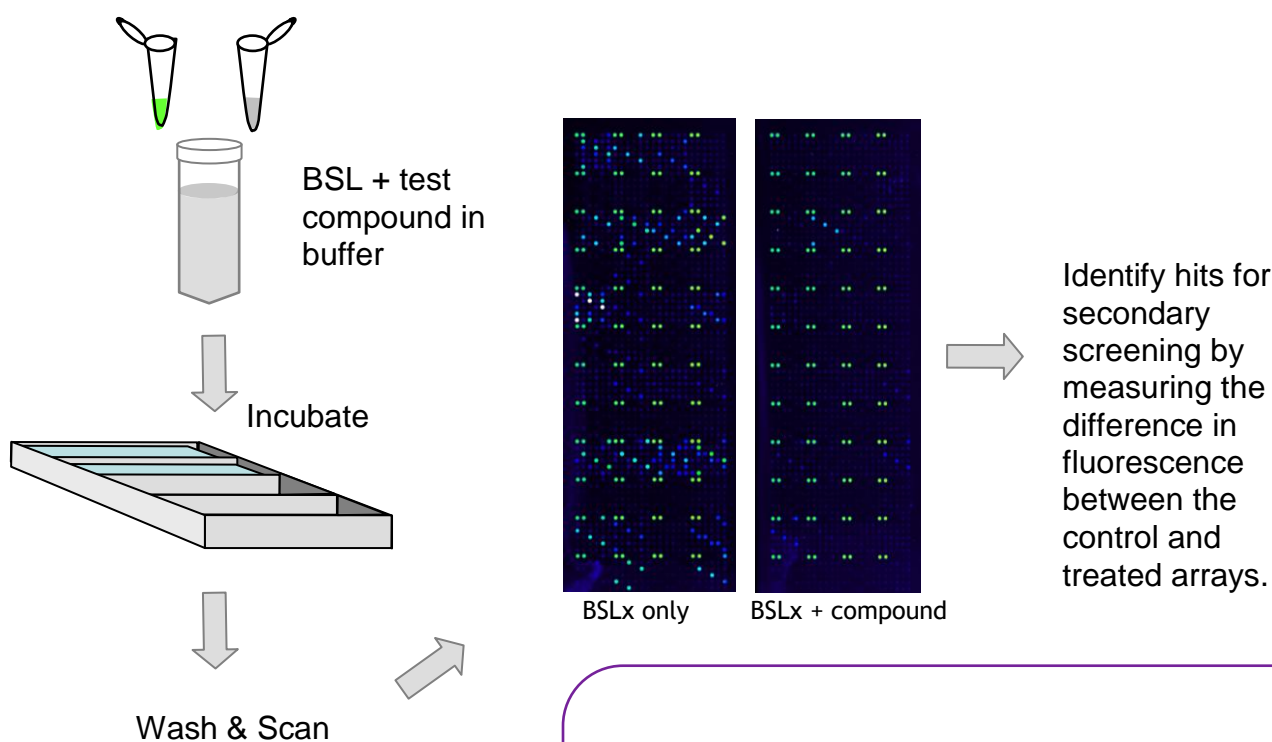


figure 3: Combine fluorescent BSL ligand (green) with 40 μ M test compound in the assay buffer. Array 1 is BSLx only (control). Array 2 is BSLx + compound.

new target discovery and new indications

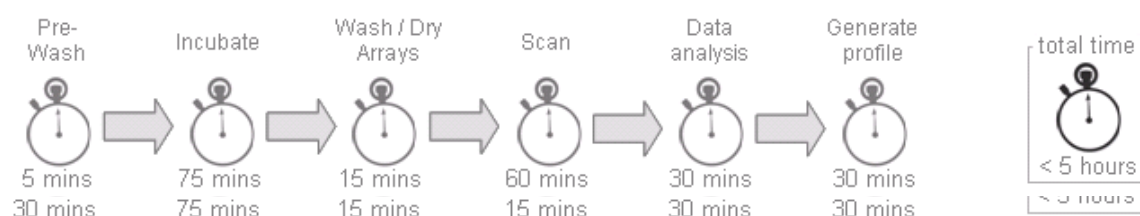
Are there potentially new indications for your kinase inhibitors? Do you need to identify the target of a compound found in a cellular screening assay? Screening focused libraries or subsets of libraries of kinase inhibitors could lead to novel leads and new therapeutics. A recent review discusses how most drugs found to



results in hours, not weeks

By doing the work in-house, screening programs benefit from an increase in speed and flexibility. The simple, straightforward assay is user-controlled and can be completed in less than 5 hours. The cost and delay of preparing compounds for shipment to a service provider and waiting for results is eliminated. Drug discovery timelines are improved by eliminating assay development time and speeding up medicinal chemistry optimization.

> delivers highly parallel results within a few hours



low price per data point

Add more kinases into your workflow without spending more on a service and without the labor and time involved in protein expression. Price per data point and compound can be reduced by as much as 6 to 10-fold depending on your experimental design. For more details, contact a Sense Proteomic representative by emailing info@SenseProteomic.com.

potency results in multiplex

Determine inhibition constants (K_i) for each kinase that binds your compound in one experiment. By assaying a dilution series of your compound across 10 arrays, an IC_{50} curve can be fitted. Using the binding constants (K_d) provided for each ligand:kinase binding event on the array, a panel of consistent K_i values are determined.

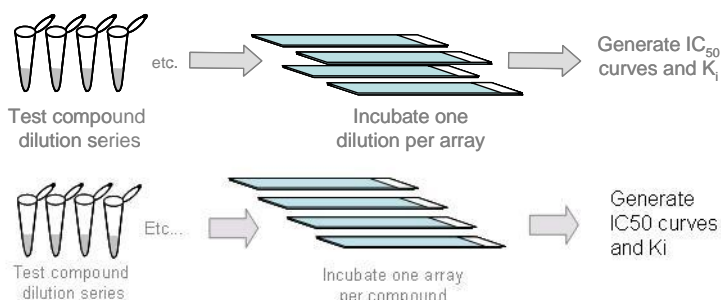


figure 4: Add a dilution series of the test compound to a set of arrays to determine IC_{50} s in multiplex.





better data comparison between experiments

There are no variables in ATP concentration and ligand concentrations to consider when using the Kinome 2.0^{plus} compound profiling kits. In addition, inhibition constants (K_i) are determined for each kinase using the K_d values provided. This is a higher quality constant than IC_{50} values for comparing your various compounds' potencies.

$$K_i = IC_{50} / (1 + ([BSL] / K_d))$$

technology is readily accessible

The Sense Proteomic technology requires only a standard microarray scanner capable of excitation and detection of the CyTM3 or Cy3B fluorophores (excitation at 532nm), which has a resolution of at least 100 microns and which is compatible with a standard 25 x 75mm (1 x 3 inch) microscope slides,. The assay requires no specialist skills and the data analysis tools we provide are easy to use and their open format enables integration with other analysis software.

kit components

Cat. No. PFA1003- Kinome 2.0^{plus} compound profiling kit

Kinome 2.0 protein function arrays x10
 Broad Spectrum Ligands
 Kinome 2.0 Analysis Tools CD x1
 Product Manual x1

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References

- (1) Park et al, PNAS 102, 2005, pp 8114-8119. "Building a human kinase gene repository: bioinformatics, molecular cloning, and functional validation".
- (2) Ashburn, T.T. and Thor, K.B. "Drug Repositioning: Identifying and Developing New Uses for Existing Drugs," Nature Reviews, Drug Discovery, Aug. 2004 (3), pp 673-683.

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product note | AN012-02-07

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