CASE STUDY

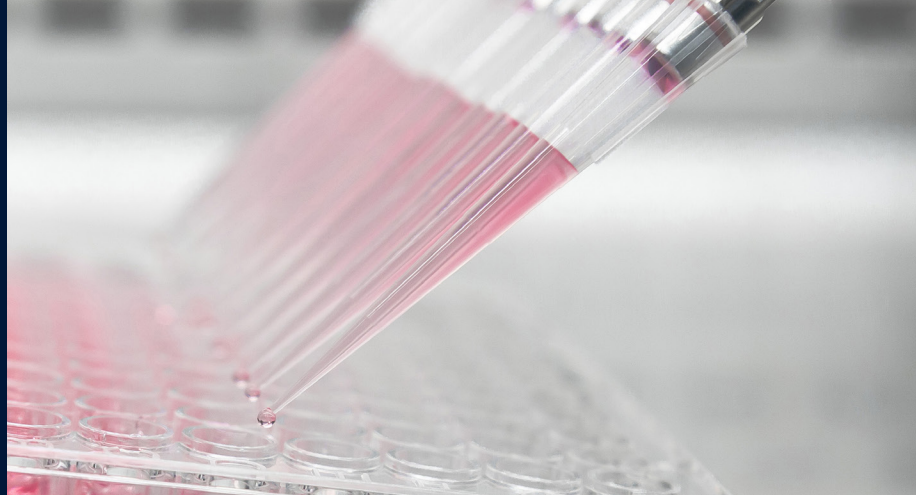
How Syngene accelerated drug discovery against a protein target using HTS

Syngene

Putting Science to Work

The Challenge

A biotech company had developed a fluorescence polarization assay. The company approached Syngene to transfer the assay in an HTS-ready manner and screen a library of 200,000 compounds against a single protein target. Syngene was required to deliver the relevant compounds against a very tight deadline while ensuring high-quality output.



The Solution

Syngene has different instruments to enable HTS solutions. We have multiple HTS-ready plate readers of different makes (PerkinElmer® EnVision®, Tecan Spark®), which can read in autonomous mode once the plates are stacked on the instruments. Further, we have multiple liquid handlers and dispensers (Tecan Freedom Evo®, Beckman Coulter Echo, Thermo Multidrop Combi, Integra Assist Plus), which can be programmed to dispense volumes ranging from nano to micro-liters.

During the HTS assay transfer, the Syngene team encountered a plate uniformity problem. This was due to the inappropriate hardware configuration of the plate reader for the unique fluorophore we were using. Our team worked closely with the manufacturer's engineering team to make the necessary changes and reconfigure the hardware. As a result, we resolved the issue within a week.

We successfully demonstrated HTS assay transfer by meeting the pre-set assay transfer criteria. As part of the screening, a total of 570 384-well plates were screened within nine days (60 to 90 plates/day). Platewise quality control (QC) parameters, Z' values are shown in Figure 1. Consistent Z' values (0.8±0.03) and signal-fold (0.8±0.03) were observed throughout the screen. A summary plot with the percentage inhibition values for all the 200,000 compounds is shown in Figure 2.

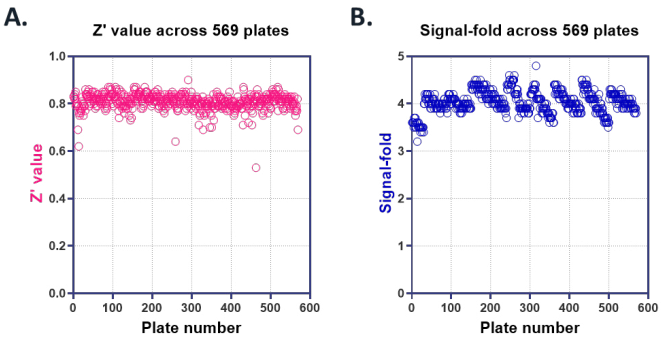


Figure 1: Quality control parameters – scatter plots of (A) Z' values and (B) signal-fold.

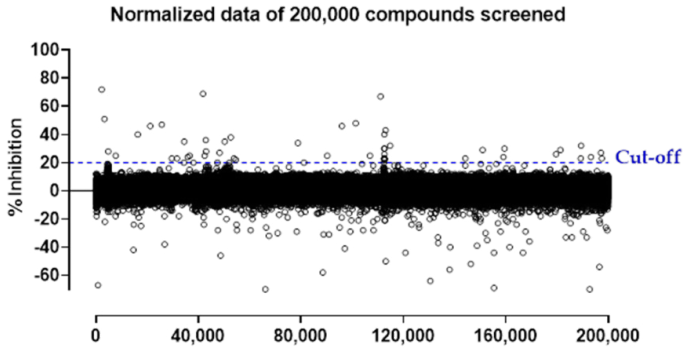
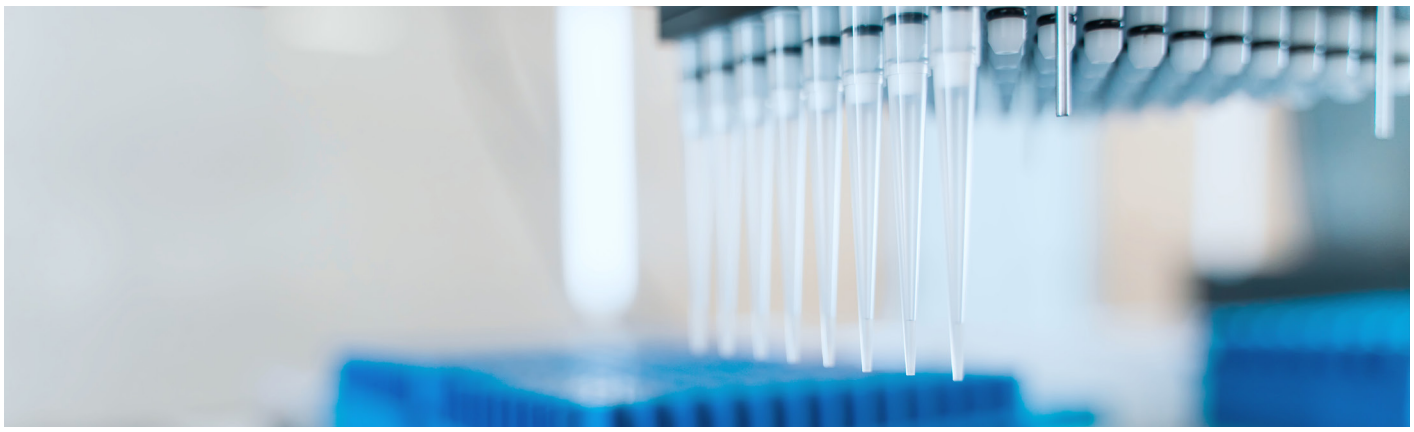


Figure 2: Summary of 200,000 screened compounds and identification of potential hits showing a scatter plot of inhibition values for compounds screened (circles) with a cut-off value (dashed line) for hit identification.



Syngene
Putting Science to Work

The table below provides a summary of the screenings focusing on critical parameters.

Description	High Throughput Screening
Library size	200,000
Targets	1
Counter screen	None
Total number of 384-plates screened	**569**
Type of HTS assay	Fluorescence Polarization (Biophysical)
HTS assay development	client
Automation and plate uniformity	In-house
HTS readiness demonstration	Assay transfer
Number of 384-well plates screened/day	60 to 90
Number of compounds screened/day	21,120 to 31,680
Total number of days of plate screening	9
Average signal-fold observed	4 ± 0.2 (569 plates)
Average Z' for the entire screen	0.8 ± 0.03 (569 plates)

Table 1: Summary of the high throughput screening project

Results Delivered

Syngene leveraged in-house expertise and automation capabilities to deliver high throughput screenings of high quality within the agreed-upon timelines and at optimum costs. The client was well satisfied with the quality of our output which enabled them to identify hits and proceed to hit triage at an accelerated pace. Commending Syngene on the quality of the work delivered, the client said it was at par with similar work executed by large pharma companies. Further, even after completing this project, the client continued to work with us for routine screening of compounds as part of the hit-to-lead phase.

To learn more about our drug discovery services, contact our team

Syngene

Putting Science to Work

About Syngene

Syngene International Ltd. (BSE: 539268, NSE: SYNGENE, ISIN: INE398R01022) is an integrated research, development and manufacturing services company serving the global pharmaceutical, biotechnology, nutrition, animal health, consumer goods and specialty chemical sectors. Syngene's more than 5200 scientists offer both skills and the capacity to deliver great science, robust data management and IP security and quality manufacturing at speed to improve time-to-market and lower the cost of innovation. With a combination of dedicated research facilities for Amgen, Baxter and Bristol-Myers Squibb as well as 2 Mn sq. ft of specialist discovery, development and manufacturing facilities, Syngene works with biotech companies pursuing leading-edge science as well as multinationals, including GSK and Merck KGaA.

For more details, visit www.syngeneintl.com or write to us at bdc@syngeneintl.com

Stay Connected