Miniaturization of Hit Confirmation Run of 12,000 Concentration Response Curves using the TEMPEST® Liquid Handler

Introduction:

Industry academic partnerships have enabled more targeted and cost-effective drug discovery approaches. With this high degree of collaboration, academic institutes throughout the world have gained access to compound libraries containing hundreds of thousands of compounds. Limited budgets and highly variable projects drive the need for cost effective and easy to use tools to facilitate efficient assay development and screening. Furthermore, these projects need to be run to industry standard and therefore automation of high throughput screens need to be reproducible in order to maintain the feasibility of this drug discovery process.

This application note highlights the use of the TEMPEST®, a versatile microfluidic reagent dispenser designed to execute assay development and high-throughput screens in miniaturized assay volumes, driving down the cost of assay reagents by 60% while generating high-quality screening data. At UCL, the Drug Discovery Group demonstrates that a hit confirmation run of 12,000 concentration response curves can be run with only 1.6 µL total reaction volumes when automated with the TEMPEST liquid handler resulting in a cost reduction of 26,000 GBP in detection reagent when compared to past liquid handling approaches.

Materials:

- Labcyte Echo Liquid Handler
- FORMULATRIX® TEMPEST® Liquid Handler
- Hidex Sense Plate Reader
- 375x 384-well plates

Methods:

Using the TEMPEST® Liquid Handler the reaction volume was miniaturized to 1.6 µL from 4 µL. This meant the volume of detection reagent required was reduced from 12 µL to 4.8 µL with no increase in error or loss of assay window.

Fidelity of the assay was determined using concentration response curves of an activating peptide. Data was read on a Hidex Sense Plate Reader and analyzed using Graphpad Prism and Genedata Screener.

Figure 1. FORMULATRIX® TEMPEST® Liquid Handler
Results:

The primary purpose for reducing the dispense volume was to reduce detection reagent costs for the screen. For this screen of 12,000 compounds in 10 point concentration response curve being able to reduce the volume of detection reagent by nearly 1/3 saved 26,000 GBP. It was anticipated there would be no reduction in assay fidelity, however, using the TEMPEST® Liquid Handler reduced error in the assay and improved the robust Z’ from 0.3 in a pilot study to 0.66 for the 375 plate screen.

Conclusion:

Academic industry collaborations have enabled academics access to large compound libraries which require cost-effective, easy to use liquid handling to screen. By using the TEMPEST® Liquid Handler we have reduced the volume of a hit confirmation screen by 1/3 thereby saving 26,000 for the 375 plate screen. Additionally there was an improvement in data quality in the screen with a robust Z’ of 0.66 through the screen. Finally the ease of use of the system make it ideal for a multi-user laboratory and to scientists with limited experience of automated liquid handling solutions.

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UCL’s Translational Research Office (TRO) builds on an increasingly vibrant translational culture across the School of Life and Medical Sciences (SLMS) and the wider university community by providing integrated support for translational research, industrial partnerships and drug discovery.