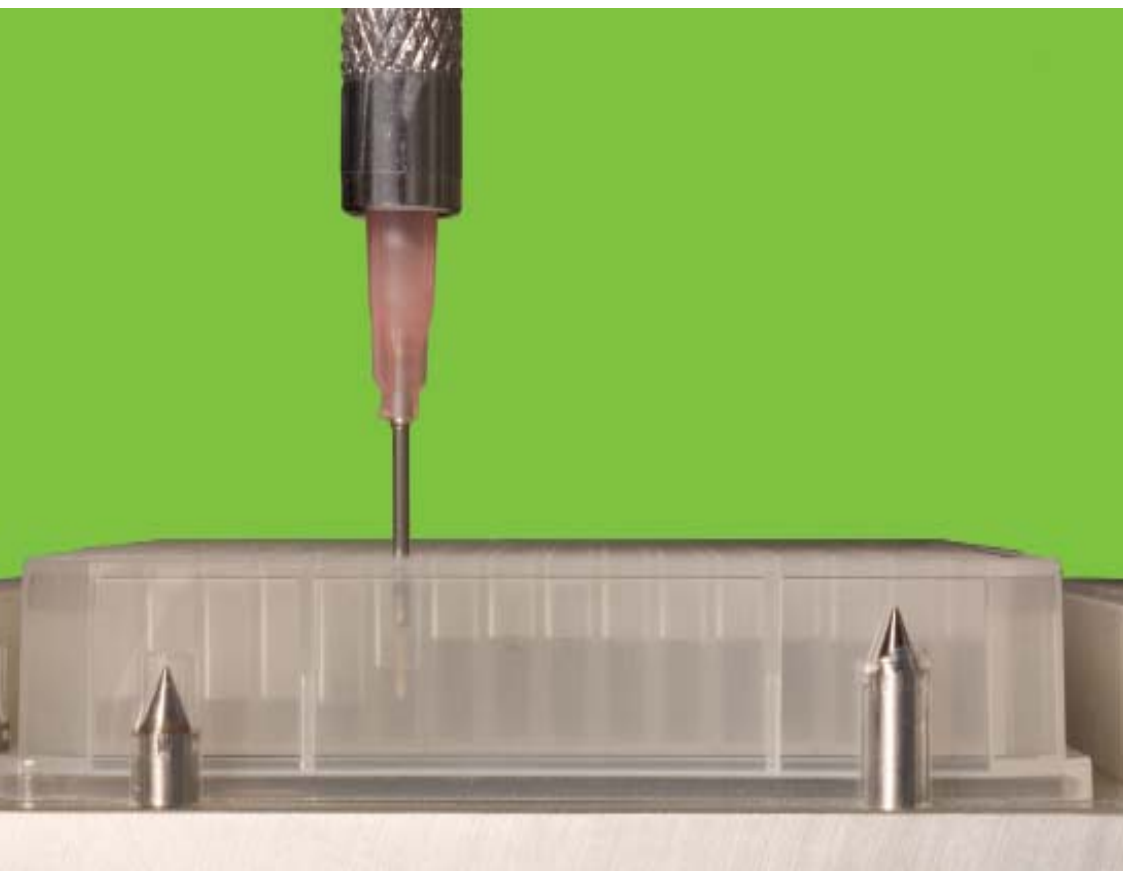


RapidFire® Lead Discovery Applications



Analyze even the most difficult targets

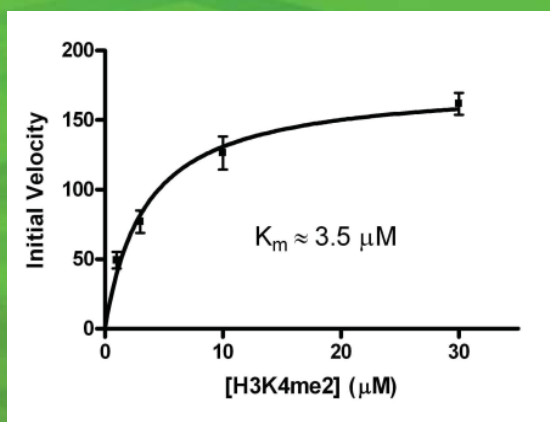
In the highly competitive drug discovery field, the time to identification of lead compounds is critical. Many new therapeutic area targets are challenging to investigate with traditional fluorescent or luminescent assays and the alternatives are too slow for processing the large sample volumes required for screening programs. The RapidFire® technology enables drug discovery researchers to process these intractable analytes with truly label free mass spectrometry detection at speeds 10x faster than traditional HPLC-MS. Incorporating on-line SPE cleanup directly coupled to the mass spectrometer, RapidFire eliminates bottlenecks in the drug discovery process enabling the analysis of difficult analytes such as lipids, fatty acids and epigenetic targets. Since RapidFire requires no labels or surrogates, native molecules can be investigated. Integrating easily into existing laboratory workflows and standard LIMS, RapidFire enables quick go/no-go decisions on potential lead compounds and gives researchers a competitive edge in the drug discovery process.

Achieve More Results

Once a target is selected, RapidFire screening assays can be developed in your laboratory or in collaboration with BIOCIUS scientists. These assays may then be used in primary screens, hit verification, and IC₅₀ determinations.

- **Enzymatic and Kinetic Parameter Determination-** Determine K_m and linear kinetic ranges
- **HTS Assay Development-** Determine Z' scores, reagent and assay stability, and rank order test compounds
- **Primary Screening-** Screen test compounds as singletons or in compressed format
- **Secondary Screening & SAR-** Support SAR programs through retesting and IC₅₀ determination
- **Hit-to-Lead Characterization-** Determine K_i values and mechanisms of inhibition

Binding constant determination from dimethylated peptide titration



The K_m value for LSD1-catalyzed demethylation of H3K4me2 (a dimethylated histone 3 peptide) as calculated from RF-MS results.

Enhance Productivity

RapidFire has successfully been used to screen for lead compounds in an ever-expanding variety of therapeutic areas, including:

- Metabolic Disease
- Cardiovascular Disease
- Anti-infectives
- Central Nervous System Disorders
- Oncology
- Inflammatory Disease
- Epigenetic Targets

Address Intractable Targets

RapidFire has the ability to investigate reactions that are not amenable to traditional high-throughput screening techniques. Additionally, the RapidFire technology eliminates some common confounding effects such as auto-fluorescence. Examples of targets screened using RapidFire include:

- Oncology
 - Protein kinases: ATK1/PKBα, Lck Kinase
 - Protein hydroxylases: FIH
- Epigenetics
 - Protein deacetylases: SIRT1, HDACs
 - DNA and protein demethylases: LSD1
- Metabolic Disorders
 - Diacylglycerol acyltransferase (DGAT)
 - Stearoyl-CoA desaturase (SCD)
- Cardiovascular Disease
 - Phosphatidylethanolamine N-methyltransferase (PEMT)
- Anti-Infectives
 - UDP-3-O (R-3-hydroxymyristoyl)-deacetylase (LpxC)
- Neurology
 - Fatty acid amide hydrolase (FAAH)
 - Phosphatidylserine decarboxylase (PISD)
 - Acetylcholinesterase (ACE)
- Inflammation
 - Prostaglandin-E synthase (PGES)