Product Focus: Biochemistry

Assaying Ahead

Biochemical Services and Instruments

As the understanding of the complexity of human biology increases, so does the need for experiments that analyze larger swaths of data. A number of different technologies have matured into commercial services and instruments that can handle greater throughput.

Mass Spectrometry Services

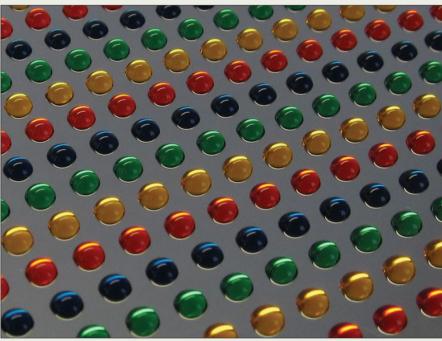
High-throughput screens against enzyme targets typically utilize antibodies, fluorescence or radiological labels, which can interfere with enzyme activity and place unwanted restrictions on assay parameters. Surface plasmon resonance, impedance, mass spectrometry, and other label-free technologies are appealing because they do not suffer from these limitations. Yet, these methods are typically low-throughput. A few recent iterations of label-free technologies address the throughput-limiting bottlenecks.

One such approach for high-throughput mass spectrometry, available as a service from **SAMDI Tech**, can eliminate the use of labels and allow up to 30,000 assays per day.

"The key is our highly efficient sample preparation method for mass spectrometry," says Michael Scholle, Director of Technology and Operations at SAMDI Tech.

The approach uses self-assembled monolayers (SAMs) of alkanethiolates on gold. Some SAMs contain tags that capture substrates (typically small molecules, peptides, proteins, or nucleic acids). The substrates are captured onto high density SAMDI 384 or 1536-spot biochips, rinsed to remove salts and other components, and then analyzed by matrix-assisted laser desorption/ionization time-of-flight (MALDI TOF) mass spectrometry.

Originally developed by Professor Milan Mrksich at the University of Chicago, the SAMDI method can identify the products, yields, and rates



SAMDI Tech's biochip for high-through mass spectrometry

of reactions involving kinases, proteases, glycosyltransferases, methyltransferases, and many other enzymes. Since the method uses mass spectrometry, multiple enzymatic events or products can be monitored simultaneously.

"We can screen for new modifications and monitor methylation, ubiquitination, and acetylation in the same assay. We use a universal format for all assays of interest to our drug discovery clients," Scholle says.

Substrate discovery is also an option, in which peptide libraries are immobilized in a grid pattern, subjected to a solid-phase enzymatic reaction, and sequentially read by MALDI TOF to produce a heat map of an enzyme's kinetic activity for hundreds of substrates in one pass.

Scholle notes this option helps provide an accelerated path for developing a

high-throughput screening program. "We can identify an optimal peptide substrate, determine the biochemical properties of the enzyme on that substrate, and then feed that into a high-throughput screen."

Another application of mass spectrometry is

Material compiled by Harris D. McKinney, Inc.

