



MASS SPEC CRO SERVICES

**ASMS Binding Assays / Covalent Binding Assays
Chemoproteomics / Small Molecule Analysis
Biomolecule Analysis**

Mass Spectrometry CRO Services



ASMS Non-Covalent Binding Assays

- Affinity selection mass spectrometry (ASMS)
- Kd determination and competition assays
- Protein, nucleic acid and complexes as targets



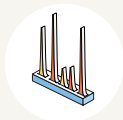
Covalent Binding Assays (Protein & RNA)

- High-throughput Intact Mass Analysis
- Potency determination
- Protein and nucleic acid targets



Chemoproteomics

- Purity & sequence determinations
- On- & off-target covalent modification
- Targeted and Global profiling



Small Molecule Analysis

- Functional assay design and development
- Quantitation of lipids, amino acids, metabolites, etc.
- Metals analysis by ICP-MS



Biomolecule Analysis

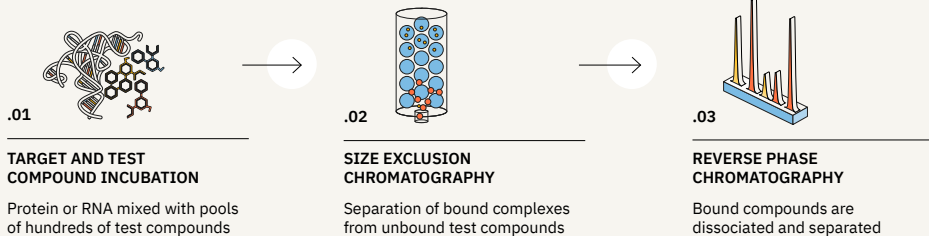
- Functional assay design and development
- Target purity
- Sequence confirmation



ASMS Non-Covalent Binding Assays

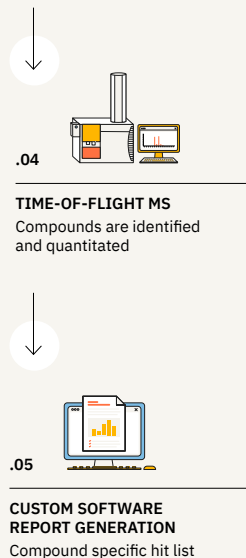
Recent advances in RNA and protein degraders, molecular glues, protein-protein interaction (PPI) disrupters, RNA binders and other target classes have led to increased interest in non-covalent binding assays. Momentum uses Affinity Selection Mass Spectrometry (ASMS) to identify ligands that bind a protein or oligonucleotide target from pools of hundreds of small molecule test compounds. This approach uses on-line 2D size exclusion/reversed-phase chromatography coupled to a high-resolution time-of-flight mass spectrometer to identify unique binders within each pool. Hit identification utilizes Momentum's proprietary custom software. Confirmed hits can be further interrogated at multiple concentrations to determine binding stoichiometry and affinity. Because the same format can be used for selectivity, competition, and counter-screening assays, hit characterization and hit-to-lead experiments can be performed rapidly.

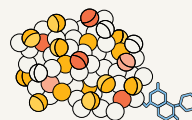
Lead Identification by ASMS



Advantages of ASMS Binding Assays

Minimal assay development required	▶	Ideal platform for selectivity screening
High-throughput	▶	100K compounds in pools of 320 screened in 38 hours
Low protein/RNA usage	▶	100K compounds in pools of 320 requires less than 1mg of a 50 kD target for primary screen
Solution-phase binding with native target	▶	No need to tag target or immobilize to a surface
Compatible with protein/protein or protein/oligo complexes	▶	Large targets can be challenging for SPR or interferometry
Broad chemical space coverage	▶	Positive ion ESI-MS covers ~95% of most drug-like test compounds

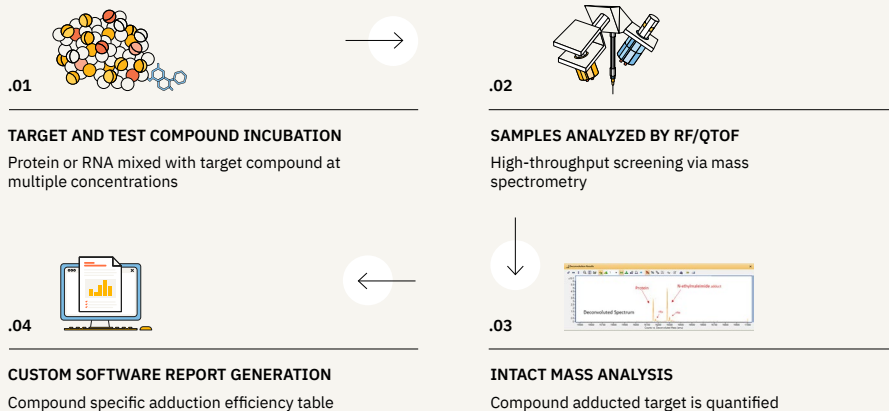




Covalent Binding Assays (Protein & RNA)

Targeting the covalent modification of proteins with compounds containing reactive functional groups has led to the development of several new potent and selective drugs. Though historically covalent compound discovery has been conducted via structure guided design, direct covalent ligand screening of electrophilic compound libraries has gained popularity as a primary approach. Momentum has integrated mass spec hardware and software into an automated workflow that enables the primary screening of electrophilic libraries at a rate of 5,000 compounds daily. Additionally, the generation of “hit” lists from these screens has increased the demands on secondary assays defining and rank ordering compound potency. With minor modifications to plate prep protocols, Momentum can determine compound potency parameters: apparent K_{inact}/K_i .

Covalent Protein Binding Assay Workflow



Advantages of Momentum's Covalent Binding Assays

Detection of covalent binding to targets	▶	Automated workflows utilizing commercial hardware and software
High-throughput	▶	1000's of compounds interrogated, per 24-hour day
Full electrophile library screening	▶	>10k compounds screen in 2-3 days
Potency determination	▶	Drug Concentration/Time courses allow apparent K_{inact}/K_i determination
Target versatility	▶	Minor protocol variations enable nucleic acid workflows



Chemoproteomics

Chemoproteomics encompasses an array of methods used to identify and interrogate protein-small molecule interactions. Momentum's chemoproteomic applications are an extension of our binding assay screens allowing our clients to further characterize their targets, hits and leads.

An example of the extension of services enabled by chemoproteomics is irreversible covalent binding analysis. Momentum has been offering a high-throughput intact mass shift assay to identify electrophilic test compounds that bind protein targets for several years. We help our clients characterize the binding site of the covalent adduct by doing peptide mapping. We can further characterize those test compounds in cellular assays showing on and off target binding *in vivo*.

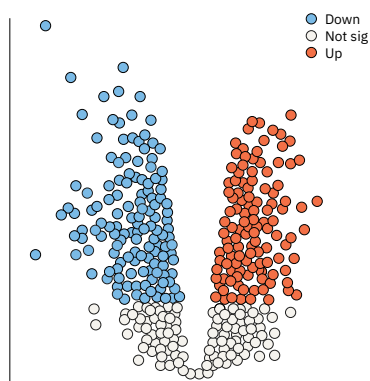
We deliver chemoproteomics results by leveraging several mass spectrometers including QqQ, QTOF, and Orbitrap Ascend Tribrid systems – equipped with nanoLC, extended mass range, ETD, and FAIMS capabilities. These instruments collectively produce high resolution MS data with speed, specificity, and sensitivity. To accelerate turnaround time, we also have several automation solutions for sample preparation including Integra, Tecan, AssayMAP Bravo, and AccelerOme.

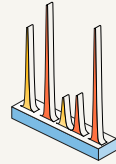
Chemoproteomics Applications

These applications are an extension of our binding assay screens enabling:

- ✓ On- and off-target covalent modification *in vitro* and *in vivo*
- ✓ On- and off-target covalent modification site specificity *in vitro* and *in vivo*
- ✓ Targeted quantitative profiling
- ✓ Global quantitative profiling

Volcano Plot Showing Differentially Expressed Proteins





Small Molecule Analysis

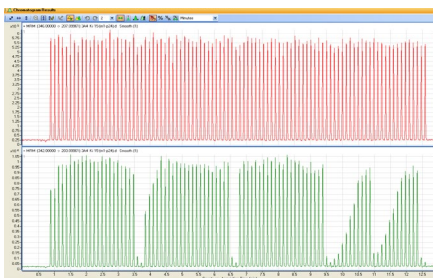
Momentum offers assay development and analysis for small molecule quantification on both HPLC-MS and RapidFire-MS. The RapidFire-MS system allows ultrafast, automated, label-free functional screening. We provide functional cell-based and biochemical screening generating 20,000 datapoints per day and up to 80,000 using BLAZE-mode. These analyses are often a follow-up or related experiments to our screening research. We can perform biomarker quantification, potency assays, and pharmacokinetic studies. We have extensive experience measuring lipids, amino acids, sugars, and metabolites. Momentum has limited to no lead time, efficient methodologies, and extensive LCMS experience meaning results are delivered in days to weeks, instead of months.

We offer ICP-MS analysis to measure trace metals, perform pharmacokinetic studies on metallo drugs, quantify biomarkers for rare diseases and characterize zinc finger proteins. We can analyze hundreds of samples daily.

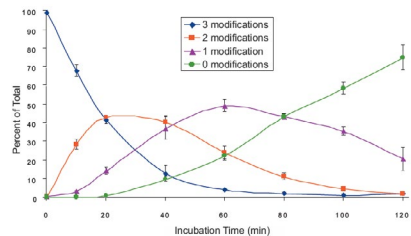
Small Molecule Analysis Assays

- ✔ Biomarker validation and screening from cell culture, biological fluids, or tissue
- ✔ Functional assay design and development for rare diseases
- ✔ Potency assays
- ✔ Small molecule library QC
- ✔ Metals analysis by ICP-MS

RapidFire-MS Analysis



Enzymatic Assay Results





Biomolecule Analysis

Momentum's biomolecule analysis applications are an extension of our binding assay screens allowing our clients to further characterize their targets. Momentum offers quality control services on proteins and oligonucleotides using high-resolution MS platforms. Data delivery is as fast as 2-4 business days after sample receipt at our Billerica, MA location.

Protein Analysis

We can work with purified protein or cell lysates to provide:

- ✓ Protein identification
- ✓ Protein mass determination
- ✓ Protein purity determination
- ✓ Protein sequence confirmation

Oligonucleotide Analysis

We can work on DNA/RNA samples with both standard and modified chemistries to provide:

- ✓ Intact mass determination/confirmation on oligos > 100 nucleotides in length
- ✓ Target purity
- ✓ Component profiling
- ✓ RNA cap and tail analyses
- ✓ Sequence confirmation

About us

Momentum Biotechnologies is a drug discovery partner that delivers innovative mass spec solutions to overcome research challenges for biopharma clients globally. Our core team of scientists and engineers started working together developing the RapidFire high-throughput MS platform and have been serving clients with MS-based services since 2004 including PureHoney Technologies (2015-23).

Momentum Biotechnologies' goal is to accelerate our partners' drug discovery & development programs through superior mass spec based CRO services. We help clients identify and characterize leads for degraders, molecular glues, protein-protein interaction (PPI) disrupters, RNA binders and other target classes. We use innovative techniques including affinity selection MS (ASMS), intact mass MS, chemoproteomics and small & biomolecule analyses. We pride ourselves on rapid turnaround of the highest quality data, accelerating the momentum of our clients' research projects. For more information, please visit momentum.bio

CONTACT US

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