



Position	Principal Scientist, Mass Spectrometry
Supervisor	Jim Barsoum, PhD
Department	Biology
Prerequisites	PhD in a relevant scientific field with 8+ years of relevant experience

Position Summary:

The principal responsibility for the new incumbent will be to build, maintain, and run mass spectrometry screening capabilities enabling rapid and high-throughput analysis of small molecule libraries to identify novel ligands that bind selectively to RNA (e.g., SEC-MS, RapidFire, SAMDI, etc.). This work encompasses the use of such screening methods for both primary and secondary (confirmatory) assays. The second broad responsibility will be to build an industry-leading drug metabolism-pharmacokinetics (DMPK) capabilities in support of internal drug discovery programs.

Associated responsibilities and skills include: (1) selection and maintenance of all MS instrumentation, (2) broad knowledge of known MS techniques across a wide range of applications, especially as they pertain to high-throughput assessment of biomolecule/small molecule interactions, (3) deep technical expertise on novel and established MS methods and protocols, (4) broad understanding of the principles and concepts of high-throughput screening, (5) build a close and productive relationship with informatics colleagues to build and manage the requisite databases, (6) extensive working knowledge of the wide range of issues and associated experimental protocols to provide all necessary DMPK data to support ongoing drug discovery and development programs, and (6) oversight of external MS work.

Of particular importance is that the candidate bring to the role the intellect and insight to apply new and emerging MS techniques and instrumentation to the problems of RNA screening. This, in turn, requires the ability to interpret and integrate a wide range of heterogeneous datastreams to expand and improve the platform. Accordingly, the candidate should have a strong working knowledge of the fields of mass spectrometry, drug metabolism, pharmacokinetics, biochemistry, and molecular and cell biology.

Responsibilities:

The responsibilities of this position include but are not limited to the following

1. Build the Arrakis MS screening capability from “bare walls”. When appropriate, hire and develop additional scientists to expand the capacity and capability of this function.
2. Devise and articulate the concepts and methods to enable rapid, high-throughput screening of small-molecule libraries against RNA targets using affinity selection MS (SEC-MS, aka AS-MS).
3. Devise, articulate, implement, and execute the constellation of DMPK assays that will most effectively advance Arrakis’ drug discovery programs.
4. Collect, analyze, interpret, and present screening and DMPK data to colleagues and leadership at Arrakis. Such assays might include (a) drug levels in plasma or blood, (b) drug levels in

microsomes, (c) proteomic analysis, (d) covalent modification of endogenous biomolecules, (e) identification of metabolites.

5. Design key experiments where novel tools or molecules can expose underlying molecular mechanisms and guide platform development.
6. Regularly survey the MS, screening, and DMPK literature to identify salient new concepts and techniques.
7. Act as an internal consultant on MS and screening for colleagues across all departments at Arrakis.
8. Identify external collaborators, both academic and industrial, that could provide cutting edge methods and insights to advance the programs and Arrakis' broader mission.
9. Oversee the work of outside vendors and CROs when internal capacities or capabilities are not adequate to emerging needs at Arrakis. This would include identification, initiation, and oversight of external work on new MS technologies, DMPK studies, and MS-mediated HTS methods.
10. Routine use of an electronic laboratory notebook.
11. Presentations of ideas and results, including issues & possible solutions, at project team or company-wide meetings.
12. Work with Arrakis colleagues and leadership to ensure that project goals are met.

Skills/Knowledge Required:

1. Comprehensive knowledge of how to implement MS techniques across a wide range of applications.
2. Deep technical expertise on the design, assembly, maintenance, and improvement of mass spectrometers and their associated protocols.
3. Broad understanding of how to carry out screening and create and manage the resulting databases.
4. Extensive working knowledge of the wide range of issues and associated experimental protocols to provide all necessary DMPK data to support ongoing drug discovery and development programs.
5. Broad understanding of the drug discovery and development process.
6. Fluency in working with chemists, biologists, pharmacologists, and toxicologists to devise experiments that illuminate critical problems.
7. Ability to interact and communicate effectively with laboratory colleagues, research management, and project team leaders.
8. Ability to effectively manage time and priorities over multiple lines of work.
9. Strong problem solving and trouble shooting skills.
10. Excellent oral communication and writing skills.
11. Ability to work in a dynamic & changeable environment.

Other Characteristics & Traits:

1. Demonstrates independent, scientifically directed, and innovative thinking.
2. Anticipates the need for contingencies and develops alternative strategies.
3. Recognized as Subject Matter Expert within function.

4. Role model for scientific excellence.
5. Outstanding team member.