QUANTITATIVE BIOSCIENCES AT MERCK

Greg Adam, Principal Scientist
Allison Kemper, Senior Scientist
William Rose, Associate Principal Scientist
Laura Struzyna, Associate Scientist, Postdoctoral Fellow

February 06, 2020
Rutgers University - Robert Wood Johnson Medical School
Quantitative Biosciences Panel Members

Greg Adam  
*Principal Scientist*

Allison Kemper  
*Senior Scientist*

William Rose  
*Associate Principal Scientist*

Laura Struzyna  
*Associate Scientist  
Postdoctoral Fellow*
Locations of Merck Research Laboratories

- Boston, MA
- Cambridge, MA
- Kenilworth, NJ
- South SF, CA
- West Point, PA
- Singapore
- London
The Drug Discovery Process: A High Level Overview

Indication with Unmet Need

Target ID/Validation

Disease Model Development

Compound Screening/Lead ID and Optimization

Clinical Studies and Approval

12-15 years’ worth of time and up to $1B USD
What is Pharmacology?

The branch of biology concerned with the study of drug action

• Pharmacodynamics studies the effects of a drug on biological systems

• Pharmacokinetics studies the effects of biological systems on a drug.
Quantitative Biosciences at MRL’s West Point Facility

In support of Infectious Diseases, Neuroscience, Cardio-metabolic, Oncology

In Vitro

- Characterize and differentiate lead series using biochemistry, biophysics, receptor pharmacology, etc.
- Assay development and execution

In Vivo

- Link *in vitro* activity of compounds to efficacy in animal models of disease (IVIVC)
- Establish relationship between compound exposure and efficacy in animal model (PK/PD)
- Large and small animal species
Drug Discovery and Development at Merck - Enabled by Pharmacology at All Phases

Will engaging this target likely produce the desired pharmacological effect?

What classes of molecules can engage the target?

Are there active molecules with desired drug-like properties?

Is there an active molecule with all of the desired drug-like properties?

Does the molecule have desired human PK? What types of side-effects are observed and at what dose? Is there evidence of efficacy in small studies?

Is the molecule safe and effective in larger clinical trials?

Are there opportunities to expand the drug's indications? Are there new safety signals that emerge post-approval?
Quantitative Biosciences Goal: Deliver High Quality Preclinical Candidates

Research Operating Plan (ROP):
• Drive Structure-Activity Relationships (SAR)
• Fully Characterize Biology of Compounds

Biochemical Assays: intrinsic potency against target
• Selectivity!!

Cellular Assays: estimate potency in cellular milieu
• Selectivity
• Toxicity

Receptor Pharm Assays: intrinsic activity against target
• Agonist
• Antagonist
• Modulator
• Selectivity!!

Ion Channel Assays: intrinsic activity against target
• Blocker
• Use-dependence
• Selectivity!!

In vivo Assays
• Link in vitro and in vivo potency and efficacy
• Demonstrate target engagement
• Establish PK/PD relationships

# of compounds
1000s
100s
10s
1
Our department collaborates with multiple functional areas

- Screen Strategy
- Assay Development

- Compound Evaluation
- Issue Driven Experiments

- Target ID/ validation
- Assay development
- Tool compounds

- ROP design/ execution
- PK/PD

- Contract Research Orgs
  - In vitro Assay / In vivo Model Outsourcing

- Leverage unique capabilities or expertise

- Disease Area Biology

- Quantitative Biosciences

- Compound Screening Group
  - Screen Strategy
  - Assay Development

- Medicinal Chemistry
  - Compound Evaluation
  - Issue Driven Experiments

- Pharmacology at other sites

- Program Teams
Merck Research Laboratories (MRL) Postdoctoral Research Fellow Program

Provides an academic focus in a commercial environment

Work alongside outstanding researchers and collaborators as part of Merck’s industry-leading R&D organization

Postdoctoral Fellows at Merck:

• Work in unique laboratory environments with top capabilities, equipment, expertise and knowledge
• Obtain experience in drug discovery and development
• Generate innovative science resulting in high-quality external publications
• Participate in seminars, lectures and meetings, and interact with the local scientific community
• Receive a competitive salary, and access to the full benefits programs offered by Merck

Learn more at: www.merck.com/research/fellow
Merck Internships and Co-Ops

The Future Talent Program:
• Internships – 9 to 12 weeks between June and August
• Co-Ops: 4 to 6 month assignments

“During my twelve weeks at Merck, I had high expectations to advance my technical skills in the laboratory, to receive guidance on graduate degrees, and to discover new career aspirations. This internship greatly surpassed my expectations. My assignment in the department of Infectious Diseases and Vaccines focused on exploring Next Generation Sequencing capabilities for targeted viral genome sequencing. Preliminary steps included extracting RNA from virus samples, performing PCR amplification, and running agarose gel electrophoresis. My supervisor quickly awarded me independence in planning and completing sequencing runs. After analyzing gigabytes of data, I proudly presented our findings to the department. However, this program goes beyond teaching technical skills. The Future Talent Program additionally encouraged the development of skills in communication and leadership, but most importantly the creation of a personal brand. The program accomplished this through assigning each intern a personal mentor, as well as hosting various networking events, panels, and seminars. Simply put, this eyeopening experience rewarded me with a clear vision of my career goals in research and helped me establish the skills, as well as the mindset, to achieve them.”

– Jessica McAnulty

Apply online at:  www.merck.com/careers