

# A View from Inside Pharmaceutical Development: Perspective on Career Paths

# Disclaimer

The views, comments and thoughts in today's presentation about working in pharmaceutical industry do not represent Merck: *Merck Research Laboratories (MRL)* or *Merck Sharpe & Dohme (MSD)*. They are the opinions of each speaker.

# Outline

- Welcome
- Introduction of Speakers / Careers they represent
- Split into 2 group: half tour bioprocess plan, half tour the Neuroscience assay labs
- Switch activities: tour bioprocess / tour labs
- Conclusions

# Practical Information

- Bathrooms are down the hall behind us
  - Women's room to the right
  - Men's room to the left
- In case of emergency, proceed left down hallway to exit building
- **Photography is strictly prohibited**; please be mindful of cell phone use, particularly during the tours

# Future Jobs in Academics?

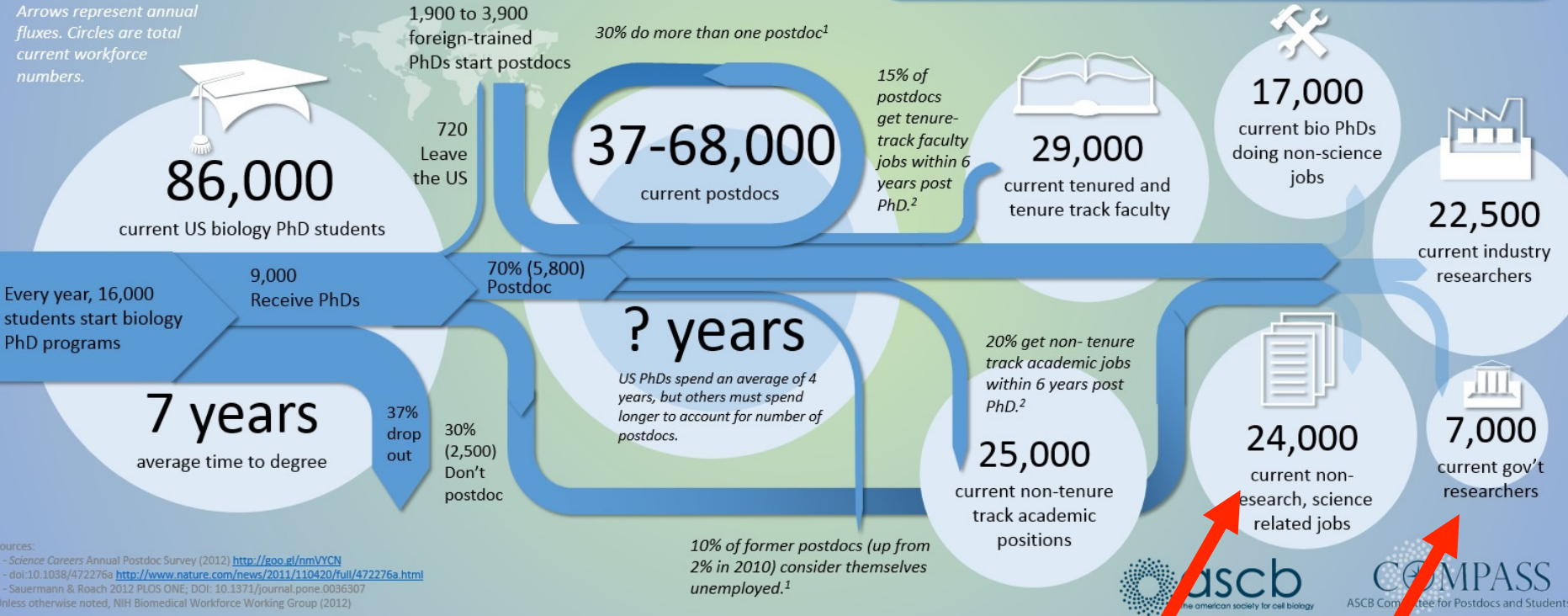
## Where will a biology PhD take you?

Arrows represent annual fluxes. Circles are total current workforce numbers.

A faculty job is an "alternative" career.



At this rate, <8% of entering PhD students will become tenure-track faculty. Yet, 53% rank research professorships as their most desired career.<sup>3</sup>

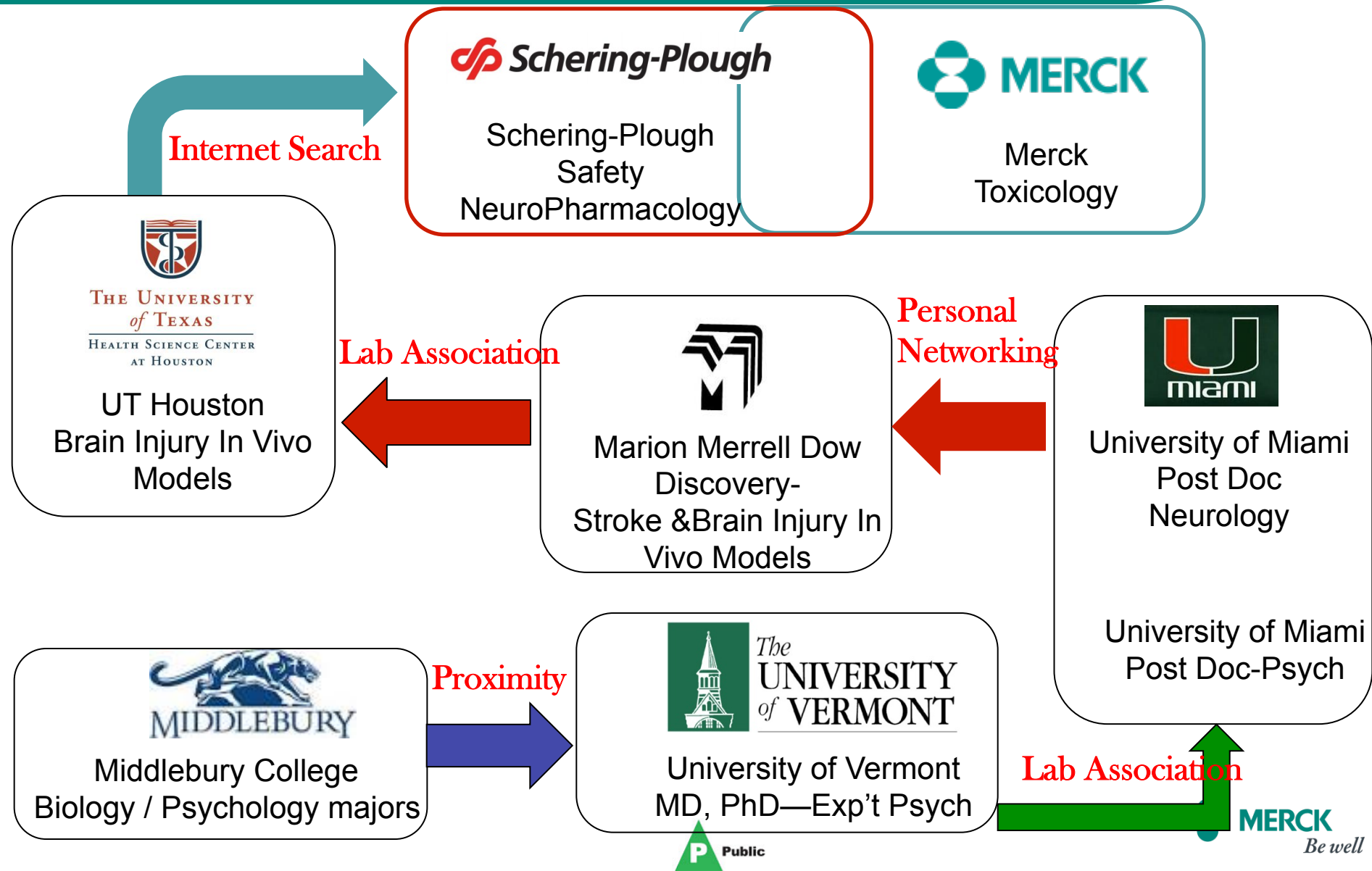


Sources:  
 1 - Science Careers Annual Postdoc Survey (2012) <http://goo.gl/nmVYCN>  
 2 - doi:10.1038/472276a <http://www.nature.com/news/2011/110420/full/472276a.html>  
 3 - Saueremann & Roach 2012 PLOS ONE, DOI: 10.1371/journal.pone.0036307  
 Unless otherwise noted, NIH Biomedical Workforce Working Group (2012)



- Carrie Markgraf
- Discovery Program Lead and Compound Leader

# Carrie Markgraf: Background



# Positions in Drug Discovery

- High School / College education: Lab technician
  - \$27-35K<sup>a</sup>
- B.S. / B.A.: Scientists / Biologist
  - \$40-71K<sup>a</sup>
- PhD: Principal Scientist, Senior Principal Scientist
  - \$75-95K starting + annual bonus \$5000-\$10,000<sup>a</sup>
  - Average \$138K + annual bonus ~20% salary + stocks<sup>a</sup>
  - Head of laboratory
  - Responsible for running compounds in your assay / model
  - Analyzing / reporting results
  - Participating in teams to represent your area of expertise
  - Keeping management informed of progress, issues, upcoming milestones
  - Attend scientific meetings, publish papers when approved

*a: American Association of Pharmaceutical Scientists, 2013 report*





# Positions in Preclinical Development

- **Laboratory positions**

- PhD, DVM: Lab Head, Principal Scientist, Sr. Principal Sci.
- Starting salary 75-95K starting + annual bonus \$5000-\$10,000<sup>a</sup>
- Average \$150K + annual bonus ~20% salary + stocks<sup>a</sup>
- Oversee assays run in your lab, develop new assays to address issues, keep current with literature and competitors' technologies
- Manage colleagues in lab



- **Non-laboratory scientific positions**

- PhD, DVM: Study Director, Compound Leader
- Starting salary 75-95K starting<sup>a</sup> + annual bonus; Average \$150K + bonus ~20%
- Design and oversee studies (SD) or a compound's program (CL)
- Requires knowledge of GLP regulations and of broad nonclinical development
- Develop study design, analyze & interpret data for standard and investigative studies
- Write sections of documents for FDA, EMA etc. that will support clinical trials
- Keep management apprised of issues and upcoming milestones, presentations

# Other Positions



- **Project Management**

- Co-leads project team
- Tracks all activities and keeps all parts moving on time
- BA/BS, MA, PhD. PMP certification preferred
- \$91-165K, average \$126K + bonus<sup>a</sup>

- **Regulatory Affairs**

- Interacts with regulatory authorities in all countries
- Knowledge of regulations, sets strategies for advancing a compound
- \$75-85K starting salary<sup>a</sup>

- **Scientific Writer**

- Works with Study Director or Research Physician to write sections of regulatory documents (IND, IMPD, NDA, study protocol)
- Scientific Writing certificate

- **Medical Science Liaison**

- Liaison with outside experts in academics, hospitals
- Develop relationships with Key Opinion Leaders (KOL) in disease area
- \$100-\$150K + bonus/stocks<sup>a</sup>

# Conclusions

- Variety of positions within pharmaceutical industry, both laboratory-based and non-lab based
- Industry offers opportunity to work in multi-disciplinary teams and have real impact on bringing new human medicines to market
  - Good scientific support with resources necessary to do the job
  - Typically, regular hours (8-4) with additional effort for important regulatory interactions, for example with FDA
  - Well-paid, good benefits, smart and interactive colleagues
- Challenges include finding company with compatible style of management
  - Attend a lot of meetings
  - Mergers, change of management or disease area are out of your control

# Training, Courses and Certifications

- Review guidances on ICH and FDA websites
- Review Scientific Reviews for approved drugs (FDA website)
- **Nonclinical Safety Assessment: A Guide to International Pharmaceutical ...** edited by William J. Brock, Kenneth L. Hastings, Kathy M. McGown
- <http://www.diahome.org/en-US/Meetings-and-Training/About-our-offerings/Certificate-Programs.aspx>
- <http://www.amwa.org/certification>
- <http://www.raps.org/education-training/online-learning/regulatory-medical-writing-bundle/>

# Scientific Meetings with Large Industry Presence

Society	Annual Meeting	Website
Society of Toxicology (SOT)	US <i>March</i>	<a href="http://www.toxicology.org/">http://www.toxicology.org/</a>
American College of Toxicology (ACT)	US <i>November</i>	<a href="http://www.actox.org/">http://www.actox.org/</a>
Safety Pharmacology Society (SPS)	US / EU alternate years <i>September</i>	<a href="http://www.safetypharmacology.org/">http://www.safetypharmacology.org/</a>
American Heart Assoc. (AHA)	US <i>October</i>	<a href="http://www.heart.org/HEARTORG/">http://www.heart.org/HEARTORG/</a>
College on Problems in Drug Dependence (CPDD)	US or Canada <i>June</i>	<a href="http://www.cpdd.org/">http://www.cpdd.org/</a>
Interscience Conference of Antimicrobial Agents and Chemotherapy (ICAAC)	US <i>September</i>	<a href="http://www.icaac.org/">http://www.icaac.org/</a>

- Krupali Prevete
- Program Coordinator



# Program Development

## Therapeutic Area Lead (TAL)

- Responsible for a particular Therapeutic Area (e.g. Cardiovascular, Infectious Disease, Biologics/Vaccines, Woman' Health, Neuro)
- Oversee/advise CL on their programs
- Responsible for all regulatory and internal documents within assigned area.
- Requires an advanced degree (e.g. Ph.D. in relevant field, D.V.M. (or equivalent Veterinary Medicine degree) with highly advanced level of knowledge and understanding of the drug discovery process.

## Compound Leader (CL/DPL)

- Safety representative on the Early Development Teams and EDT and Product Development Teams
- Responsible for preclinical development strategy and risk
- Oversee design and timely reporting of SA studies to support clinical trials and marketing application
- Contribute to Regulatory/Internal documents
- Requires a Ph. D. in relevant field with advanced level of knowledge and understanding of the drug discovery process

## Program Coordinator (PC)

- PC's are considered operational experts in non-clinical drug development
- Coordinate all non-clinical studies and Regulatory submissions in SALAR
- Determine drug requirements for studies
- Provide monthly tracking in a pipeline management tool for the status, issues, and resolution plans on all active programs
- BS/BA degree in relevant area with commensurate experience



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# Pharmacology (Biology) Management

Eric Parker, Ph.D.

Department of Pharmacology, Screening and  
Protein Sciences (Pharmacology/SPS)

October 28, 2015

# My Career Path



1977-1987  
UNC-Chapel Hill  
B.S. Pharmacy, 1982  
Ph.D. Pharmacology, 1987  
Dr. Luigi Cubeddu

1987-1991  
Post-doc, UT-Soutwestern  
Dr. Elliott Ross

# My Career Path – Part 2



Bristol-Myers Squibb

1991-1996  
Neuroscience



Schering-Plough/USA

1996-2009  
Neuroscience, Obesity, Diabetes, CV

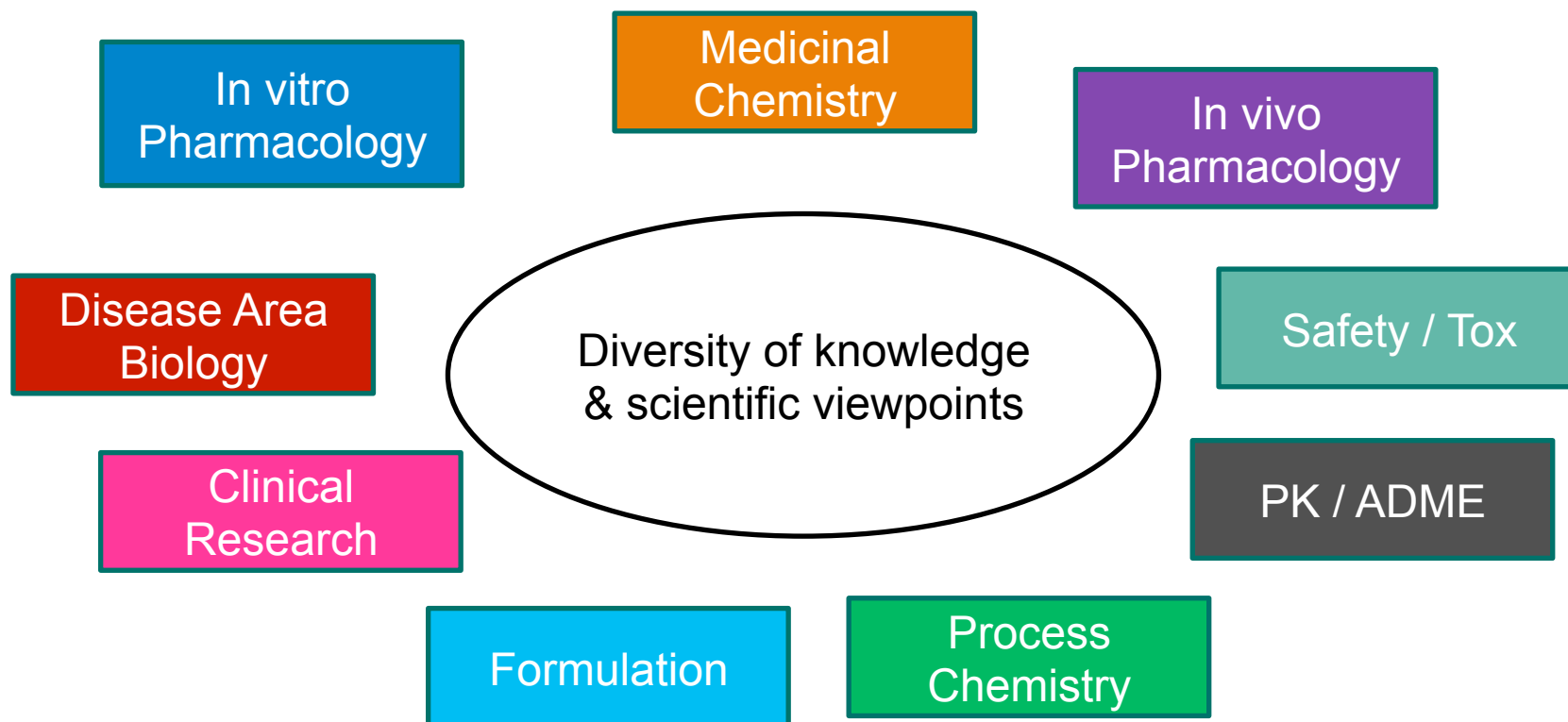


2009-present  
Neuroscience Site Lead  
Distinguished Scientist, Pharmacology



# Drug Discovery Projects are Complex

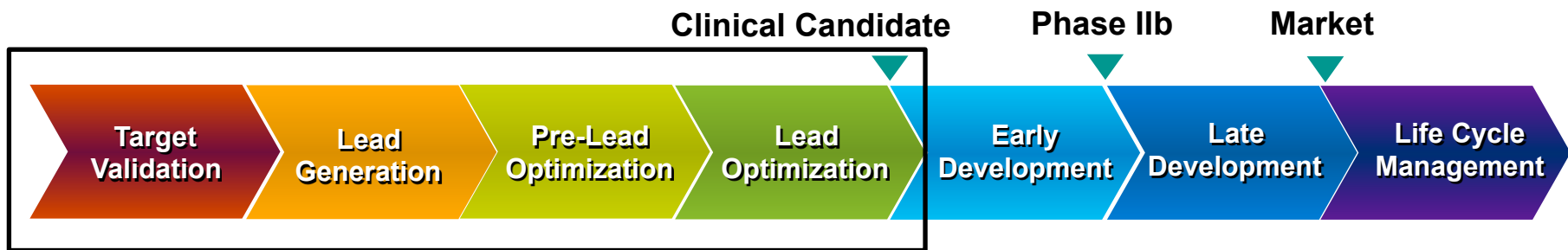
*A team approach is required*



Managing this complexity is one of the key jobs of a manager in a biology group like Pharmacology/SPS

# The Drug Discovery Process

*A 10-15 year effort for projects that succeed*



ID proteins appropriate for drug intervention in medically-relevant pathways



Find non-optimized compounds, antibodies, etc. that modulate target activity



Chemistry & mechanistic studies: Can the lead be converted to a drug?



Optimize the lead for efficacy & safety sufficient to test in humans



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?

# Pharmacology/SPS at Merck Research Labs

Characterize drug mechanism of action & enable chemical optimization

Assess safety & efficacy of lead compounds in animal models of disease

In vitro Pharm

In vivo Pharm

Protein Sciences

High-Throughput Screening

Generate protein reagents to fuel studies across MRL, from structural studies to assays

Convert *in vitro* assays to high-throughput, automated platforms & screen millions of compounds

# What Does a Scientific Manager Do?

- Set overall strategic direction for projects
  - Is this a tractable target? What resources (people/money) do we need to prosecute a drug discovery program on this target? How long will it take? Etc.
  - Need a sufficiently broad and detailed scientific background to understand the science involved in projects under his/her direction.
- Be a conduit for communication – both up the management chain and back down to your team.
- Connect dots, identify opportunities
- Remove obstacles so your team can function at its best.
  - Compromise, yield, confront as necessary
- Recruit the best talent and then develop that talent to its fullest potential.
- Basically, roll up your sleeves and do whatever is necessary to help your team succeed.



# Some Advice for Graduate Students and Postdocs

- Focus on research in a hot area, but be flexible. Your hot area will not always be hot.
- Get a broad scientific background. Don't overspecialize.
  - Read, go to seminars, etc. outside of your immediate area of interest.
- Learn to communicate well!
  - Presentation skills are key – practice as much as possible!
  - Teaching is a great way to develop presentation skills.
  - Become a good writer – there are fewer and fewer good scientific writers.
  - Never stop publishing!!!!!!
- Learn to collaborate, function as part of a team, but also balance with a strong dose of self-motivation and independence.
- Develop a large and diverse network (internal and external)
- Balance in your life
  - Scientists (including me) tend to be workaholics.
  - Family, hobbies, etc. are important!

# Merck Research Laboratories Postdoctoral Research Fellow Program



Learn more at: [www.merck.com/research/fellow](http://www.merck.com/research/fellow)

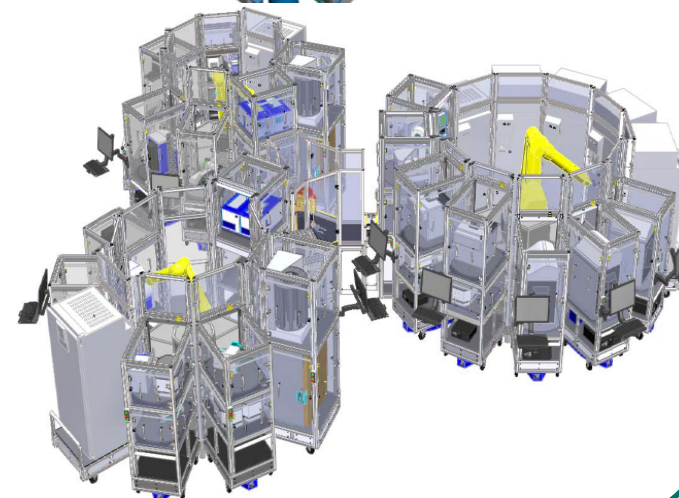
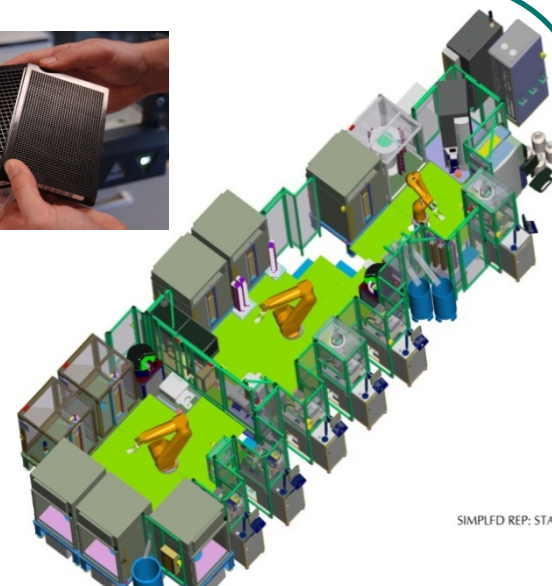
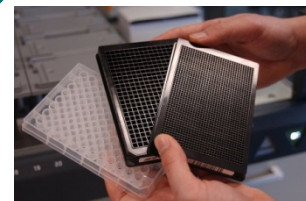
- Academic focus in an industrial environment
- Focus on building your career & publication record
- Paired with an accomplished mentor
- Postdoctoral Fellows at Merck
  - Receive competitive salary & the same access and benefits as regular full-time employees
  - Have direct access to core capabilities, equipment, and expertise across MRL
  - Work exclusively on publishable topics
  - Obtain real experience in drug discovery and development
  - Participate in seminars, lectures and meetings, and interact with the local scientific community

# Questions ?

# High-Throughput Screening

Lead  
Generation

- **7 robotic platforms capable of supporting a wide variety of screening modalities**
  - 384-, 1536- and 3456-well plate formats
  - biochemical, cell-based and phenotypic screens
  - primary screening of millions of compounds completed in < 2 weeks
- **Special technology platforms available that can support focused library screening**
  - High-throughput mass spectrometry
  - Plate-based imaging assays
  - Electrophysiology
  - GPCR ligand bias



# Pharmacology Goal: Identify, Characterize and Differentiate Lead Series

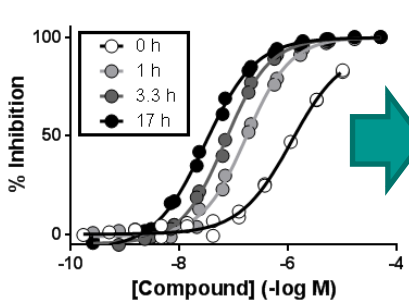
Lead Generation

Pre-Lead Optimization

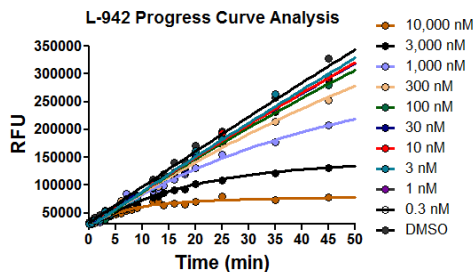
## HTS Generates Thousands of Hit Compounds!!

- What is real?
- How do they work?
- What should we work on?

## Biochemistry: characterize compound *in vitro* enzyme inhibition mechanism and potency

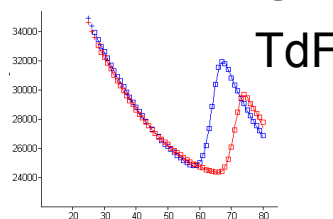


Potency improves as enzyme-inhibitor pre-incubation time is lengthened

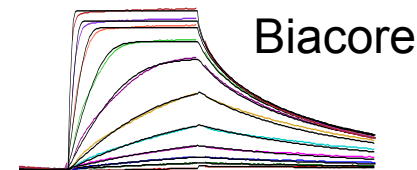


Time-dependent inhibitors can have beneficial pharmacological properties

## Biophysics: demonstrate *in vitro* target engagement

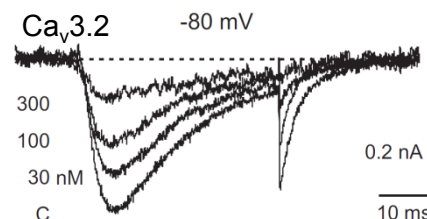


Monitor ligand-induced changes in protein melting temperature

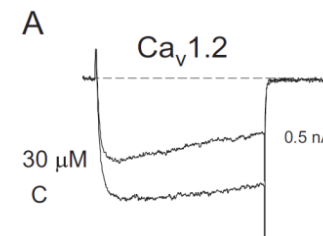


Monitor binding kinetics to immobilized target

## Cell Pharmacology: characterize ability of compound to modulate receptor or channel function



Demonstrate subtype selectivity of Ca<sup>2+</sup>-channel blocker



# Pharmacology Goal: Deliver High Quality Preclinical Candidates

Pre-Lead  
Optimization

Lead  
Optimization

## Build and Execute Assays to:

- Drive Structure-Activity Relationships
- Fully Characterize Biology of Compounds

### Medicinal Chemistry

#### 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

 MERCK

# In Vivo Pharmacology - Support Multiple Therapeutic Indications

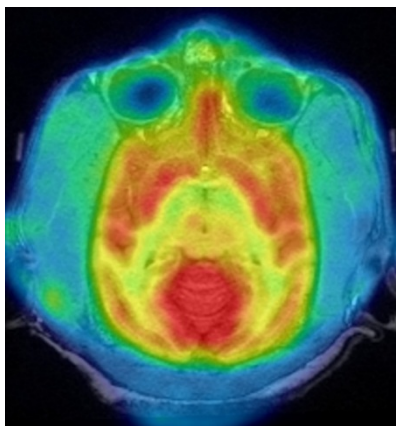
Pre-Lead  
Optimization

Lead  
Optimization

- **Target Engagement** – receptor occupancy
- **Pharmacodynamic Effects** – *e.g.* neurochemistry, physiology, etc.
- **Efficacy** – *e.g.* behavior in a validated assay/model
- **Translation** – compound exposure → target engagement → efficacy

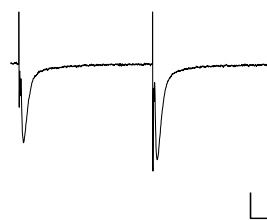
## Example: Neuroscience

### Receptor Occupancy

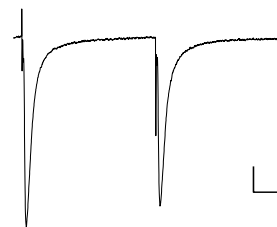


### Electrophysiology

Pre compound



Post compound



### Complex Behavior



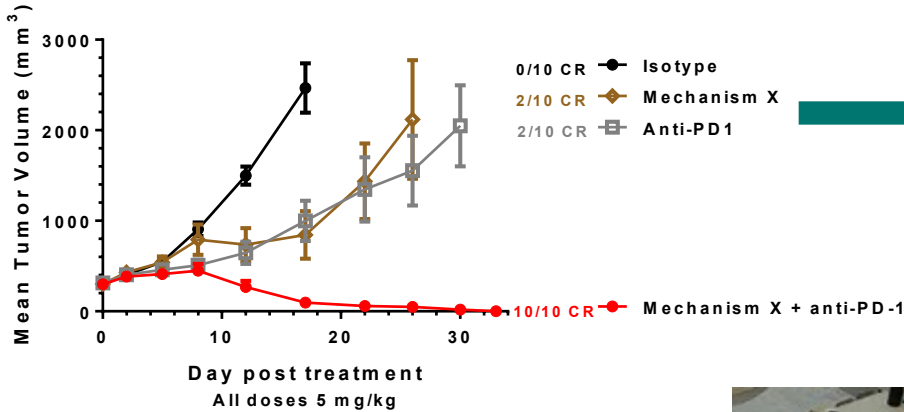
# Pharmacology Goal: Provide Data to Inform Clinical Trial Design

Early  
Development

Late  
Development

Lifecycle  
Management

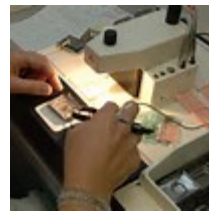
MC38 tumors



Oncology

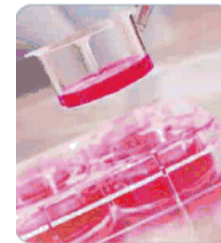


Tumor (fresh)



Tissue  
Processing

IHC, ISH, LCM, Immuno-  
LCM



Histoculture  
(+/- tx e.g. Keytruda)

ELISA (e.g.  
cytokines)



Tissue  
Disassociation

FACs sorting/  
immunophenotyping  
In vitro functional assays

Gene Expression (qPCR, Nanostring, NextGen sequencing)

Perform  
preclinical  
studies that can  
point to new  
indications for  
approved drugs