Quantitative Virology and Evolution Unit Laboratory Manual

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The purpose of this document is to lay out general expectations and provide information for members of the Quantitative Virology and Evolution Unit (QVEU). This is a living document that will change as the lab changes. Please read it thoroughly. If anything in this document seems incorrect, outdated, or you think a process or policy can be improved, please bring it up to Patrick or the group. Even though this is not a permanent document it is important that we all agree to follow the expectations as defined here and respect the process as it's set forth.

1 Introduction

1.1 Welcome

Welcome to the Quantitative Virology and Evolution Unit (A.K.A., the Dolan Lab) in the Laboratory of Viral Diseases at NIH. Whether you are a student, fellow, or staff member, I am incredibly honored and excited that you've chosen to continue your scientific work here. I look forward to supporting your development as a scientist, and look forward to learning with and from you during your time in the lab.

1.2 The Mission

The mission of the QVEU is to explore questions related to virus evolution, emergence, and pathogenesis through rigorous quantitative experiments and computational biology.

The three concepts I want to motivate the lab are:

Heterogeneity - how does diversity and selection in viral and host cell populations affect the outcome of infection and evolution?

Constraint - what are the forces (biological, genetic, or biophysical) that shape evolutionary processes?

History - how can historical data (either measured or inferred computationally) be used to enhance our understanding of viral diversification and emergence?

1.3 Motivating Values

Core values are the beliefs that motivate us. In my scientific training, I've found my two core values are Curiosity and Responsibility. To me, scientific curiosity is the fuel that runs this machine. Without it, we have no new questions and can easily find ourselves just "punching the clock" and doing the same experiments on the same variables we always have. When things aren't working, it is my own curiosity that will keep me asking new questions and spurring me on through the difficult times. Responsibility is what makes us do the rest of the job - the paperwork, cleaning, organization, and participation - when we might rather not. I encourage you to think about your own core values and how they motivate you and shape your interactions. My core values shape this document. I also want to understand how your core values motivate you.

1.4 Setting: The LVD, NIAID, and the NIH

The Quantitative Virology and Evolution Unit is part of the Laboratory of Viral Diseases (the LVD). The LVD operates under the Division of Intramural Research, the intramural reseearch arm of the National Institute of Allergy and Infectious Diseases (NIAID). NIAID is one of

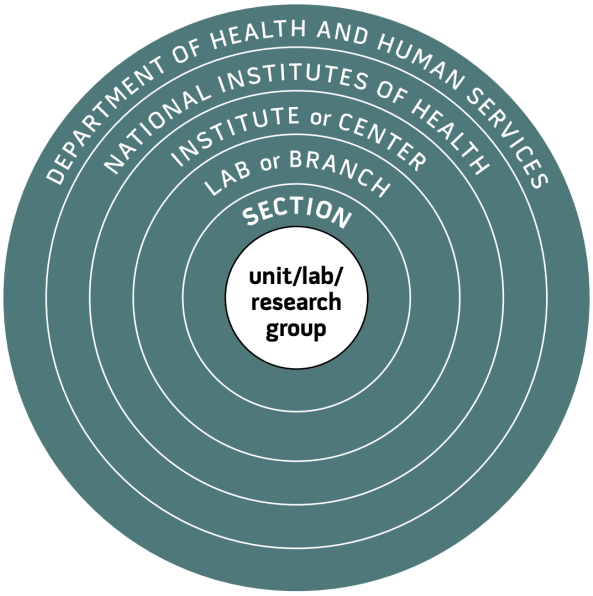

Figure 1: *Diagram of NIH organizational structure. From the very helpful Post-bac handbook. ()*

Institutes that makes up the National Institutes of Health (the NIH).

To put it in terms of academia, you should think of the LVD as your "Department" and the Lab Chief as the Department Chair.

2 General Lab Information

2.1 Contact Information

Lab Address :
Building 33, Room 1E13
33 North Drive, MSC 3210
Bethesda, MD 20892-3210
Patrick's Cell Phone : 989-600-0117

2.2 Onboarding Tasks

Here is a brief outline of what to expect once you have received an offer to join the lab. Because we are a government lab, and because our building requires special clearance, there are a few extra steps that will be required, especially if you are planning to do any BSL3 work. NOTE: If you are planning, or might plan, to do any BSL3 work, we should discuss this and make sure the admin team knows.

1. Receive initial E-mail from LVD Admin team.
2. Complete DPSAC background check through eQIP.
3. Activated in NED NIH system.
4. Get fingerprints recorded (can be done remotely).
5. Get PIV card ("ID Badge") at NIH security office .
6. Complete necessary trainings in lab safety, security, and bloodborne pathogens (online or in-person).
7. Complete computational bootcamp. Learn basics of GitHub, R, and python. Get necessary software (see 'Software') installed on your Government-issued device. Get access to storage space and BioWULF server, learn how to submit jobs.
8. Complete lab tour and orientation. Learn where things are, how things work, where to order, where to shop on campus for equipment and reagents.

3 Expectations

3.1 Lab Policies

It is my responsibility to provide you with a safe, supportive, and productive environment for you to work, train, and study. I hope all lab members will become active participants in creating a lab culture of curiosity, rigor, and shared success. These are a few expectations I hope will provide a substrate on which that culture can grow.

3.1.1 Working Hours

There are no specific "working hours" for the lab, but official lab activities will operate ona 9-to-5 schedule. This means lab meetings, discussion, 1-on-1's, seminars, and trainings will be scheduled between 9AM and 5PM Monday-Friday. Schedules are sometimes irregular due to experimental timelines, variable workloads, equipment schedules, or commitments at home. You can keep a schedule that works for you as long as you are productive and you attend the scheduled lab meetings. If there is an important conflict with the scheduled lab meetings we will find a new time that works for all lab members. The lab will not close on weekends, but I do expect you to use your weekends to recharge for the week as needed.

3.1.2 Working remotely

Working remotely is sometimes conducive to completing a writing or coding task, but being in the lab helps to foster communication, coordination, and creativity through organic conversation between lab members and others on the NIH campus. Working remotely is a privilege and not a right. All members of the lab are expected to be in the lab for all lab meetings and seminars. **COVID-19 note:** The unique situation presented by COVID-19 means that remote work will be a necessary part of the lab indefinitely. It is critical that we prioritize the wet-lab work onsite, and perform writing and coding projects off-site as necessary. This will require extra coordination

and organization across the lab group. We will rely on the lab Slack and other scheduling tools as necessary to facilitate this coordination.

3.1.3 Lab absences

If you expect to be out of the lab for more than a day, please put this on the lab calendar along with whether you are available to be contacted. You can also put up a status on Slack. This helps everyone know not to bother you (except in an emergency), or to store deliveries that may need special handling.

3.1.4 Illness

You should make every effort to avoid coing to lab if you have a contagious illness. Contact your labmates to cover for you, if necessary. If you do need to come to work for an urgent reason, minimize contact with your co-workers, wear a mask, and wash your hands regularly to avoid transmission.

3.1.5 Vacation

I expect you to take advantage of the weekends and vacation time you have. I want you to balance your mental health and well-being with your productivity. Please do your best to plan vacations around important deadlines and give yourself and your collaborators ample time to plan ahead.

3.1.6 Language

Since English will be the language we use to write and present our work, please speak and write in English in the lab and office with your colleagues and coworkers. It is important to avoid misunderstandings, facilitate interactions, and prevent isolation. It also gives those for whom English is not a first language more opportunities to practice speaking about their work in English.

3.1.7 Dress code

There is no dress code beyond any set forth by the NIH, but you should be presentable when on campus and dress with safety in mind. There are lockers available for those who may want to change into lab clothes, lab shoes, or scrubs prior to work. You can request a locker with the admin team when you arrive on campus.

3.1.8 Food/drink

Food and drink are banned from lab bench areas. Do not store food in the office area, and do not leave any empty containers or food waste anywhere in the office area.

3.1.9 Professionalism

Punctuality is expected at lab meetings and seminars. All members of the lab are to treat others with respect inside and outside of the lab. When representing the lab at a conference, symposium, or NIH function, lab members are expected to exhibit behavior that exemplifies our values.

3.1.10 Discrimination and Harrassment

Abuse, harrassment, or discriminatory behaviour of any kind will not be tolerated. It is my priority that this lab be an example of tolerance, compassion, and acceptance. No one will be treated differently due to the race, color, religion, sexual orientation, gender, socioeconomic background, or any other reason. I ask that everyone respect the boundaries of their labmates. We will not tolerate the display of racist or offensive signs or images; offensive jokes based on race, gender or other grounds that result in awkwardness, embarrassment or unwelcome attention.

3.1.11 Lab maintenance and repairs

Working at the NIH is a tremendous privilege and it is critical that we treat the taxpayers' lab and equipment with respect. It is also critical to your work, the work of your colleagues in the lab, and that of our neighbors in the LVD that we maintain our equipment in excellent condition. Any broken or malfunctioning equipment should be discussed as soon as possible, preferably by the party who discovered the issue. In order to encourage the maintenance of the lab in good working order, the lab will have a shutdown each spring where we thouroughly clean, declutter, and inventory the lab and any equipment that requires repair, replacement, or to be sent to surplus can be identified. We will also regularly clean the lab space with 5% bleach and then 60% ethyl/isopropyl alcohol.

3.1.12 Being a good lab citizen

Science is sometimes difficult, but made easier through the support of our labmates. I want members of the lab to be generous with their time, resources, and expertise. I expect you to participate in group meetings, give constructive feedback, ask questions, suggest experiments, offer assistance, and generally support the work of your labmates. You should expect the same of them. We should be understanding of others' working styles and, when possible, flex to work with them in a way that they are comfortable. I want us all to build a culture of shared success and not one of intra-lab competition.

3.1.13 Conflict Resolution

Working together for years, sometimes under pressure, in small spaces can naturally lead to disagreements and conflicts. As adults, we should all be willing to be deal with issues directly, professionally, and honestly. We should also be aware and understanding of others' boundaries, preferences, and customs, and avoid issues where possible. When serious interpersonal issues arise in the QVEU or LVD, they should be brought to Patrick's attention as soon as possible.

3.1.14 Criticism

Criticism and feedback are an important part of the scientific process. It improves our work and forces us to think from new perspectives. The ability to give and receive feedback effectively comes from trust between team members. To encourage that trust, we must always give criticism in a thoughtful and constructive way. I understand not all members of the lab may be comfortable giving and receiving feedback or criticism in the same way, so I encourage you to find and communicate an approach that works for you.

3.1.15 Mistakes

Mistakes are a natural part of learning, but making the same mistake is not. I want everyone to own up to their mistakes so that they and others can learn from them and we can take any steps possible to avoid them in the future.

3.1.16 Safety

As virologists, the work we do has some inherent risks. It is critical that we all observe key safety rules to keep us all safe and compliant.

Situational awareness is the key to safety. Everyone is expected to exercise situational awareness in the lab.

Perception - of the elements in the environment
Comprehension - of the situation
Projection - of future status

Some general safety guidelines for the lab (Adapted from Safety in a Microbiological Laboratory, CDC guidance (U.S. Department of Health and Human Services, 2020)):

1. Hygiene:

   Wash your hands coming in and going out of the lab and between tasks.
   Do not eat or drink in lab area.
   Isolate your lab surfaces from your computers and personal devices in the office area.

2. Equipment:

   Do you have the necessary equipment and PPE to do the experiment safely? Think about this far ahead of time so we can get what you need.
   Appropriate equipment for the job?
   Reduce risk where possible.
   Minimize splashing and aerosolization.
   Secondary containment when necessary.

3. Decontamination:

   Clean work surfaces.
   Place all contaminated items in leak-proof containers.
   Use secondary containment when transporting infectious materials (e.g. a locked, plastic container to hold your tube rack).
   Regular decontamination is critical to high quality work and we will keep a tidy, regularly decontaminated work area (regularly 10% bleach and 60% Ethanol).
   Be aware of what come into the work area and what goes out.

4. Signs and Labels:

   Make sure you are working in designated areas appropriately.
   Make sure your work area and reagents, and waste are appropriately labeled.

5. Training:

   Are you properly trained to use a piece of equipment?
   Have you done adequate preparation (i.e. reading), planning, and visualization to foresee potential risks?

If you do not know the appropriate *hygiene, equipment, decontamination or labeling* necessary for a given task, you still require some *training*. That's OK, just ask!

3.2 Lab Meetings

Traditional lab meeting/journal club models are not always effective at engaging all members of the lab effectively. In addition, our lab is small and we are just getting started so there will be a lot of troubleshooting and optimization, so we are going to experiment with a modified version of the "Scrum" or "Agile" project management style (May and Runyon, 2019) which will allow us to collaborate effectively as we set up the lab. This will probably take a few months to get right, but we will improve it together.

In this framework, work is broken into "cycles" of some length of time (e.g. 2-3 weeks). At the beginning of each

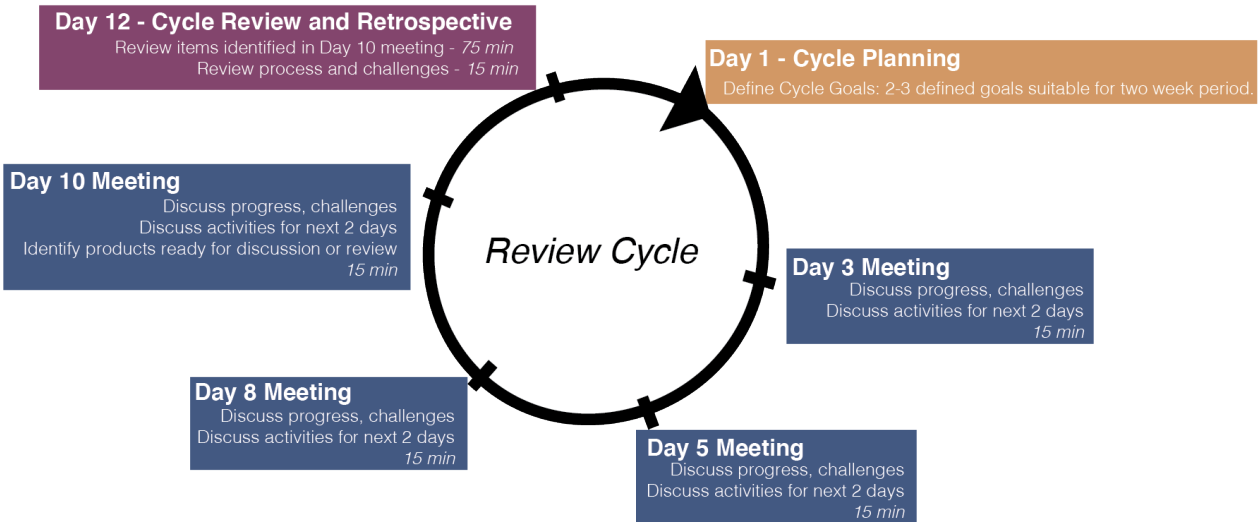

Figure 2: *Biweekly cycle schedule.*

cycle each individual in the lab, including the PI, chooses goals for that cycle (2-3 goals appropriate to the cycle length) that are part of their larger project. Then, the team will meet regularly (every 2-3 days) to discuss their progress and identify any challenges in short, 15 minute meetings. At the final short meeting in a cycle (Day 10), the team will nominate items to be discussed at the "Cycle Review". Cycle Review is a more formal 90 minute meeting where we discuss the nominated results, manuscripts, recent publications, or practice presentations in more depth (more like a traditional lab meeting). At each Cycle Review, we will also have a Cycle Retrospective where we will evaluate any challenges we encountered and discuss whether the process itself can be improved or adapted to better suit our needs.

This structure should only form the minimum interactions you have with me and your other labmates. My door (and Slack) is always open to brainstorm, troubleshoot, plan, or write. If you feel you need to structure our interactions in a way that works better for you (e.g. daily check-ins or weekly 1-on-1's), put that on the calendar or talk to me and we can arrange it.

3.3 Communication

NOTE: All communications are monitored on campus and on government-issued equipment. Please keep this in mind and behave appropriately.

3.3.1 Slack

Slack is the preferred method for communication in the lab. It's an instant messaging app that allows you to manage topic-specific channels for discussion with specific groups of users. It's incredibly useful for sharing data and papers, sending calendar reminders, or quickly alerting the lab of freezer malfunctions. When you are added to the lab slack, you will be automatically added to general channels: 'general', 'science-literature', 'lab-organization'. If there are channels that might be useful, feel free to add them and invite the group. You can send messages to specific people with the "@username" function, or you can callout to the group with "@here", "@channel" or "@everyone". You can download the app to your phone or computer. Notifications can be muted outside of specified hours.

The lab Slack channel can be found at: https://QVEU.slack.com

Request access using this link.

3.3.2 Lab Mailing List

In addition to Slack, which should be the most reliable method of communicating, the lab e-mail list is [INSERT LAB MAILING LIST]. This is especially handy for looping other folks outside the lab into lab-wide conversations. Patrick will add you.

3.3.3 Google Calendar

Our lab calendar is the official word on meetings, lectures, presentations and social events. You should also put any planned vacations or extended work-from-home

Table 1: *Current cycle schedule*

Day	Time Limit	Description
M Day 1	30min	Cycle Planning - Set 2-3 goals for 12 days cycle.
W Day 3	15min	Cycle Meeting
F Day 5	15min	Cycle Meeting
M Day 8	15min	Cycle Meeting
W Day 10	15min	Cycle Meeting - Nominate any projects for review, either due to progress or challenges.
F Day 12	90min	Cycle Review and Retrospective

time, so that others can be aware if you receive packages or are relying on you for collaborations. We will also develop specific calendars for equipment signup using Google Calendar as needed. Please subscribe to the calendar on your own device to make changes easier. Calendar updates will also be fed continuously on Slack "lab-calendar" channel. Subscribe here.

3.3.4 Ordering

This section is still a work in progress as we decide which purchasing policies work best for us. At present, please ask Patrick before making any purchase above $500. The NIH has many specific protocols and rule for procurement. Orders are entered into the system and then approved by an Administrating Official (AO). Purchases over $10,000 require special justification and are subject to bidding by competing manufacturers and suppliers. These justifications should be discussed before submission to make sure they are sufficiently specific.

3.4 Data Management

3.4.1 Data Integrity and Dishonesty

Robust results require rigorous science and reproducibility. I will not tolerate dishonesty or manipulation of results. Backup data often, keep the raw data, and track the changes you make.

3.4.2 Lab Notebooks - Benchling

Currently, the lab standard for lab notebooks is Benchling https://benchling.com/organizations/ptdlab/projects. Benchling is a free, cloud-based lab notebook that has lab organization (e.g. plasmid, virus, cell stock location and annotation) and molecular biology tools (plasmid maps, restriction enzyme databases, CRISPR gRNA design) built in.

3.4.3 Computational and Sequencing Data

As a computational and systems biology lab, we are users, creators, and stewards of a large amount of data. Our goal is to maintain the integrity, usability, and reproducibility of the data we generate. All data generated in the lab should be regularly backed up. We will develop SOPs around this process including backing up data from each individual's lab computer and instrument computers. The lab also has a shared drive [INSERT shared drive information here]. Data will be uploaded to public servers during sequencing analysis in coordination with the NIAID Bioinformatics Core

3.4.4 Version Control with GitHub

Use GitHub for version control. Our lab uses GitHub for version control and software documentation. We have a github repository for the lab at: https://github.com/QVEU To create an account: https://github.com/join The lab website is also currently hosted on GitHub: qveu.github.io/qveu/
There is a desktop app for

3.4.5 Pipelines and Computational Workflows

Computational work should always be done using the current established workflows in the lab when possible to facilitate comparison across datasets. Any compputational work shoudl be collected in a shell script or notebook for version control. Links to this information should also be incorporated along with any graphical results in your Benchling notebook.

3.4.6 Computational Resources

Each person will be given an NIH computer. You can have a Mac, Windows, and, perhaps upon negotiation, a Linux computer. Some nice pre-configured options are available from the IT shop, but you may also want to design something specific, especially for computational work. Just talk to Patrick to arrange this. In addition to resources in the lab, we also have access to the computing cluster at NIH, "BIOwulf": https://hpc.nih.gov/systems/. Access can be requested through the IT. Jobs are submitted using Slurm job submission: https://hpc.nih.gov/docs/biowulf-cheatsheet.pdf.

NOTE: All communications are monitored on campus and on government-issued equipment. Please keep this in mind and behave appropriately.

3.4.7 Software

A few of the software you can install for use in the lab are:

GitHub Desktop : Graphical User Interface (GUI) for updating and organizing GitHub repositories.
Atom : Text and code editor that works well with GitHub repositories. Excellent for editing latex files.
bbedit : General purpose text and code editor.
R : General purpose, open-source statistical computing language. Many packages are also available for specific tasks, e.g. explore "BioconductoR" packages and the "tidyverse".
RStudio : Interactive Development Environment (IDE) for R scripting and plotting. Cheatsheets for R packages can be found online.
Jupyter Notebook : Interactive (browser-based) notebook for python, R and Julia scripting.

3.5 Publishing

Publishing is the core of what we do, and we need to be efficient in translating our work into publications. When a project is nearing the point of minimum publishable unit (2-3 figures), the author or authors should put together figures and an outline of the narrative together for discussion. Once we have agreed on a general outline for the manuscript, I want the author(s) to organize a first complete draft. This should happen early and with a critical eye - where can we make improvements or ask new questions? It also encouragess you to go back to the literature and see if you missed anything useful. I will read the draft and we will discuss within two weeks. You can also put your drafts or figures up for discussion at Cycle Review. I also encourage you to organize your paper in a LaTeX document for submission and revision (like this one - available on GitHub).

3.5.1 Authorship

We will subscribe to the "discuss early, discuss often" philosophy for authorship. When a project begins to take shape, the scientists involved should consider and discuss what they think is fair and come to an agreement. As the project develops, things can change and when these changes shift the balance of work shared between collaborators, its reasonable to discuss how that might change the balance of credit. I am very open to shared authorship arrangements but only when justified. I do not believe sharing reagents consitutes authorship (e.g. using a plasmid you generated for another application), especially among lab members. The reagents you generate in the lab belong to the lab and are available to everyone. Computational work is real work - I do not consider wet or dry lab work more deserving of first-authorship.

3.5.2 Presubmission Approval

The NIH will need to approve all manuscripts before submission, including collaborators' manuscripts. This is mostly to make sure we have the appropriate funding descriptions and to check for any conflicts of interest or biosafety issues.

3.5.3 Preprints

I'm open to posting preprints of papers, but submission must be discussed and approved by me beforehand.

3.6 Meetings and Trainings

I want every trainee to attend a scientific meeting every 1-2 years. American Society of Virology (ASV), American Society of Microbiology (ASM), Society Molecular Biology and Evolution (SMBE), and Ecology and Evolution of Infectious Disease (EEID), and Keystone Positive-Sense RNA viruses are all great choices depending on your interests. Let the lab know if you find other opportunities. If eligible, please apply for travel awards to supplement the cost of your attendance.
I also encourage you to pursue topic-specific trainings to enrich your experience in the lab. The Smmmer Institutes in Statistical Genetics (SISG), or Summer Institutes in Modeling of Infectious Diseases (SISMID) in Seattle are excellent for learning computational skills. I encourage you to search for scientific, career, and leadership trainings that may be of interest to you on campus, in the US, or internationally.

3.7 Member Roles and Responsibilities

3.7.1 Postdocs and Fellows

1. Develop as an independent scientist. Learn new techniques, ask new questions, pursue new opportunities. Develop a niche.
2. Develop mentorship skills. Mentor junior members of the lab. Be generous with your time and expertise.
3. Develop leadership skills. Pursue formal and informal opportunities to practice and learn leadership skills.
4. Participate in cycle meetings and present regularly at cycle review (at least twice per quarter).

5. Develop and manage 2-3 projects. I will have input at various stages but you will be the owner of these projects.
6. Write papers. Ideally you should have something in press at least twice a year. Reviews, perspectives, collaborations are all fair game, but first author publications are the priority.
7. Network. It's incredibly important for any career path, so find a way that works for you. Also, don't be afraid to use your network when you need it!
8. You will be in the lab between 2-5 years, focus on the career you want early and set the appropriate goals. Set up regular 1-on-1 meetings with Patrick to talk about those goals.

3.7.2 Post-bacs

1. Work with Patrick and senior members of the lab to develop a project.
2. Set-up a weekly 1-on-1 meeting with Patrick to discuss research, the post-bac program, and career goals.
3. Participate in cycle meetings and present in cycle review.
4. You will be working on something connected to the current projects in the lab. However, if there techniques or questions that interest you we should talk about that in our 1-on-1 meetings. We want to invest in your development as a scientist, wherever that takes you.
5. Network. Make connections with other post-bacs, your colleagues, and other PI's when you can. Take advantage of opportunities to meet visiting speakers.
6. Learn! You are in a fantastic environment to explore scientific questions and careers. Go to seminars across campus, network, and learn as much as you can!

3.7.3 Graduate Students

1. Develop a broad set of research skills. Wet lab, computational, robotics, all of it. Make mistakes, but work towards excellence.
2. Develop leadership skills.
3. Participate in cycle meetings and present in review often (at least once per quarter).
4. Expand your network. Attend conferences, seminars, events, etc. to connect with as many professionals in (and outside) your field as possible. Take advantage of opportunities to meet with visiting scientists.
5. Graduate in no more than six years, and ideally in about five. Engage Patrick and postdocs/fellows in your career planning - they have been there and can help with networking.

3.7.4 Lab Technician

1. Keep regular hours (roughly 9-5).
2. Work with lab members to schedule and carry out animal experiments.
3. Prepare, infect, euthanize, and dissect mice for viral studies.
4. Interface with mouse facility staff on animal issues and communicate any issues to Patrick.
5. Organize orders and procurement of animals and animal equipment.

3.7.5 Unit Chief

1. Supervise the research program in the QVEU. Set the long-term vision and direction of the lab.
2. Mentor post-bacs, graduate students, and post-docs.
3. Advocate for the scientific, professional and personal interests of the lab and its members.
4. Manage the finances, personnel, and facilities of the QVEU.
5. Develop independent research projects and pilot studies.
6. Write, review and edit manuscripts.

In execution of those responsibilities, I will do my best to:

1. Treat each member of the lab with respect, and value their contribution to the team.
2. Respect your time. I will do my best to be punctual to meetings, and to always communicate if I am running late or need to reschedule.
3. Turn around feedback on documents as soon as possible (ideally within one two-week cycle). I want us publishing often and I do not want to be the bottleneck.
4. Attend and engage in all lab meetings, seminars and events.
5. Make myself available to you on Slack, by e-mail, or by phone as much as possible.
6. Give you credit for your work in public presentations and ensure you get appropriate authorship at the time of publication.
7. Understand your career goals and help you identify paths to achieve them.
8. Provide life-long mentorship in whatever capacity you wish. I am invested in your success and want to keep in touch.
9. Maintain the lab's reputation by acting with integrity and generosity, being a careful steward of our funds, recruiting the best people I can, and promoting our work actively.

3.8 Acknowledgements

This document was heavily influenced by similar lab expectation documents shared Gavin Sherlock (Stanford), John Boothroyd (Stanford), and resources and materials provided by the Office of Career and Professional Development (OCPD) at UCSF. It was also improved by many rounds of comment and revision by colleagues at different career stages.

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