Research Rotations

The primary goals for the research rotations are to provide the student with an experience that will allow informed selection of a PhD thesis mentor and to provide the mentor with sufficient familiarity with the student to determine the fit of the student with the laboratory. Together, these goals will enable effective placement of students in labs for their PhD thesis research. A secondary goal is to expose students to a variety of research problems and laboratory techniques.

While rotating, students should participate in as many lab activities as possible (research, lab meetings, journal clubs, seminars, etc.) to get an idea of what it will be like to be a member of the lab.

The student should work on a substantive project, produce some data, and do data analysis to engage in a good breadth of research experience. The mentor should identify a project that will allow this level of engagement, even if done in collaboration with other trainees or staff in the lab, yet is realistic for what is attainable in the short amount of time allowed for a rotation. If publishable data are produced, that is a great accomplishment, but that may not be attainable in many rotations.

The student and rotation mentor should discuss the student's time commitment before beginning the rotation to allow design of a rotation project of appropriate scope. For reference, BSTP students are expected to devote 15 hours per week for 6 weeks for rotations (approximately 90 hours total). For fall or spring semester rotations, MSTP students may stretch their rotations over 6-10 weeks, so their hours/week may be less than 15. MSTP students may need to reduce time in the lab in some weeks, for example during exam preparation times.

At the end of a rotation, it is expected that the student will (1) give an oral lab presentation of the project; and (2) write up a short rotation report. (A sample report is below.) The report should be submitted with the evaluation form (below) to the rotation mentor at or near the end of the rotation. The mentor will review the report and complete form.

The student should have an "exit" interview with the mentor to discuss the rotation and review the evaluation and report. The interview is meant to be constructive and to provide useful feedback. It is expected that the rotation mentor will be honest and indicate the degree to which he/she is interested in accepting the student for PhD thesis research in his/her lab, but it should be recognized that the mentor may have other student rotations planned that may result in placements that will reduce slots available in the lab. The student may also want to indicate the degree of interest in joining the lab. Honesty is best, and it is fine to indicate interest in the lab but more time is needed for exploration, or the rotation was appreciated but research interests are evolving in different directions. After both you and the mentor have signed the form, email it along with the report to mstp@case.edu.

Evaluation forms signed by the student and mentor should be submitted for all rotations completed by the student within two weeks of the end of the rotation. Timely submission of these materials is required to get a grade of “Pass” in MSTP 400.

**MSTP RESEARCH ROTATION MENTORSHIP AGREEMENT**

**Purpose of agreement**

The primary purposes of this document are to:

1. establish clear and uniform expectations for M1/M2 MSTP students and mentors during laboratory rotations and preliminary work in the thesis laboratory;
2. allow for students and mentors to enter into explicit agreement regarding these expectations; and
3. provide a mechanism for the resolution of conflicts that may arise between the expectations stated herein and the practices that are adopted by students and/or mentors.

A secondary purpose of this document is to enable the MSTP to maintain a written record of student-mentor pairings and ensure ongoing compliance with the policies outlined herein.

**Expectations of students**

Students must complete research rotations during the M1 academic year (beginning in Block 2) or during the intervening summer between M1 and M2. Except in the case of extenuating circumstances, students are expected to select their thesis laboratories by the fall of the M2 year.

During the academic year, students are expected to be present in lab weekday afternoons following the completion of medical school classes, except when:

1. students have official, pre-arranged medical school activities (*e.g.*, Physical Diagnosis, Field Experiences) during the afternoon; or
2. the student must be absent for another reason (*e.g.*, medical appointment, vacation, university holiday, exams), which should be discussed in advance with the mentor.
3. The student needs to focus more time on work for the MD curriculum (e.g. for preparation for MD curriculum exams).

Students and mentors should understand the need for flexibility in lab schedules. Work may occur in the evening or on weekends depending on the nature and schedule of experimentation for the project. During the fall and spring semesters, students should commit approximately 15 hours per week for a minimum of 6 weeks (the same as BSTP rotation expectations), or an equivalent amount of time spread over a larger number of weeks in that semester.

During the summer, students are expected to be present in lab full-time (approximately 40 hours per week), except for (1) and (2) listed above. Summer rotations should last a minimum of 5 weeks (with two rotations in the summer). Students may elect to make their summer rotation longer and do a single summer rotation.

**Expectations of mentors**

Mentors are expected to acknowledge that M1 and M2 MSTP students are, first and foremost, medical students, and that all required medical school activities, as well as requisite time for class preparation and mastery of the material, take priority over a student’s laboratory responsibilities. Mentors are expected to honor the hour limitations given above and create a positive experience for students during these times. The mentor is also expected to convey these guidelines to any training personnel (graduate students, postdoctoral fellows, etc.) who will directly oversee the student on a day-to-day basis. In addition, mentors are expected to speak candidly with students about their funding, laboratory space and personnel, and the feasibility of accepting them into their lab – THIS CONVERSATION SHOULD OCCUR BEFORE THE ROTATION TO ENABLE STUDENTS TO CHOOSE ROTATIONS THAT DEVELOP POSSIBLE LAB PLACEMENTS. Above all, mentors are expected to provide a welcoming atmosphere, strong guidance, a safe laboratory work environment and the resources necessary to facilitate the execution of a rotation and/or thesis project.

**Resolution of conflicts**

Should conflicts arise between the expectations outlined in this document and those imposed by mentors or self-imposed by students, students and mentors should make every effort to resolve these conflicts themselves, using this document as a reference for the expectations of the MSTP. For cases in which a resolution cannot be reached, a member of the student’s primary MSTP advisor will serve as a mediator between the student and mentor to devise a solution that adheres to the expectations outlined herein.

**Contact information**

Clifford Harding, MD, PhD, Director

Email: cvh3@case.edu

Phone: (216) 368-3611

Diane Dowd, PhD, Administrative Director

Email: dxd57@case.edu

Phone: (216) 368-2674

**Statement of acknowledgment**

*I agree to the guidelines and expectations outlined above and attest that I will follow the processes described herein in the event that a conflict of expectations should arise.*

Student signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_

Student name (type or print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Mentor signature \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date \_\_\_\_\_\_\_\_\_\_\_\_\_\_

Mentor name (type or print) \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Please sign and return to mstp@case.edu

# ROTATION EVALUATION: MEDICAL SCIENTIST TRAINING PROGRAM

STUDENT NAME

FACULTY NAME DEPT.

DATES OF ROTATION

1. Did the student spend the expected time per week in the lab? (Summer: Full time for 5-10 weeks; Fall or Spring: ~15 hrs/week for 6 weeks or equivalent) Yes No
2. Did the student learn any new techniques? Yes No
3. Did the student get any new results or data? Yes No
4. Did the student do a lab group meeting presentation or

other presentation of their rotation project? Yes No

1. How would you rate the students overall performance in this rotation?

Poor Average Good Excellent

1. Based on this student’s performance and compatibility with the laboratory as a whole, would this student be suitable for placement in your laboratory? Yes No
2. Comments. Please address the following questions (**add additional pages if necessary**).

What are the strengths of the student? What areas need improvement? Other comments or information?

Faculty Signature Student Signature

Date

After the student and faculty member have reviewed and signed this form, it should be emailed, along with the report, to mstp@case.edu. Students should submit a rotation evaluation within two weeks of the end of the rotation.

SAMPLE ROTATION REPORT

Effect of a broad-spectrum vaccine on evolutionary rate of simian-human immunodeficiency viral protein gp120 in a macaque pathogenesis model

MSTP student: ; Preceptors: Dr. Gabrielle Nickel and Dr. Eric J. Arts Abstract/Summary

From July – August 2013, I worked under the direction of Dr. Gabrielle Nickel, a post-doctorate researcher in the laboratory of Dr. Eric J. Arts, to analyze sequencing data from a collaborator’s project investigating population-level changes in the viral sequence encoding glycoprotein 120 (gp120) of simian human immunodeficiency virus (SHIV) in a macaque pathogenesis model. To assess the effect of a broad-spectrum vaccine on the evolution and infectivity of the virus, the collaborator vaccinated monkeys with replication-defective SHIV pseudovirus representing the env variants of 10 different HIV-1 subtypes. As controls, animals were vaccinated with pseudovirus expressing only the B-subtype env variant. These monkeys were then infected with a SHIV clone expressing the B-subtype env variant. After 1 and 3 weeks, blood lymphocytes were collected from each monkey, and the gp120 region in a sample provirus population was PCR-amplified and deep-sequenced. As a measure of evolution in gp120 over time, we tracked changes in the frequency of predicted N-glycosylation sites. Preliminary results show differences in the rate of loss or gain of N-glycosylation sites in gp120 between different animals, presumably due to differential selection pressure of the vaccination treatment on the virus, though at this point we are still blinded to the vaccination treatment of each animal.

Introduction

The development of an effective preventive HIV-1 vaccine has proven to be an elusive goal for many reasons, including the heterogeneity of the virus, the high mutation rate of the viral genome, and the inaccessibility of virion surface proteins to host antibodies. However, promising results from a landmark 2009 HIV-vaccine trial (RV144) that lowered the risk of acquiring HIV-1 by 31% have spurred renewed attention on this goal, with specific focus on gp120.

Gp120, a virion surface envelope glycoprotein encoded by the env gene, plays an essential role in HIV-1 infectivity, by binding the CD4 receptor and co-receptor of target CD4 T-lymphocytes and mediating viral entry. Glycosylation of this protein at arginine residues is important for this function, as the N-linked glycans are essential for the receptor binding-induced conformational changes in gp120 necessary for membrane fusion. In addition, glycosylation provides a “glycan shield” that masks epitopes from the host immune system. This immune escape strategy makes the sequence encoding gp120 one of the most variable regions in the HIV-1 genome.

To measure the efficacy of a broad spectrum vaccine, our collaborator vaccinated 6 monkeys with a combination of pseudovirus representing the gp120 variants of each of 10 HIV-1 subtypes. After infection with the B-subtype SHIV, the gp120 region of a sample provirus population was sequenced at various time-points post-infection. I contributed to the sequence analysis for 2 of the 6 samples. As the reads covered specific sub-parts of the full-length gp120 sequence, I first mapped each read to the known, full-length sequence using an alignment tool, MUSCLE. Next, I calculated the frequency of predicted N-linked glycosylation sites from the translated sequence reads, by developing and running a customized Perl script which finds in the sequence all matches to the pattern predictive for N-linked glycoslyation sites (Nx[ST]).

Results

Table 1. [unpublished data redacted] Positions of predicted N-linked glycosylation sites and their frequencies in a sample population of gp120 sequences, 1 week and 3 weeks after infection, for 2 different animals. In red and green are positions lost and gained, respectively, between the two time-points.

|  |
| --- |
| Animal 1 |
| Week 1 Week 3Position Frequency Position Frequency |
| … | … | … | … |

|  |
| --- |
| Animal 2 |
| Week 1 Week 3Site Frequency Site Frequency |
| … | … | … | … |

The distribution of predicted N-linked glycosylation sites in gp120 is shown for two different animals in Table 1. In Animal 1, between weeks 1 and 3, X sites were lost, and X sites were gained in the population of gp120 sequences. In contrast, in Animal 2 in the same period of time, X sites were lost in the population of gp120 sequences, and X were gained. Though quite preliminary, these results may be consistent with our hypothesis that the rate of evolution in gp120 is accelerated in subjects of the broad-spectrum vaccine, because of higher selection pressure on the virus from antibodies against all gp120 subtype variants compared to antibodies against a single gp120 subtype variant.

Future directions

I will confirm each monkey’s vaccination treatment to associate rate of change in the distribution of N-linked glycosylation sites with vaccination treatment. I am currently working with Dr. Nickel to assess the genetic diversity of the gp120 populations at each time-point using the Kimura 2- parameter model, which estimates the evolutionary distance between two sequences from the frequency of nucleotide substitutions. We expect that genetic diversity of gp120 populations will follow similar trends as the rate of change in the distribution of N-linked glycosylation sites, comparing the subjects of the broad-spectrum vaccine with controls. In addition, we will correlate evolutionary rate in the gp120 sequence with viral load measurements to assess whether accelerated evolutionary rate indeed contributed to increased viral fitness in this study.