Research Rotations

The principal goals for the research rotations are to provide a foundation for selection of a PhD thesis mentor and to provide exposure to a variety of research problems and laboratory techniques. While rotating, students should participate in all lab activities (research, lab meetings, journal clubs, seminars, etc.) to get an idea of what it will be like to be a member of the lab. During a research rotation a student should work on a substantive project and ideally should aspire to generate publishable data. The student and rotation mentor should discuss the student's time commitment before beginning the rotation and design a rotation project of appropriate scope.

After you have completed a rotation it is expected that you will (1) give an oral lab presentation of your project; and (2) write up a short report of your rotation. (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.

You should have an "exit" interview with the mentor to discuss the rotation, going over the evaluation and report. The interview is meant to be constructive and to give useful feedback to you. It is expected that the research advisor will be honest and indicate the degree to which he/she is interested in having you as a student in his/her lab. You may also want to indicate your degree of interest in joining the lab. 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 at least three rotations. Typically the rotation report and evaluation should be completed and returned to the MSTP office 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.

Students are also expected to exercise flexibility with their lab schedules, particularly if extra work is needed in the evening or on weekends depending on the nature and demands of their project. During the academic year, students should commit approximately 15-25 hours per week for a number of weeks that is determined through mutual consent of the student and mentor (generally 6-10 weeks).

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 5-10 weeks, and this duration should be determined through mutual consent of the student and mentor.

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.) that 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. Above all, mentors are expected to provide a welcoming atmosphere, strong guidance, 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 MSTP Executive Leadership (Derek Abbott, Cliff Harding, Agata Exner) will serve as a mediator between the student and mentor to devise a solution that adheres to the expectations outlined herein.

Contact information for MSTP Executive Leadership
Derek Abbott, director
Email: derek.abbott@case.edu
Phone: (216) 368-8564

Cliff Harding, co-director
Email: cvh3@case.edu
Phone: (216) 368-3611

Agata Exner, associate director
Email: agata.exner@case.edu
Phone: (216) 368-6727

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 4-6 weeks; Fall or Spring: ~20 hrs/week for 8-12 weeks) 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____
5. How would you rate the students overall performance in this rotation?

   Poor_____ Average_____ Good _____ Excellent _____
6. 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____
7. 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 MSTP Director

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

Animal 1			
Week 1		Week 3	
Position	Frequency	Position	Frequency
…	…	…	…

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

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.

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- paramter 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.