MHC Haplotype Activity: Instructor Notes

Learning Outcomes

1. **Differentiate** between individual and community haplotypes
2. **Predict** how MHC haplotype will be shaped over evolutionary time by a pathogen

Instructor activity notes:

Pre-class preparation:

Instructors for printing and painting models can be found at https://stembuild.ncsu.edu/resource/MHC-haplotype.

Prior to class, the instructor should assemble a classroom set of activity kits. Each activity kit is shared by a group of four students and contains:

- A set of all 11 peptide antigen models
- Four MHC arrays
- A set of 5 index cards each numbered (0-4) with writing as large as possible
- Four MHC Activity Handouts
- One Group Haplotype Sheet

The activity kits can be assembled in Ziplock bags or any other small container.

Activity facilitation:

1. Introduce activity.
    a. Depending on the topics that have already been covered in the course, the instructor may choose to present a short introductory lecture.

2. Pre-assessment.
    a. The instructor may provide a short pre-assessment prior to the activity. An example pre-assessment is included with this lesson.

3. Activity part 1: individual and population haplotypes

a. Students form groups of 4.
b. Each group receives an activity kit.
c. Each student follows the instructions on page 1 of the MHC Activity Handout to determine their individual haplotype.
    i. To do this, the student completes Table 1 by circling the shape and color of the binding site of each of their 3 MHC molecules.
    ii. To ensure that all MHC arrays are oriented in the same direction, all students have either a red circle or a blue sphere in position 1.
d. Reporters collect data from each group member and complete Table 1 of the Group Haplotype Sheet by tallying the total number of group members who have each of the different MHC molecules.
e. Reporters use index cards to report haplotypes to class:
    i. Instructor calls out each MHC molecule (for example, “Red Circle”), and the reporter raises the index card that indicates the number of individuals in their group with that MHC molecule.
f. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled “Starting Population” in the Population Haplotypes tab and projects the graph created by the spreadsheet.
g. Students complete questions 6-12, which includes Table 2, in which students determine which peptides can be presented by their MHC molecules.
    i. Group discussion during this part of the activity is encouraged.
    ii. Each student will need to test the ability of their MHC molecules to bind each of the 11 peptide antigens shared by the group. It is most efficient to take an assembly approach, where student 1 tests peptide antigen 1, and then passes it to student 2 while moving on to peptide antigen 2, etc.
h. The instructor facilitates a class discussion:
    i. Is the number of peptides that can be presented by the individuals in the population equal to the number of different MHC molecules within the population haplotype? That is, can one MHC present only one peptide?
    ii. How are MHCs encoded in the genome?
        1. This part of the discussion may be a review of information that has already been covered in the course, or may require a short mini-lecture focusing on the MHC-I and MHC-II loci.
    iii. Do you think the composition of the population’s haplotype can change?
        1. The instructor may take a yes or no vote on this question, either by a show of hands or using a classroom response system.
    iv. Suggested additional question: Do you think the composition of an individual person’s haplotype can change?
        1. The instructor may again take a yes or no vote.

4. Activity part 2: Outbreaks and haplotype analysis

a. Smallpox epidemic.

i. The students are instructed that a smallpox epidemic has occurred, and none of them are vaccinated, nor do they have any treatments available. The peptide antigen derived from smallpox is the **multi-colored triangle**.
ii. Students work through questions 13-16 on the MHC Activity Handout, ending with predicting whether they will survive the epidemic.
iii. The instructor facilitates a class discussion:
    1. What's the difference between MHC I and II? Which kinds of antigens are presented by each? Which kinds of T cells are activated by each? Will the smallpox antigen be presented by MHC I or MHC II?
    2. Who has an MHC that can present the smallpox peptide?
    3. How does the ability to present the peptide affect the development of an immune response?
        a. Only those who can present smallpox antigens will be able to activate T cells. Note here that in reality, there would be more than one antigen being presented.
    4. In this scenario (no vaccines or drugs), who lives and who dies?
        a. The individuals who can present the antigen live.
iv. Each group's reporter fills in Table 2 in the Group Haplotype Sheet, recording the number of surviving group members, and tallying the number of surviving group members with each MHC molecule in their haplotype.
v. Reporters use index cards to report the total number of surviving group members to the class.
vi. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "Smallpox" in the Survivorship tab and projects the graph created by the spreadsheet.
vii. Reporters use index cards to report haplotypes of survivors to the class:
    1. Instructor calls out each MHC molecule (for example, "Red Circle"), and the reporter raises the index card that indicates the number of surviving individuals in their group with that MHC molecule.
viii. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "Smallpox" in the Population Haplotypes tab and projects the graph created by the spreadsheet.
ix. Students answer question 18 on the MHC Activity Handout.
x. The instructor facilitates a discussion of question 18 (how does the population's haplotype change after the smallpox outbreak)?

b. Ebola epidemic:
    i. The students are instructed that an Ebola epidemic has occurred, and none of them are vaccinated, nor do they have any treatments available. The peptide antigens derived from Ebola are the **pink 9-pointed star and black 3D pentagon**.
    ii. Students work through questions 19-21 on the MHC Activity Handout, ending with predicting whether they will survive the epidemic.
        1. Only individuals who survived the smallpox epidemic will participate. Those who did not survive will observe and help their group members.
    iii. The instructor facilitates class discussion:
        1. How did this scenario differ from the smallpox epidemic? Who survived this time?
            a. Individuals with MHC molecules that can recognize either of the antigens will survive. Because multiple MHCs can present Ebola-derived peptides, more people in the population are able to survive.
    iv. Each group's reporter fills in Table 3 in the Group Haplotype Sheet, recording the number of surviving group members, and tallying the number of surviving group members with each MHC molecule in their haplotype.
    v. Reporters use index cards to report the total number of surviving group members to the class.
    vi. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "Ebola" in the Survivorship tab and projects the graph created by the spreadsheet.
    vii. Reporters use index cards to report haplotypes of survivors to the class:
        1. Instructor calls out each MHC molecule (for example, "Red Circle"), and the reporter raises the index card that indicates the number of surviving individuals in their group with that MHC molecule.
    viii. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "Ebola" in the Population Haplotypes tab and projects the graph created by the spreadsheet.
    ix. The instructor facilitates class discussion of the observed changes in the population haplotype.

c. *M. tuberculosis* epidemic:
    i. The students are instructed that an *M. tuberculosis* epidemic has occurred, and none of them are vaccinated, nor do they have any treatments available. The peptide antigens derived from *M. tuberculosis* is the **purple 6-pointed star**.

d. Students work through questions 23-25 on the MHC Activity Handout, ending with predicting whether they will survive the epidemic.
    i. Only individuals who survived the smallpox epidemic and the Ebola epidemic will participate. Those who did not survive will observe and help their group members.
    ii. Each group's reporter fills in Table 4 in the Group Haplotype Sheet, recording the number of surviving group members, and tallying the number of surviving group members with each MHC molecule in their haplotype.
    iii. Reporters use index cards to report the total number of surviving group members to the class.
    iv. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "*M. tuberculosis*" in the Survivorship tab and projects the graph created by the spreadsheet.
    v. Reporters use index cards to report haplotypes of survivors to the class:
        1. Instructor calls out each MHC molecule (for example, "Red Circle"), and the reporter raises the index card that indicates the number of surviving individuals in their group with that MHC molecule.
    vi. The instructor records these numbers in the MHC Haplotypes Activity Spreadsheet in the column labeled "*M. tuberculosis*" in the Population Haplotypes tab and projects the graph created by the spreadsheet.
    vii. The instructor facilitates class discussion of the observed changes in the population haplotype. Final discussion points should focus on:
        1. How the haplotype of the population impacted the ability of the population to survive each epidemic. What would have happened if no one in the population had a multi-colored triangle MHC? What would have happened if only one or two people had a multi-colored triangle MHC?
            a. If only a few individuals survived the first epidemic, how does that impact the likelihood that MHCs able to interact with the antigens presented during the next epidemic are present within the surviving population?
        2. How the individual haplotypes were impacted by the epidemics. Did an individual's haplotype ever change?
        3. How the population haplotype was impacted by the epidemics. Did the population haplotype change? Which MHCs persisted or became more abundant within the population? Which MHCs did not persist?
        4. Depending on the size of the class, the instructor may wish to ask the students to compare the dynamics of individual groups to the larger, class-wide population.