INTRODUCTION

The interactions of immune cells during lymphocyte activation is beautifully orchestrated, but learning how the “alphabet soup” of cell receptors and cells interact with each other can be daunting. Active learning and kinesthetic strategies that support traditional lectures can make topics easier to conceptualize. Such physical activities have been used throughout science education, yielding improvements of 20% to 50% based on pre/post assessment analysis (1–6), and benefits extend to both the student actors and the audience (1). They have been used to successfully teach quorum sensing (7), membrane transport (2), the spread of sexually transmitted infections (STIs) (3), and other biological concepts (4, 5), including the immune system (1, 8). The 25-minute activity described here focuses on the specific function and interactions of various immune cell receptors leading to lymphocyte activation, building on a previously published role play activity looking broadly at lymphocyte activation (8). It also demonstrates how linked recognition occurs with complex antigens. The study took place at a primarily undergraduate institution with classes of 10 to 64 students, and most participants were from a second-year nursing student cohort. The primary learning outcome is that students are able to map activation of the humoral immune response.

PROCEDURE

Setting the stage

Prior to the activity, students learned about B-cell activation and T-helpers through traditional lecture methods. To begin the activity, enlist eight volunteer actors and provide them with the name tags of immune system components (instructions for name tags and gloves can be found in the supplemental materials). Throughout the activity, nonactor students provide instructions for actors and answer questions. One by one, gloves/receptors are introduced and the class identifies which actors/cells should have each glove, e.g., gloves representing major histocompatibility complex class II (MHC-II) will be given to antigen-presenting cells and B cells. [Note: While B cells do have C3b receptors, the instructor should explain they are not as important as the B-cell receptors (BCR) in activation, and students’ hands are needed for BCR and MHC-II.] The student representing complement is given a pink marker, which will deposit C3b as marks on the antigen. Once all gloves are distributed, students identify where each actor/cell should wait for new antigenic material (stage right is the peripheral tissue and stage left is a lymph node).

Inflammation

Introduce the first antigen (all red) to the peripheral tissue. The complement student should “deposit C3b” by marking the antigen with their complement marker. The neutrophil and macrophage students bind the opsonized antigen by grabbing the marked part with their C3b receptor glove. The phagocytes rip the antigen paper down the middle, with the neutrophil putting the parts in their pocket or bare hand and the macrophage holding the parts on their MHC-II glove. The neutrophil does not show antigen on MHC-II and soon becomes irrelevant.

Lymphocyte activation

The neutrophil, the macrophage, and the instructor (carrying additional copies of the antigen) move to the lymph node on stage left, representing the movement of white blood cells and antigen after inflammation. The class is asked which cells can interact with the antigen. B-cell students with the red BCR bind, digest/rip, and present the antigen with their MHC-II hand. Then the macrophage attempts to interact with each T-helper, the MHC-II is grabbed by the CD4 of each T-helper, and the colored T-cell receptor (TCR) checks for a match of the epitope color (Fig. 1). When
a TCR color matches the presented peptide, that T-helper is activated, symbolized by flipping the name tag to “activated” status. Then, the activated T-helper moves to interact with B cells. Only the red B cell is showing an antigen, so it interacts with the red T-helper just as the macrophage and T-helper previously interacted. Upon recognition, the red B cell is activated and the class confirms it produces antibodies with a red paratope, the same color as the BCR glove fingertips.

Repeat and increase antigen complexity

Next, introduce the all-green antigen, paralleling the process of the red antigen. For the combination green-and-red antigen (third round), both green and red B cells are involved, and the green or red T-helpers may activate both of these B cells. However, students must recognize that the antibodies produced will be the color of each B cell’s paratope. The all-blue antigen is sugar only and will not be shown off on MHC-II, resulting in no memory cell production. The final antigen is blue and red (sugar and peptide representing an encapsulated bacterium or conjugate vaccine) and elicits a strong response by two B cells.

Recap and Review

As the activity progresses and students master the flow and concepts, they assume more ownership in guiding the scenarios. Periodically and at the completion of the activity, students are asked to confirm, “Which cells interacted?”, “How did each cell interact?,” and “What was the result of the interaction?” When students are intensely animated about the acting, these questions are necessary to bring the class back to the biology rather than the role play itself. Suggestions for modifications can be found in the supplemental materials.

RESULTS

Pre-survey, post-lecture, and post-intervention data demonstrate the effectiveness of this activity. Over an 18-question survey, average scores increased from a baseline of 5.4 (31%) to 7.2 (40%) after the lecture to 11.4 (62%) after the role playing activity (distribution is shown in Fig. 2). The highest gains related to the interaction between CD4 and MHC-II receptors, order of cell activation, and location of cell activation. Based on individual response patterns, we suspect outliers on the post-intervention survey represent a few students who made random selections, since the survey scores had no correlation to actual course points. Despite outliers, the average scores increased by 1.7 (SD = 2.4) after lecture and an additional 4.2 (SD = 3.2) points after the intervention (t-test, p < 0.05).

Students perceived the activity as worthwhile (86%) and enjoyable (85%). Additionally, the activity provided longer-lasting learning. A unit exam, given 2 weeks after the lymphocyte activation sessions, has included a question about linked recognition of conjugate vaccine antigens for the past 3 years. Analysis of this question showed students in the intervention cohort (n = 78) scored an average of 17% higher than those who were not in the cohort (n = 223) (t-test, p < 0.05).

Student improvement was consistent with previous role playing studies (1–6). Additionally, based on conversations with students and in-depth analysis of survey questions, it became evident that confusion about basic vocabulary (e.g., epitope vs. paratope) was the root of incorrect survey answers in many cases—students were able to properly describe the relevant processes when using their own terminology. This served as a reminder of the importance of clarifying technical terms and foundational material.

SUPPLEMENTAL MATERIAL

Appendix 1: Instructions and template for making props
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