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**ABSTRACT:** Jerome Bruner proposed the Spiral Curriculum as a method for creating deep understanding of scientific concepts. Bruner writes that five year olds intuitively create grammatically correct sentences and are therefore prepared to understand sentence structure more deeply when it is formally introduced in school. Immune Attack is a three-dimensional video game that provides a place to gain an intuitive understanding of cellular biology and molecular science. Proteins, molecules and cells behave in Immune Attack as they do in nature. Objects in the game, such as white blood cells, are drawn to look like the schematics that scientists use in their own models. Game actions, such as the capture of white blood cells by proteins on blood vessel walls, mimic actions that occur in nature, and are described using vocabulary similar to that of scientific literature. Our Scientific Advisory Group of 20 active scientists reviews our game outline and contributes to the faithful and exciting presentation of molecular science. We have successfully developed a method of communication, a guided wiki-like document, that allows these scientists to contribute meaningful information in a time efficient manner. We collaborate directly with teachers to conduct controlled evaluations, using the Medical Mysteries Series (MedMyst, which covers non-molecular aspects of infectious disease) as a negative control. We tested students' knowledge, comprehension of game dynamics and confidence with the material ( $n = 180$  Immune Attack,  $n = 142$  MedMyst). We found highly significant gains in confidence with molecular science related materials and significant gains in knowledge of the cell biology and molecular science presented, in the groups that played Immune Attack as compared to the control game. We are building on the results of these studies to create an evaluation tool for the Fall of 2009. Additionally, we have used Immune Attack to inspire high school computer programming classes to create their own new video games based on Immune Attack. Immune Attack provides an intuitive introduction to molecular and cellular biology for 7th grade students, thus significantly lengthening the "Spiral Curriculum."

### Immune Attack present the cellular and molecular world in an accurate and engaging video game.



**Figure 1.** This is a view of how Micro and Nano scale objects and action will be presented in Immune Attack 2.0. The player is manipulating the Nanobot on the surface of the vein endothelial cell, while the change in behavior of cells can be observed in the Microbot's camera.

#### Introduction

Molecular science is not introduced to American students until advanced high school classes or college. This means that most of the general public do not understand the molecular aspect of environmental or health issues. For example, the debate about flu vaccination policy cannot be informed by a straightforward explanation of the genes that H and N stand for. If the average person understood the central dogma we would at least be debating the flu vaccination based on facts and not trying to come up with metaphors that leave everyone annoyed and possibly suspicious at the vagary of the whole debate. How to teach intuitively? As Jerome Bruner points out, make it a game. Players can learn the rules of a game and apply them to new scenarios without being aware of or even being able to comprehend the implications or the formal science learning behind the game. As Mihaly Csikszentmihalyi has pointed out, people stay in task and enjoy what appears to be hard work requiring intense attention when they are in a state of "Flow." Flow is the state of being challenged but still close to our level of competence. As Bowman points out that video game, such as Pacman and Donkey Kong are so popular because they meet the requirements for Flow. Finally, Kurt Squire has demonstrated that video games like Civilization can take advantage of the state of Flow to teach and to inspire interest in history. Additionally, James Paul Gee has pointed out that games can teach players how to think like an expert, which would be the end goal for a Cell Biology game, but we must first introduce the molecular and cellular world before we can train students to design experiments in it.

Making a video game to introduce cells and proteins and the entire molecular world requires us to first make a list of the concepts we wish to teach, take advantage of modern game engines and graphics to create an accurate Micro world and an accurate Nano world, recruit many scientists in fields such as immunology, chemical engineering, cell biology, organic chemistry, etc. in order for the game to be "peer reviewed," and then finally to design an evaluation method that allows us to determine whether the core concepts are learned by players.

Preliminary data presented here demonstrate that our goals can likely be met. Immune Attack successfully integrate accurate object presentation with engaging game play. Scientists in many fields have volunteered their time and expertise not only to reviewing the game, but to making the game play more intricate. And finally, preliminary studies demonstrate that learning occurs and that players gain confidence with cellular and molecular diagrams, which may extend beyond the topics directly portrayed in Immune Attack.

# Immune Attack: A Video Game in the Molecular World

Melanie A. Stegman and Michelle L. Fox

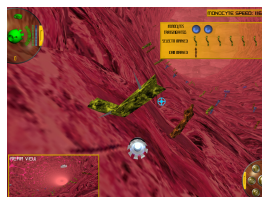
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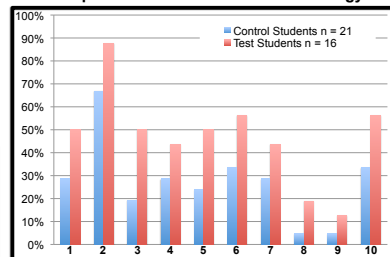
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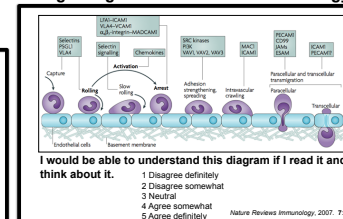
### Immune Attack teaches students core concepts of Cellular and Molecular Biology.



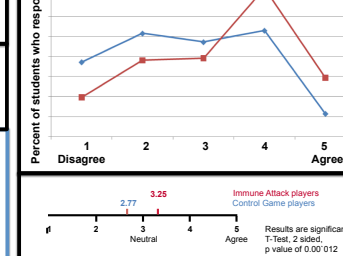
**Figure 2.** Some results of our current evaluation. Each class is randomly divided into two groups. One group plays Immune Attack for two 40-minute sessions, separated by 1 week, while the control group plays an unrelated computer game. 1 or 2 days after the second session, all students take an online survey. The questions are designed to determine whether players comprehend the core concepts, see below.

1. What does the word "macrophage" mean? (Vocabulary)  
Big eater. Big cell.  
Big antibody. Big killer.
2. The walls of veins are made of what? (Concepts 1 and 6)  
Muscle. Fibers.  
Collagen. Cells.
3. What is the first line of defenses the body employs against potential pathogens? (Concepts 1 and 4)  
Antibodies. White Blood Cells.  
Cells. Cough.
4. How do cells of the immune system get to the site of an infection? (Concepts 2 and 3)  
They exit the blood vessel through spaces in the vessel wall.  
They diffuse to the site of the invading bacteria.  
They accumulate due to swelling at the site of infection.  
They travel from lymph nodes to the infected tissue.
5. Which cells are the first to respond to a bacterial infection? (Concepts 2 and 3)  
Red Blood Cells. Monocytes.  
T-Cells. Infected Cells.
6. How do Macrophages summon other cells to help fight an infection? (Concepts 2 and 3)  
They divide into specialized cells that recruit other cells.  
They convey a message through red blood cells.  
They send a special chemical signal to the lymph nodes.  
They send a special chemical signal that other cells follow.
7. What changes happen to the cells of the vein when there is an infection nearby? (Concepts 2 and 3)  
The cells start making...  
... a protein that sticks to white blood cells.  
... a chemical signal that attracts white blood cells.  
... new antibodies.  
... a chemical signal that attracts red blood cells.
8. What is the name of the protein that will make a slowed Monocyte come to a stop? (Concepts 2 and 3)  
Peptin. ICAM.  
Pseudomonas. Selectin.
9. When a white blood cell exits the blood stream what is the process called? (Concepts 2 and 3)  
Transmigration. Transvessel movement.  
Transportation. Transference.

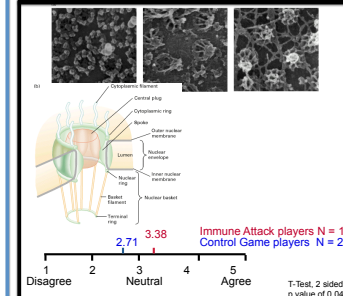
### Immune Attack increases students' confidence regarding cellular and molecular biology.



**Figure 3.** To determine whether Immune Attack provides intuitive learning, we designed a test for feelings rather than actual knowledge. The TOP figure demonstrates an increase in confidence due to playing Immune Attack. This figure, despite its complexity, contains many IA related aspects. The BOTTOM figure is preliminary data that indicates that the confidence gain may not be limited to topics in the game, but may also be transferred to any three dimensional depiction of molecular structures. We will follow up on these results.



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#### Conclusions

A video game can teach basic facts and vocabulary about Cellular and Molecular Biology.

A video game may be used to create an understanding of the Core Concepts of Cell biology.

A video game about this complex topic can make students more confident in their ability to understand the topic.

#### Future Goals

1. To build more levels of Immune Attack that more explicitly require the player to understand and employ the core concepts of Cellular and Molecular science.
2. To demonstrate that Immune Attack provides a deep understanding of cellular biology and molecular biology. We will continue to develop our evaluation, focusing on whether Immune Attack conveys a deeper understanding of the core concepts. **We are recruiting 7th - 12th grade teachers now.** We plan a large scale evaluation in 2013-2014 and 2014 and 2015.
3. To create an online database that mirrors the in-game "Mission Intelligence Database" that will serve as an place where students and scientists submit "datacards" on the topics of molecular chemistry, cellular biology, chemical engineering, etc. This database will be part of IA2.0... coming in 2010.

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