Immunology Stories: How Storytelling Can Help Us to Make Sense of Complex Topics

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Abstract
The immune response is a wonderfully complex aspect of our physiology that can sometimes confound students and instructors alike. How do we wade through the layers of detail to help our students develop an understanding of immunology? In this article, I will share some of the stories about immunology research that helped me strengthen my own understanding and improve my approach to helping students learn and understand this topic. In addition, we will explore some of the research on the power of storytelling, and how learning through stories might be a defining characteristic of what it means to be human. https://doi.org/10.21692/haps.2020.105

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Introduction
I have been trying to understand the immune response for a long time. Like many Anatomy and Physiology instructors, I did not have an immunology background beyond what was covered in my undergraduate physiology courses. When the time came for me to teach students about the immune system, I relied heavily on the information presented in our textbooks. I was able to present students with the key pieces of information and help them to remember a few facts, and the students did well on their exams. However, I felt that perhaps I was missing the point; perhaps I was not helping them truly understand the immune system. Maybe this was because I did not actually understand it very well myself.

One summer, I had the opportunity to take the American Association of Immunologists (AAI) Introductory Course in Immunology. After six intensive days full of lectures on the immune system, I had learned many new facts and gotten a sense of what the "hot" areas of immunology research were at that time. It was 2016 and the majority of participants were researching cancer immunotherapy treatments. In some way I felt a lot more competent in my understanding of immunology, but I still felt like I was missing the bigger picture.

Then one day I heard a radio interview with Daniel Davis about his 2018 book *The Beautiful Cure*. It sounded interesting, so I picked up a copy from the public library and started to read. I enjoyed it so much that I soon found myself telling everyone I knew about it, and soon after I read his earlier (2014) book, *The Compatibility Gene*. These two books greatly improved my own understanding of the immune system and helped to transform my approach to teaching these topics as well. What was so special about these two books that they had such an impact on me? It was the stories. Not just stories about how our immune system works, but stories about the researchers that shaped our current understanding of immunology.

My personal journey to develop a better understanding of the immune system was a compelling reminder to me of the power of storytelling. Suddenly I saw examples of storytelling everywhere that I saw authentic learning. In this article, I will share some of what I have learned about learning through stories, some of the fun and fascinating immunology stories from Davis' books, and my current approach to helping students understand the immune response.

Learning through stories
Once I had recognized the link between stories and my own learning, I started to see examples of it all around me. I also did some reading to learn a bit more about the research that has been done on the power of storytelling. In her recent book, *Transcendence: How humans evolved through fire, language, beauty, and time*, Gaia Vince (2020) writes about how it has been a combination of genetic and cultural evolution that has transformed our species. Using language to share information through story, between individuals and between generations, has been essential to our ability to survive times of significant environmental change, including a great ice age 20,000 years ago (Vince 2020).

As described by Vince, "our brains evolved with reflexive use of narrative as a part of our cognition. Stories shaped our minds, our societies, and our interaction with the environment" (Vince 2020, p.82). Not only do we appear to be hard-wired to use stories, we use more regions in our brains to process information told through a story rather than from a list. Language processing areas of the brain (including Broca's area and Wernicke's area) will be active in both cases, but when the information is told through story, other areas of the brain are also involved, including areas of the motor cortex for stories that involve movements, and areas of the sensory cortex for stories that include descriptions of physical sensation (Vince

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2020). All of this brain activity might be why information told through story can be up to 22 times more memorable than the same information given in a list (as summarized in Vince 2020).

Humans have been telling stories for tens of thousands of years, and storytelling continues to be an important way of learning and sharing knowledge among indigenous peoples. Vince (2020) describes the songlines of Aboriginal groups in Australia, oral stories that serve as archives to describe things such as ceremonies, laws, and geographical information. In describing the roles of the songlines, she writes "This explains the prevalence and importance of human stories: they work as collective memory banks, storing detailed cultural information encoded in narrative" (Vince 2020, p.82). Ancient stories can convey facts and information, but they can also help to provide perspective and perhaps shape our thinking. In her book, *Braiding Sweetgrass: Indigenous wisdom, scientific knowledge, and the teachings of plants*, Robin Wall Kimmerer, a botanist and member of the Citizen Potawatomi Nation, writes:
"In the public arena, I've heard the Skywoman story told as a bauble of colorful 'folklore'. But, even when it is misunderstood, there is power in the telling. [Can we] understand the Skywoman story not as an artifact from the past but as instructions for the future? Can a nation of immigrants once again follow her example to become native, to make a home?" (Wall Kimmerer 2013, p.9).

I am sure that I am not alone in telling short, personal stories and anecdotes when I teach. It helps me to feel more engaged with my students, and students often report that they "enjoy" the stories; it helps them to connect to the course material and remember it better. In my experience, it also helps to create a class environment where students feel more comfortable sharing their own stories, so that we all have the opportunity to learn from these new examples and ideas.

Moitra (2014) describes how the use of stories to convey course content in a genetics class helped to increase student engagement, and other studies have shown that when post-secondary students have the opportunity to tell their own stories as part of an assignment or project, they feel more engaged in their studies and their college experience overall (Everett 2017). While there is a considerable amount of research about the effectiveness of storytelling in the education of younger children (see Engel et al. 2018 for example of storytelling in children's science learning), storytelling has also been shown to be effective in higher education (Abrahamson 1998; Rossiter 2002). Aside from conveying information, research has shown that when teachers share personal stories, their students find them more approachable and authentic (Johnson and LaBelle 2017), and scientists can increase comprehension and engagement in their "nonexpert audiences" by using narrative and storytelling (Dahlstrom 2014; Saffran et al. 2020). It is no wonder, then, that as a "nonexpert" in the field of immunology I would find myself engaged in the stories of immunology discovery.

Some immunology stories

Daniel Davis' two books, *The Compatibility Gene* (2014) and *The Beautiful Cure* (2018), contain many engaging stories. Some of the stories describe how landmark discoveries in immunology were made, sometimes in dramatic "ah ha" moments, but more often through slow, steady progress and collaboration between creative individuals.

One discovery story that had an impact on me was about the work of Charles Janeway. When teaching students about the scientific method, we tend to teach them that you start with an observation which leads to the formation of a hypothesis, and then you design experiments to test that hypothesis. However, in Janeway's case, his observations on the role of adjuvants in vaccines led him to predict that there was (at that time, in 1989) something "missing" from our understanding of the immune response (Davis 2018). He hypothesized that there must be some sort of "pattern recognition" that enabled our body to determine when non-self-molecules were a sign that potentially dangerous pathogens were present, and to then stimulate our adaptive immunity. There was no way to test his hypothesis at the time. "Quite simply, at the time, nobody could say if Janeway's ideas were revolutionary or fanciful bunkum" (Davis 2018, p.19). It would take nearly another decade for researchers to develop experiments that could prove Janeway's hypothesis and increase our understanding of the role of innate immunity (Davis 2018). This later work was not without controversy, involving the collaborative efforts of many individuals, only a small subset of whom were awarded the Nobel Prize for this work on innate immunity (Davis 2018).

Other stories were memorable simply because they made me shout out, "that's so cool!" and then proceed to share that story with anyone who was willing to listen. One such story was about fever in cold-blooded animals. Even though cold-blooded animals cannot change their body temperature by altering their metabolic activity (like warm-blooded animals can), they can change their body temperature by changing behavior and seeking out a warmer environment. They increase their heat-seeking behaviors during an infection. Even more amazing is the fact that medicines that reduce fever in warm-blooded animals reduce the heat-seeking behaviors of cold-blooded animals (Davis 2018; Evans et al. 2015). "This means that at least some of the chemical and biological processes causing a reptile or fish to seek a warmer habitat during an infection are similar to those within us during a fever" (Davis 2018, p.112).

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Most of the stories in *The Compatibility Gene* (Davis 2014) describe the discoveries and functions of our MHC (major histocompatibility complex) genes. Collectively, the stories in this book helped me to gain a greater understanding of how MHC genes (and MHC proteins) work, and how their variation contributes to differences in susceptibility to different diseases and infections. One well-documented example describes the connection between one MHC gene variant (HLA-B*27), susceptibility to the autoimmune disease ankylosing spondylitis, and protection against AIDS. People who have inherited HLA-B*27 are more likely to develop ankylosing spondylitis than people with other forms of HLA-B, but are they are also more likely to be HIV Controllers, individuals who do not progress to AIDS after HIV infection.

The research on ankylosing spondylitis was performed many years ago (see Brewerton et al 1973, for example), and the research on HIV followed many years later (The International HIV Controllers Study 2010), but the two were woven into one cohesive narrative that helped to explain the connections between the two, and the overall significance of variation in our HLA genes. As Davis (2014) explains, the different forms of HLA genes result in slightly different-shaped proteins in the region of the HLA (MHC) class I protein that presents antigen. Differing antigen presentation between individuals can make one individual have a strong immune response to a certain antigen compared to a different individual; differences that could lead to inflammatory disorders or affect susceptibility to infection (Davis 2014).

While most of the discussion of HLA-B*27 is found in one chapter of the book (Chapter 5: Differences between us that matter), Davis returns to this in the book's epilogue, with a story about how he and his wife had a genetic test done to determine their own HLA genes. With much humor related to other aspects of these results (including some friendly competition about whether their results were "common" or "rare"), he also describes their reaction when it was revealed that his wife has the HLA-B*27 gene (Davis 2014). Does it mean that she is likely to develop ankylosing spondylitis? No. However, will they consider this possibility if she were to start developing back pain, in the hopes that they could begin appropriate treatment early? Yes.

Through these stories, and the others in these two books, I was able to see immunology in a new way, and the big themes became more apparent. As Davis writes in *The Beautiful Cure*: "Textbooks about the immune system tend to discuss the role of each molecule or cell in turn, but that's like explaining a bicycle by describing what a wheel is, and then what a handlebar is, and then what a brake is. None of these single elements are properly understood without the others; their meaning lies in the relationships between them." (Davis 2018, p.5)

By reading these immunology stories, I gained a deeper appreciation and understanding of both the marvelous details and the overarching themes of our immune response.

My approach to teaching immunology now

"Someday we may find a grand unified theory of the immune system, a few principles that capture precisely how it all works, or one diagram that fits on a T-shirt. But that dream may never work out. And it might even be the wrong thing to aim for." (Davis 2014, p.196)

In all of my earlier endeavors to understand the immune system, I had been aiming to learn enough to be able to create one, magical summary of the whole immune response that I could then share with my students. Eventually, I realized that this was not really possible, and that it would probably not be very helpful either! I did make a variety of summary drawings, flowcharts, and other diagrams to help put things together for myself, but just giving one of these summaries to students deprives them the opportunity to put it together and figure it out for themselves.

Of course, the problem is that they do not have nearly enough time as a student in a typical Anatomy and Physiology course to study the details, discover the big themes, and then put it all together for themselves. That process would probably take months. In the end I decided on a compromise: guide them through a visual summary of the immune response to bacterial infection, share some of the stories I have heard and read to help provide some context and generate additional interest in the topic, describe a reasonable amount of detail (cell types, receptors, etc.), and introduce them to some of the big themes.

There are four big themes that I use as anchors for the information I share with students in class, as well as for my own ongoing learning about the immune system.

<u>Innate vs. adaptive immunity</u>. There can be a tendency among students and instructors to overlook the importance of our innate defenses and focus instead on the details of our adaptive defenses. However, it is worth remembering that our innate defenses essentially keep us alive long enough for our adaptive defenses to be activated. I also try to remind students that it is not a matter of "either/or" but "both/and". Innate and adaptive defenses work together in many aspects of our immune response.

<u>Cell-mediated vs. antibody-mediated immunity</u>. This theme is often emphasized in first-year Anatomy and Physiology textbooks as well. This can be a helpful way of categorizing and thinking about adaptive immunity and the different cell types that are involved, but as with the innate vs. adaptive dichotomy described above, it is helpful to remember that there are some overlapping elements here as well.

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Systemic vs. mucosal immunity. I do not spend much time in the first-year Anatomy and Physiology classes I teach discussing systemic vs. mucosal immunity, but it is something that has interested me since I took the AAI Introductory Course in Immunology. The majority of research into the immune response has focused on the body's response to antigen exposure through the skin (systemic immunity). But the majority of infections that the body must fight involve antigen exposure through one of our mucous membranes (Parham 2015). And while there are many similarities between systemic and mucosal immunity, there are many important differences too. I think it is worth highlighting this fact while teaching immunology as part of an Anatomy and Physiology class, even if we do not study many details of mucosal immunity, because it could at least prime the students to know that what happens at the mucosae will not be exactly the same as what happens at the skin. It can also help to set the stage for topics that may be covered in pathophysiology courses, which many Anatomy and Physiology students will eventually take as they continue in their program of study.

The balance between illness, immunity, and autoimmunity. For me, this really is the big picture idea that we should keep in mind while studying the immune response. Our ability to fight infection, prevent cancer, and yet avoid excessive inflammation and destruction of "self" cells is at the heart all aspects of health and disease.
With any luck, my students will remember these "big ideas" in immunology, even if they forget some of the finer details.

Has my personal journey to learn about immunology helped me to develop a better understanding of the immune response? Yes, but with one significant caveat: I am not an expert. But I am OK with that. I will continue to read about immunology, broaden my knowledge and deepen my understanding. I will continue to revise how I approach these topics in the Anatomy and Physiology courses that I teach. And I will keep telling these stories.

About the Author

Jennifer Giuliani, MSc, is an Instructor in the Biology Department at Camosun College. She primarily teaches courses in Human Anatomy and Physiology, including Human Anatomy, Human Physiology, and Anatomy/Physiology for Nursing.

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