COFFEE BREAK WITH A SCIENTIST

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What is the focus of your current research?

My laboratory studies how outer membrane and secreted proteins from the Gram-negative bacterium *Fusobacterium nucleatum* contribute to multiple human infections (i.e. mouth, brain, liver) through the induction of inflammation, and, ultimately, how this contributes to the onset and progression of colorectal cancer. *F. nucleatum* is highly overrepresented within the cancerous tissue of a significant percentage of patients with colorectal cancer, and transferring isolated bacterium from human tumors to a mouse model of cancer leads to both the acceleration of tumor formation and an overall increase in tumor number. Despite a connection between this bacterium and cancer, there is currently a lack of understanding as to which proteins and genes from the bacterium or the human host contribute to disease. This bacterium is unique in that it lacks several protein secretion systems that are commonly used by pathogenic bacteria to induce infection and disease. Despite this lack of previously characterized virulence genes, strains of F. nucleatum are able to invade epithelial and endothelial cells, and these invasive bacteria are more frequently isolated from patients with Inflammatory Bowel Disease (IBD) and colorectal cancer. To determine how this bacterium enters cells and if it is important for colorectal cancer modulation, we are characterizing how a group of large outer membrane proteins and secreted toxins known as autotransporters contribute to cellular binding, invasion, pro-inflammatory signaling, and the onset and progression of cancer. These studies will contribute to our understanding of how bacteria with the human microbiome are contributing to intestinal disorders including cancer.

A major focus of our research is to create gene deletions of the autotransporter family in *F. nucleatum*, followed by infection of human cells and mice to determine if specific outer membrane and secreted proteins are necessary for colonization, inflammation, and disease. As genetic manipulation of the *F. nucleatum* chromosome has been a severe bottleneck in the analysis of this bacterium, we are developing bacterial genetic tools with the goal of being able to delete multiple genes in the same bacterial strain. After we have identified autotransporter proteins that are critical for infection, we will use a combination of biochemical techniques to determine the structure and function of each gene with the goal of determining if these proteins can be targeted with inhibitors or even targets for vaccine development. Since very little is known about this protein family in *F. nucleatum*, we are constantly surprised and intrigued by our results. This has made for very exciting discoveries that we are anxious to further develop and present to the scientific community to enable additional researchers and collaborators in the fight against bacterially induced cancer.

How did you become interested in your line of research?

My doctoral research focused on how the human innate immune system uses proteins circulating in the blood as a front-line defense against bacterial infections. I was fascinated by how our bodies are able to fight off invading pathogens, but even more intrigued as to how only a few select bacteria are able to evade this onslaught to infect and survive within the human body. To study the latter, I was awarded a postdoctoral fellowship to dissect how protein localization within the Gram-negative bacterium *Shigella flexneri* is essential for infecting and invading epithelial cells within the colon, which leads to severe dysentery. I then accepted a second postdoctoral position because I wanted to expand my training and knowledge of cancer by using structural biology to study a group of enzymes that are upregulated in inflammatory diseases including breast cancer and rheumatoid arthritis. Through this work, I gained an understanding of how epigenetic changes in chromatin structure induce inflammation and modulate cell signaling pathways during disease, which is an important part of our current studies. After working in all of these diverse areas, I knew that I wanted to shape my laboratory by combining my love for immunology, microbiology, and cancer. Serendipitously, as I was forming my ideas for this, two major studies were published in parallel that showed that the Gram-negative bacterium *Fusobacterium nucleatum* was far more frequently found within colorectal cancer tumors when compared to healthy controls. After analyzing the interesting genome and protein repertoire of this bacterium, I knew that we could carve out a niche by using bioinformatics, molecular biology, and biochemical studies to discover proteins that allow colonization of the host and subsequent tumor formation.

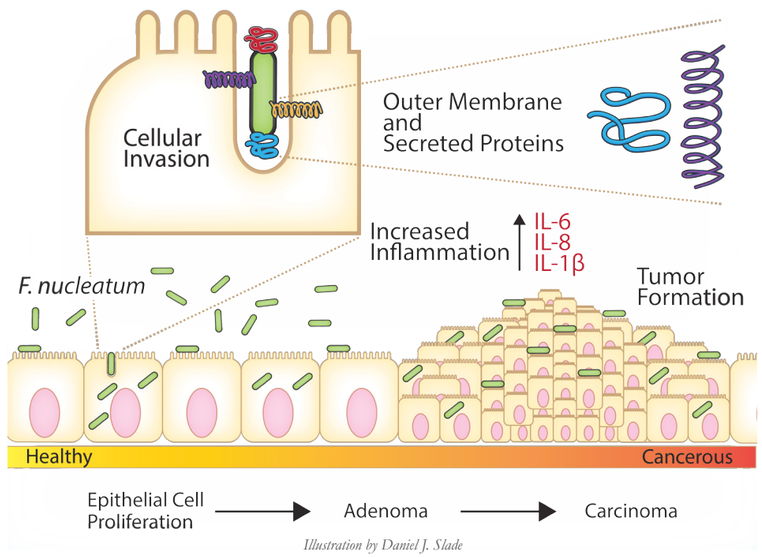

Illustration by Daniel J. Slade

How would you describe the dynamics and work environment of your laboratory?

I describe the laboratory as 'ordered chaos,' as we like to move at a fast pace because we are truly interested in finding the answers to our questions that could lead to a better understanding of bacteria in inflammation and cancer. At the moment, my team consists of one Research Scientist, two graduate students, and two undergraduate students. I am very proud to have recently trained two outstanding high school students from Virginia who are moving on to pursue degrees in the life sciences at prestigious universities. I like to think that I run my lab like Google, where scientists are encouraged to be creative and can pursue projects they are truly passionate about. While I can't provide them with unlimited free food like Google, I do provide coffee, wireless speakers in the lab, a Frisbee to throw when we get exciting results, and group meetings and outings at a local watering hole! I have learned that when people are excited about their work, they are more likely to push projects to achieve outstanding results. My team is fantastic, and I always make sure to let them know they are doing amazing work that has the potential to increase human quality of life.

Why did you choose to continue your career at Virginia Tech?

Virginia Tech fits my needs and wants perfectly as a scientist because this university excels in many areas, especially in the life sciences, bioinformatics, and engineering. Because of this, I have been able to expand the tools and techniques our lab uses to study bacterial infections by fostering interactions and collaborations with vibrant researchers at the university. After working at several universities and institutes, I am always impressed by the quality of work being performed by Virginia Tech scientists. There is a contagious energy that encompasses the campus, and new leadership and initiatives make this an exciting university to be a part of both now and in the future. When you combine the outstanding scientific vision at Virginia Tech with all that the Blacksburg community has to offer, there was no better choice for my family and me.

Which aspect of your research are you most excited about right now?

I feel that we are pushing boundaries for how to study difficult bacterial membrane proteins and how secretion systems are driving host-pathogen interactions. We are beginning to lean heavily on bioinformatics and cell biology to answer our questions, which will allow us to dissect the mechanisms of how bacteria contribute to diseases such as cancer. I am constantly pushing myself and my students to learn new techniques, with the goal of never having to limit the scientific questions that we ask to the skills that we currently have. It is exciting to give my students and scientists the freedom and encouragement to learn new techniques to facilitate their growth. We are also forming collaborations outside of our field, to study these bacteria using biomedical engineering and animal models. Virginia Tech is a great place to achieve this because the world-class science being performed here means that achieving scientific goals is only a phone call away to an experienced and outstanding colleague.

Hometown:

Bellingham, MA

Educational Background:

B.S. in Chemistry at Wofford College
Ph.D. in Biochemistry at the University of South Carolina
Postdoctoral Fellow in Microbiology at Harvard Medical School and Massachusetts General Hospital
Postdoctoral Associate in Chemistry at The Scripps Research Institute

Hobbies:

Drawing in either pencil or black pen, brewing beer, and hiking with my wife and daughters.

Favorite things to do around Blacksburg:

Lab group meetings outdoors at The Cellar, attending Hokie baseball games, and biking to work through the beautiful countryside.

A favorite book or two:

The Dragons of Eden: Speculations on the Evolution of Human Intelligence by Carl Sagan.

Oh the Places You'll Go! by Dr Seuss

A favorite quote:

"Science is not only a disciple of reason, but, also, one of romance and passion."
– *Stephen Hawking*

Favorite type of music or artist:

I have a pretty substantial vinyl record collection, and I am enamored with the grace of Ella Fitzgerald, the raw energy of Louis Armstrong, the storytelling of Frank Sinatra, and the soul of Sam Cooke.