Making the microbiome personal

Ami Bhatt is a physician-scientist and assistant professor of medicine and genetics at Stanford University. Her research deploys next-generation sequencing to explore host–microbiome interactions, including those in cancer.

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Around the time I was 10 years old, my parents put me in charge of caring for my little brother, three years my junior, for the first time while they went out for 30 minutes to take care of an errand. The moment we heard the garage door close, we parked ourselves in front of our television in a beautiful wood cabinet. Flipping through the channels, I happened upon an educational science program that was showing cartoons of squirming circles, rods and spiral-shaped organisms wiggling across every imaginable household surface. Bacteria, we learned, were all over — on sofas and carpets, and even all over us!

Fast-forward almost ten years later when, at the age of 20, I started the MD–PhD program at the University of California, San Francisco Medical School. I knew I liked organic chemistry and biochemistry in the classroom — but I had yet to find a scientific passion that sparked my sense of wonderment. Hoping for inspiration, I spent countless hours in the basement floor of an academic library. With the money I had loaded onto my plastic copy-machine card, I would carefully Xerox journal articles of interest to me. I'd take my pile of papers, still warm from the photocopier, to a nearby coffee shop.

I remember the deep amazement I felt while reading the paper that 'changed my life'. The premise of the manuscript was simple. I had been told that Epstein–Barr Virus (EBV) could cause nasopharyngeal cancer (NPC), among a list of other cancers; the manuscript I read showed that NPC was far more common in East Asia, but that the reason for this difference in epidemiology was unknown. The puzzle gripped me. How could it be possible that EBV, which I knew to be highly prevalent across the globe, predominantly results in NPC mostly in East Asia? Were the effects of viruses different in people of different genetic backgrounds? My career-long obsession of trying to understand how microbes, humans and the environment affected one another had begun.

Several years later, when I received my schedule for my internship year in internal medicine at Brigham and Women's Hospital

Credit: Mark Tuschman

on the 'bone marrow transplant' service, I was completely overwhelmed. While I had learned so much in medical school, I had never cared for a patient with a hematologic malignancy, and I had only a glimmer of an understanding of what a bone marrow transplant was.

One patient I encountered was Ms. B, a children's school bus driver with aplastic anemia who had been admitted for a bone marrow transplant. Her procedure had gone well, and her aplastic anemia was 'cured', but she had daily fevers and complained of abdominal and lower back pain. I learned that Ms. B had been driving a bus for decades and that she missed the 'kids' on her route deeply. She did not have children of her own, and her role as a bus driver had connected her to the whole community.

Her blood had been cultured daily, but this had yet to provide any positive results. Day by day, the list of antibiotics and antifungals that we administered to Ms. B grew, but her symptoms still persisted. Eventually, the blood culture grew *Candida* — so her antimicrobials were narrowed to antifungals only — but her fevers persisted. Six weeks later — during which time she had been continuously in the hospital — the cultures reported Gram-variable beading rods. The organism was sent to a special lab in Texas. It turned out to be *Mycobacterium abscessus*, an atypical Mycobacterium that infects immunocompromised individuals. Antibiotics were tailored to her infection, and it was successfully treated. She was discharged shortly thereafter, and I receive yearly updates that she is generally well and is back to her school bus route. But did we really need to culture these organisms in the 'molecular era' that had been heralded in by the advent of genomics?

When the time came for me to begin my postdoctoral training, I knew that if I wanted to leverage the power of genomics to better understand the host–microbe interface, I needed to find a mentor who was willing to jump into the field. I found this in Matthew Meyerson's lab at the Dana-Farber Cancer Institute and Broad Institute. For the first time, I used sequencing-based approaches to discover new bacteria that could be opportunistic pathogens in patients like Ms. B.

I began my independent career at Stanford in 2014, and I'm fortunate to be surrounded by some of the smartest, kindest and most curious physicians and scientists I've ever known. I'm no longer alone in being almost maniacally obsessed with the host–microbe interface and exploring the microbial 'unknowns' that are within, on and around us, especially as they relate to cancer. Although I was initially excited about the microbiome by a television show, I have been taught by the literature, trained by physicians and scientists, and inspired by my patients and students. I'm excited for what lies ahead — and there is one thing of which I am certain: after every answer that we find, I'll have so many more questions. ❐

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