Building a career during a revolution in biology

Margaret McFall-Ngai is the inaugural director of a new division in biosphere sciences at the Carnegie Institution for Science. She has explored the impact of evolving in a microbial world on the biology of animals and plants through a set of adventures that began with a lecture by Carl Woese early in her graduate career.

Margaret McFall-Ngai

I have had the privilege of building a career in the field of biology during one of its revolutionary periods. Two former revolutions set the stage. In the nineteenth century, Charles Darwin introduced the construct of organismal evolution by means of natural selection. Then, in the mid-twentieth century, work by Rosalind Franklin, James Watson and Francis Crick demonstrated that DNA is the genetic blueprint of all life forms. A revolution in the twenty-first century integrated these two major milestones into a single conceptual framework that I believe unified the field of biology. The foundational work of Professors Carl Woese and George Fox at the University of Illinois at Urbana–Champaign in the late twentieth century kick-started this frontier with the application of nucleic-acid sequencing to our analysis of the phylogenetic relationships of all organisms (N. R. Pace et al. *Proc. Natl Acad. Sci. USA* **109**, 1011–1018; 2012). This work would prove crucial in shaping my career.

In 1979, Woese, a microbiologist and biophysicist, came to speak at the University of California Los Angeles (UCLA), where I was beginning my graduate career in the Department of Biology. I intended to study comparative animal physiology, but had no thoughts about a path involving microbiology. At that time, although my home department and the Department of Microbiology occupied the same life sciences building, little or no interaction occurred between these two groups. However, word spread that all academics in these departments should attend Woese's seminar. What he described was a new structure to the relationships among all organisms in the biosphere. Gene sequencing had revealed that all life forms comprise three fundamental divisions — two entirely microbial, and the third principally microbial. This breakthrough brought evolutionary biology into the study of the microbial world, for the first time joining the field of microbiology with macrobiology, in which evolution had long been recognized as the 'glue' that joins the entire subdiscipline. Subsequent

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technological advances over the past 15 years have rendered nucleic-acid sequencing fast and inexpensive, which enabled the field to grow exponentially. Studies of Earth's microbiomes have revealed that the microbial world is responsible for the vast diversity of life, and that the health of the biosphere relies on activities of these unseen forces. At the time, I did not fully realize the impact of Woese's presentation on my career, but this one lecture and my graduate school experience would form the foundation for my view of the field of biology throughout my career — my first turning point.

I credit my openness to new ways of thinking, such as those espoused by Woese, to my educational experiences, beginning with secondary school. I attended an all-girls high school in Hollywood, California, where my classmates spanned from the underprivileged to the super-rich. Enrolled were girls whose parents had been stripped of their livelihoods and sent to Manzanar, the World War II Japanese–American concentration camp in California, to those who were daughters of high society in Los Angeles or of major figures in the movie industry. Wearing uniforms and being provided with an outstanding, unbiased education by a dedicated set of female teachers were the great levellers. Each and every student was completely empowered and encouraged to be all that they could be, to serve in any and all roles. For me personally, I cannot pinpoint one specific teacher who made an impact; rather the actions of this whole faculty, working together to provide the highest quality education, were the inspiring element. Following high school, I enrolled at a Jesuit university for my undergraduate degree. Although I had my first real taste of misogyny there (which I ignored), I am grateful for the requirement to study philosophy, with core courses including ancient philosophy, logic, metaphysics and ethics. This exposure to the humanities provided an appreciation for the evolution and limitations, as well as the positive power and potential danger, of the human thought process. Taken together, these early educational experiences provided me with the two valuable lessons that I would carry with me: (1) women are capable of doing anything; (2) but are not always encouraged to do so.

Reflecting back to my time as a graduate student at UCLA, there were 35 faculty in my department but only one woman, who was not granted tenure. Early on I knew that my path would be challenging. I was determined, however, to continue my dream to be a university professor, and I have aspired to run a research lab that would give wings to all motivated students, regardless of the 'hand of cards' that they were dealt. As the 1980s would have it, the mentors of my graduate career and postdoctoral experiences were all male, but gave me every opportunity to excel. With Professor James Morin, my graduate advisor, the concept was to learn where and how a good research question arises, and how to contribute at the horizons of a field. It was during this time that I also had my first experience with animal–microorganism symbiosis — a topic that would go on to be the focus of my career to date. I studied the impact of microorganisms on the anatomy and physiology of a host animal, and became enamoured by the biochemical mechanisms underlying my observations. As a result, I accepted a postdoctoral position in

biomedicine with Professor Joseph Horwitz at UCLA. Joe — a protein biophysicist and biochemist, and an exceptionally creative and curious individual — greatly expanded my worldview and allowed me to bring to his lab my love of comparative animal biology. Following this experience, I joined the laboratory of Professor George Somero at the University of California San Diego, whose work spans the hierarchy of life. He has pioneered the field focusing on the characterization of the biochemical mechanisms by which animals adapt to their ecological niches, and my experiences in this lab helped bring my varied research experiences into a focused vision for my faculty positions. These mentors and positions provided the roadmap for the development of a multidisciplinary approach to my research programme, one that would focus on exploration of the dynamics between the microbiological and macrobiological worlds.

Fast forward and I now have had tenured faculty positions at three institutions: University of Southern California, University of Hawai'i at Mānoa, and University of Wisconsin–Madison. It was across this time period that I developed the squid–vibrio model of symbiosis with Ned Ruby, my life-long collaborator. Ned, who brings his microbiology expertise, has been an extraordinary partner in all aspects of this journey. It is a true symbiosis — he provides the microbiology know-how and I provide my knowledge of the host animal biology. My current and past graduate students and postdoctoral associates, who have worked with us, have also been key to this journey, and I am forever grateful. Over these years, I have also had the privilege of watching the field of symbiosis and microbiome research blossom. I have countless colleagues to whom I am indebted for including me in the development of this exciting new frontier.

Looking over my career, I recognize that I have had the great fortune of contributing to what has become a forefront of biology, that is, the recognition that the biosphere has evolved as nested ecosystems, with microorganisms as critical elements at each level. This trajectory would only have been possible with the guidance of mentors, the comradery of my collaborators and the perseverance of my trainees, as well as the good luck, of course, of being in the right place at the right time. I now have the honour of beginning the next chapter of my career, as director of a new division of the Carnegie Institution for Science, which is being formed in collaboration with the California Institute of Technology. This Carnegie division will bring together three existing departments, the research of which spans from molecular biology to ecology, promising a unique opportunity to develop the new horizons of a unified biosciences. ❐

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