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Virulence profile

Alejandro Aballay

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Molecular Genetics and Microbiology; Duke University; Durham, NC USA

Tell us about your early days

I grew up and studied all the way to graduate school in Mendoza, Argentina. A beautiful city located at the foot of the Andes mountains, at only a couple of hours away from the Aconcagua mountain, which at almost 23 000 ft., is the highest peak in the American continent.

Argentina has a history of a large, very well educated middle class that has yielded fantastic scientists, including Nobel awardees. On top of that, I came from a family of educators, so since I was a small child, I participated in a number of discussions about science and philosophy.

Did you have a particular career wish as a child?

Since I was a little kid, I was fascinated by nature. I was always intrigued by the formation of the universe and the existence of life. Ever since I was in elementary school, I knew I wanted a profession along the lines of science either in physics, chemistry, or biology.

When did you first get interested in science?

Even before grasping the notion of what science was, I was intrigued by the fundamental questions that drive science.

How did you get interested in science?

My interest in science started early in childhood, but my interest in biology really developed half way through high school. I had a fantastic biology professor who really inspired me by teaching me the beauty and complexity of the biological systems. Until that point, I was more interested in physics and chemistry, but everything changed since those biology classes in high school.

When did you decide to become a scientist?

As my interest in biology developed in high school, I started reading the fourth edition of Biology by Helen Curtis, published in 1983. I still have the book in my library.

This inspiring book not only teaches you the main biological concepts but it also gives you a flavor of the scientific discoveries that lead to the development of those concepts. At that moment, I was totally convinced that I wanted to be a scientist.

Were there any people who influenced your decision?

I'd say Helen Curtis (above).

Tell us about your education and experiences at university

University in Argentina is quite rigid. Right after high school, you need to pick a major and you immediately start taking a preset number of courses that are required to obtain your degree. For the most part, students do not have the option of taking different courses based on their interests. Thus, it was challenging for me to identify a career that would prepare me to enter a PhD program in biology while keeping me excited. After looking at the curriculum of programs in medicine, engineering, chemistry, and biology, I decided that pharmacy and biochemistry represented the best compromise.

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The choice was a right one, because the studies prepared me very well for a PhD in biology, but it was not easy for me to take the corresponding courses. Since I knew I wanted to do science, everything that kept me away from a lab seemed a distraction. On top of that, at that moment there were no opportunities for undergraduate research.

What was your first position after university?

Immediately after graduation, I started my PhD in biology in Mendoza, Argentina, and after that I initiated a postdoc in Boston, USA. I started my postdoc in the laboratory of Fred Ausubel in 1999 and I started my own laboratory soon after that, in 2002. Training in Fred's lab was a fantastic experience. A previous very talented graduate student in his lab, Man-Wah Tan, had just started the field that uses *C. elegans* to study host–pathogen interactions, so there were a number of open questions in the field. In additon, Fred is an outstanding mentor who gives his postdocs a great deal of freedom to pursue their own interests.

When and where did you start your own lab?

I started my lab in the Department of Molecular Genetics and Microbiology at Duke Medical School in 2002.

How many people work in your lab?

There are currently five members in my lab, including postdocs and graduate students.

What is your function in your institution?

I'm an Associate Professor. While my main role is research, I do teach medical students, graduate students, and I serve on different committees.

What areas or topics does your lab currently focus on?

Our laboratory uses genetic and functional genomic methodologies to study the genetic basis of innate immunity. We infect the *Caenorhabditis elegans* model host with different human bacterial and fungal pathogens to understand host-pathogen interactions. We also use mammalian systems to study innate immunity and microbial pathogenesis.

Recent studies from our laboratory highlight the importance of the nervous system in the regulation of innate immune responses. Using a genetic approach we were able to demonstrate that specific neurons can regulate innate immunity. We are studying a number of signaling molecules that can be used by the nervous and immune system to communicate to each other.

What are your main goals for the next five years?

Previous studies from our laboratory have identified at least 7 neurons that may participate in the regulation of immune responses. However, those studies do not provide insights into the effects of pathogen infection on neuron activity or the flow of information required for the control of organismal homeostasis during immune activation. A unique advantage to neural-related studies in *C. elegans* is the unparalleled characterization of its nervous system at the cellular level. The precise and characteristic identity of each of the 302 neurons in the *C. elegans* nervous system, detailed anatomical reconstructions by electron microscopy, and functional data provide a map of the synaptic connectivity for the entire nervous system. My goal for the next five years is to take advantage of these resources to fully dissect the neural-immune pathways involved in the control of immune homeostasis.

Tell us about the most important stages of your professional career

Like in the case of most scientists, graduate school was crucial in my education. It gave me the strong foundation that is needed for a successful postdoc experience. My postdoctoral training was equally important as it allowed me to develop a research program to start my independent career.

Who were your mentors?

My graduate school mentor was the most outstanding scientist in Mendoza, Argentina: Luis S Mayorga. When I started graduate school, I was really interested in studying immunology, but there were no strong immunology labs in Mendoza. Thus, I decided to join a laboratory with a strong research program. At that time, Luis Mayorga had recently returned from a postdoc in the US and was starting an independent research program concerning the study of intracellular trafficking. Luis told me not only what science is really about but also a great deal of cell biology, molecular biology, and biochemistry.

My postdoc mentor was Fred Ausubel. Fred has a unique talent for big picture

Studies in the primitive nematode *Caenorhabditis elegans* demonstrate that ancient components of the innate immune system protect host cells from invading microorganisms. The picture shows a nematode infected with *Salmonella enterica* expressing GFP immersed in an image of an Inca warrior seeking the healing powers of waters in "Puente del Inca" (Bridge of the Inca) to fight pests. Artwork is by Julie Newdoll (http://www.brushwithscience.com).

research that was invaluable for me as I was transitioning to an independent investigator. Fred's record of training a number of prominent investigators who have their own laboratories now speaks for itself. He also has a number of qualities that make him an outstanding scientist and mentor, but I would like to highlight his generosity in terms of allowing postdocs to develop their own research projects to take with them when they leave his lab.

What makes a good mentor?

I believe that a good mentor in science is the one that coaches students and postdocs to be independent thinkers by providing guidance but giving them enough freedom to develop their own ideas.

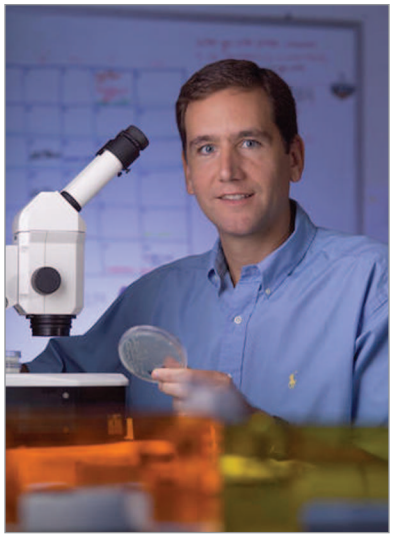
What are your research interests?

I am interested in understanding conserved mechanisms underlying conserved host–pathogen interactions and the mechanisms involved in the cell-autonomous and organismal regulation of innate immunity.

What was your most significant scientific accomplishment?

I believe the discovery that specific neurons are involved in the control of not only microbial killing pathways but also cellular stress pathways to maintain immune homeostasis during response to infections is the main scientific accomplishment of my laboratory.

Overall, during the last decade, my laboratory has performed a number of interesting studies: (1) We developed a *C. elegans* system to study immune pathways conserved in mammals that are specifically targeted by bacterial virulence factors. This work is of particular importance because it was assumed for a long time that the interactions between bacterial virulence factors and immune pathways were relatively specific. Our work with *C. elegans* changed this belief and preceded the work of several other investigators who are now performing similar studies using other model systems. (2) We have provided mechanistic insights into the function and evolution of conserved innate immune pathways. Our findings involving heat shock factor-1 provided a molecular explanation for at least one of the mechanisms by which fever works. (3) We recently developed a creative forward genetic screen to identify negative regulators of innate immunity. We developed a high throughput assay to isolate mutants based on bacterial burden rather than survival. The studies linked the nucleolus, p53, and innate immunity against bacterial infections for the first time, indicating that surveillance mechanisms may oversee core cellular activities to detect pathogens. (4) Recent studies concerning NPR-1 and OCTR-1 provide the first direct evidence indicating that specific neurons control immune responses, paving the way to the use of *C. elegans* to study neural-immune communications.



About Dr Alejandro Aballay. Alejandro Aballay earned his bachelor degree in pharmacy from Juan A. Maza University, in Mendoza, Argentina, in 1994. He finished his MS equivalent studies in 1995 and started exploring the machinery that governs early steps in endocytosis at Nacional de Cuyo University. During this period, he received a World Bank fellowship to complement his studies in endocytosis by working as a summer student for two consecutive years at Washington University, in St. Louis, MO. In 1998, he earned his PhD at Nacional de Cuyo University and moved to St. Louis to continue his studies in endocytosis at Washington University. In 1999, Dr. Aballay moved to Boston to join the Ausubel laboratory at Harvard Medical School, where he developed a novel pathogenesis system utilizing the simple well-studied nematode *Caenorhabditis elegans* and the common human bacterial pathogen Salmonella entericae. He showed that several well-studied *S. enterica* virulence factors required for causing disease in mammalian hosts are also required for *C. elegans* killing, thereby validating the use of *C. elegans* as a host to model Salmonella infection in mammals, including humans. In 2002, Dr Aballay moved to Durham to join the Department of Molecular Genetics and Microbiology at Duke University, where his studies focus on what makes bacteria pathogenic and hosts resistant. His laboratory takes advantage of the compromise between complexity and tractability of the *C. elegans*–*S. enterica* pathogenesis model. *C. elegans* is used as a host to screen thousands of bacterial clones from mutagenized libraries to identify novel *Salmonella* virulence factors and to address how they alter host signaling pathways. Since several components of innate immunity are conserved among different organisms throughout evolution, his group is also exploiting the genetic and genomic resources available for *C. elegans* to study the basis of the immune response. Dr Aballay was a recipient of the 2005 ICAAC Young Investigator Award. He also serves as an editor for the journal *PLoS One* and is a member of the editorial board for *Virulence*.

What were your "highlights" in recent research performed in your field?

Taken together, the studies performed by my laboratory and other laboratories indicate that a fine-tuned control of protein homeostasis and metabolism by the nervous system seems to be important to maintain immune homeostasis at the whole animal level.

What do you think you would do if you were not an MD or a scientist?

I always wanted to be a scientist so I cannot really imagine having another career. I do enjoy practicing sports and I love music even though I am definitely tone deaf. Something along those lines would have been fun.