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INTERVIEW

An interview with Michael Barresi

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Michael Barresi is Professor of Biological Sciences at Smith College, Northampton, MA, USA, where he uses the zebrafish to understand central nervous system development. Michael is also Program Director of the 'Student Scientists' outreach project and has made significant contributions to teaching developmental biology, including being co-author and illustrator of the textbook Developmental Biology, producing developmental documentaries and starting the Online Developmental Teaching Forums. He was awarded the 2021 Viktor Hamburger Outstanding Educator Prize from the Society of Developmental Biology (SDB). We caught up with Michael over Teams to hear more about his career and love of learning.

Let's start at the beginning: when did you first become interested in science?

It stems all the way back to when I was a kid and I'd go out and play with my best friend in the woods. We'd go searching for snakes and lived out there until dinnertime. I developed a deep personal relationship with nature and trying to understand how everything around me came to be. In seventh grade, my biology teacher had a microscope with an old film camera mounted to it. I started taking pictures of different insects and other random small things. My current career very much relies on microscopy, and that early first experience helped me realize there was a much larger and smaller world to behold.

What do you think it was about microscopy that really drew you in?

Like most, I had been immersed in the environment utilizing the only mode of observation I had available, my eyes. Microscopy opened up a whole new world, this other space that I could uniquely explore, which allowed me to actually look harder and deeper upon aspects of life that perhaps no-one else has ever witnessed. That's just plain cool. I also have an eye for detail and an interest in art so this appealed to my inclination to want to represent the microscopic world as accurately as possible. In hindsight, it's similar to how many embryologists used to work a century ago – you look and you draw. You ask what drew me in; well, in one respect, my love of drawing drew me in.

Could you tell me about your undergraduate studies as a Biology major at Merrimack College?

I wanted to go to a place that was going to expose me to a broad range of studies. Merrimack, for me, was a comfortable liberal arts college where I felt nurtured and supported. It provided me with the philosophies that I was interested in and I was able to minor in Studio Art. Although research opportunities at Merrimack were few and far between at the time, I really pushed hard to get those experiences very early in my undergraduate career. My first two summers, I got a position at a nuclear power plant in Niantic, Connecticut, in an environmental lab where we monitored the waterways around the plant. We conducted trawls where we pulled up a diversity of the life and catalogued it. I spent hours on a dissecting microscope sifting through collected plankton, specifically searching for and staging winter flounder larvae – I was doing developmental biology and didn't even know that the field of developmental biology existed. It was awesome! Like a cliché about biologists, when I started out, I wanted to be a marine biologist. I also had grown up being an avid fisherman. I just loved fish – I drew them all the time so this early research experience was really positive.

I took one semester and went to the Sea Education Association in Woods Hole, Massachusetts. I spent 3 months at that campus. I felt like I almost lived in the library at the Marine Biological Laboratory, which was an unforgettable experience: just being there around all those books, just reading about biology. We put together a research project and we went aboard a 134 foot, two-masted schooner and sailed 24/7 around the Caribbean conducting marine biological research. It was actually a lot of work, but I loved it. Although, I vividly recall looking at this huge ocean around me and realizing

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that it was not controlled enough for me – there were too many variables in this research. I wanted to do science where I could ask hypothesis-driven questions and come up with experimental designs that would give me results that I could have confidence in. So I went to the other extreme and applied for opportunities in molecular biology. I took a summer internship at the Dana Farber Cancer Institute in Boston, MA, working with Dr Linda Clayton on negative selection of T-cells in the thymus of mice. I certainly learned a lot and Linda was wonderful to me. When I returned to Merrimack for my senior year, I completed an honors thesis with Dr Josephine Napolitano. We studied a colon cancer cell line, testing whether or not a mitochondrial-targeting drug could enhance the anti-cancer properties of a currently used treatment. Again, a great experience from a different perspective. In the end, I really jumped around to different topics during my undergraduate research career gaining experiences that told me what I essentially didn't want to do.

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You seem to be quite fearless in your approach to just trying new things. Do you encourage people to try things and see what they like?

Your intuition is probably correct. My father was an electrical engineer and my mother started up her own secretarial office business from home, but despite being the youngest of seven siblings and a large extended family, there was not a biologist or other PhD scientist in my background. Regardless of the research experiences I had, coming out of undergrad I really had no idea what the science community was like nor what it really meant to be a scientist. Fearless ignorance was probably one ingredient that fueled my adventurous idealism. To me, it was really more about trying to hone in on what I enjoyed learning the most, which meant having to play around with a lot of different things – finding things that, ultimately, were not it. In all that, I did learn that the idea of studying life was essential for me, and to really get at the big questions of life, you have to go all the way back to when those tissues were first being created and figure out what's happening in those moments. It was that realization that attracted my compass toward doctoral programs in developmental biology.

How did you start your PhD?

My whole life has been about learning. So, naturally, that made me interested in becoming a teacher, but the practical prospect of becoming a teacher would necessitate continued tuition costs for graduate school. I very much liked research too, so I thought I might as well go for a PhD and, during that process, have my tuition covered and even receive a stipend. I figured, if in the end I do go on to become a high school science teacher, then I'll just be one of the more-qualified high school teachers around.

I learned from my experiences with cell culture that studying things in an *in vitro* environment wasn't for me, but the ocean was too big an ecosystem; I wanted something in between. Then, harkening back to embryology and the work I did with the winter flounder larvae, I discovered developmental biology. I'd never taken a class in it during my undergrad career, but I immediately started to look for doctoral programs. I attended Wesleyan University for my PhD, and worked under Dr Stephen Devoto, who was a new professor that brought zebrafish to Wesleyan. Because of my long-term interest in fish and marine biology, it was a perfect fit for me. He studied muscle development, and ironically, this topic was another aspect that I liked from an anatomical standpoint; I did a lot of anatomy drawing in my youth. During my PhD, I studied the role of sonic hedgehog in muscle fiber-type specification and development (Barresi et al., 2000, 2001).

You then went on to do a postdoc in neuroscience. Why were you drawn to that particular field?

I kept the idea of being a high school teacher alive for a while. I even went and got my 'alternative route to certification', but I wasn't ready to make that decision. If you ever want to delay a decision, just go do a postdoc (!). Well, not just that; my research was quite productive and I really enjoyed it – I wasn't ready to give that up. I applied for a biotech position too. I kept all my options open to investigate what was out there and what opportunities existed.

I was first interested in evolution and development. I had this larger perspective of trying to understand how form has evolved. I initially applied, and was offered, a postdoc at Yale with Günter Wagner, where we were going to study tetrapod limb evolution. But I also knew that I wanted to be a teacher and that I wanted to have this balance between research and teaching. Günter wasn't interested in allowing me any flexibility to get teaching experience. Rolf Karlstrom, on the other hand, said, 'I'll give you whatever experience you want', which he did and I am terribly grateful for. At UMass Amherst, they had a teaching documentation program that I was able to participate in and he let me teach a unit of his developmental biology course – all of which was fantastic experience for me to grow as a teacher.

Rolf studied axon guidance and I did have a significant interest in the brain; if I was to choose a system to study, it was going to be the central nervous system (CNS). I was fascinated with circuitry and how the brain is built. At the turn of the century, there was a fantastic discovery that occurred where it seemed as though the adult brain might be able to undergo neurogenesis and produce new neurons (reviewed by Owji and Shoja, 2020). The Neuroscience community long thought that the adult brain was incapable of doing that, so that was a huge result that I felt would change how neuroscience was studied moving forward. So while I was a postdoc, I also wanted to figure out what cells are responsible for building the nervous system and thereby have the potential to contribute to neurogenesis – in the embryonic CNS these cells are called radial glial cells. While in Rolf's lab and in collaboration with Dr Nancy Hopkins at MIT (Massachusetts Institute of Technology), I conducted a screen of her insertional zebrafish mutants, looking for defects in commissure development in the zebrafish forebrain. During this screen, I also used a radial glial marker to assay for alterations in radial glial development (Barresi et al., 2010). That screen was a very helpful endeavor that enabled me to identify some mutants in both of those categories that allowed us to study radial glia, which really were not being studied at all back then. That gave me the basis for my own research story and how I envisioned building my own lab's research focus.

What are the main research themes of your lab today?

From a basic standpoint, I'm still interested in how the brain is built. There are many aspects to building a brain, but there are two pretty

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important ones that we have focused the most on: how are the cells of the brain made (who's making those cells and what influences how those cells develop into certain specific cell types?) and how does the nervous system get 'wired up' (a process known as axon guidance)? My lab started trying to answer those two questions by looking at the role of radial glia as the stem cell for the late-stage embryonic brain, and how those radial glia, or other related astroglial cells, influence nervous system wiring. My lab has looked at the Slit/Robo family of guidance cues and how they facilitate commissure development in the forebrain; we recently published a paper documenting a foundational architecture of what the embryonic forebrain looks like in zebrafish; more specifically, where cells are positioned relative to commissures (Schnabl et al., 2020). That's going to be a fantastic foundation for us moving forward to start to ask more mechanistic questions. We've also documented genes that are important for the regulation of radial glia, and how they impact neurogenesis in the patterning of the spinal cord (Johnson et al., 2014, 2016).

Although our projects on axon guidance, neurogenesis and radial glial development have generally been the main 'bread and butter' work of the lab, we also have some exciting complementary projects. Briefly, we are investigating the role of bioelectric signaling and how it may influence morphogen gradients during axis determination of the early embryo. We also have a disease-modelling project using zebrafish that is probing the embryonic origins of autism spectrum disorders (Hoffman et al., 2016). In contrast, we have also completed a project focused on questions of how the environment influences CNS development (de Soysa et al., 2012). Most importantly, all three of those projects were born out of a teaching lab, which functioned as an undergraduate student-driven incubator for ideas. I also have a team of undergraduate researchers focused on developing new computational methodologies; I realized that, although I certainly appreciate the beauty of the images we produce, there is a lot of subjectivity in that beauty. I decided some time ago that we as a field need to analyze images in a different way, one that can convert them into numbers to be able to quantify what we actually see. Over the years, I've brought in computational and mathematical modeling collaborators, and statistics and data scientists, who were willing to interact with the neuroscientists and biologists in the lab. It's all extremely exciting. The math, computer science and biology all complement each other and help push our understanding of CNS development much further. These numerous projects also serve to provide real research opportunities for a huge lab (30 strong) of undergraduates with multiple teams. That's a lot of amazing opportunities for undergraduates to gain real research experience and get that perspective of what it is like to be a scientist – something I was grossly lacking as an undergraduate.

How was the transition into becoming a group leader?

It was scary. I remember sitting in my office looking around like, 'so is anyone going to come to tell me how to teach my class and tell me how to organize my lab?'. But you're totally on your own. I vividly remember that moment in deciding that it's quite possible that I won't get tenure, but I'm going to do it my way; I'm going to create the best learning experience for my students that I can provide, while also staying true to my research interests. Raising again your earlier notion of me being 'fearless', I think that was probably the one moment I forced myself to relinquish my fears – where I allowed that fearful moment to happen and then I just said, 'Nope! Not gonna consume me. We're just gonna do it this way, whatever happens, shall happen'.

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This year, you've been awarded the SDB Victor Hamburger prize for your contribution to teaching. What is it that makes teaching the center of everything that you do?

I love to learn, and I'm fascinated with how people learn. I realized early on that teaching and research have a synergistic relationship. We've been able to leverage the teaching lab as a space to identify really important questions that have completely transformed my own research lab, to the point where we've published and garnered funding. If I wasn't asked to teach, my lab would likely be asking different questions. I've been able to infuse research into those spaces in unique ways to give students a more authentic glimpse of what it is like to be within the scientific community, everything from doing web conferences with lead investigators from the papers they've read to students writing National Science Foundation (NSF) and National Institutes of Health (NIH) style grants. I have even had students produce and publish documentary movies on the various topics that we're interested in, which require them to go out and meet these investigators, interview them, and make the critical editorial choices to communicate complex biology to the broader public. These kinds of different approaches have helped my students grow an appreciation, not just for the concepts of developmental biology, but for what it is like to be part of that community. I view this Viktor Hamburger award as an accumulation of all of these different things that I've helped to bring to teaching, which is a huge honor. I'm just completely humbled to be part of that group of amazing educators, and I still have a lot more to do and a lot more to give. So I'm looking forward to leveraging this award in some way to help continue to propel and share these kinds of innovative teaching pursuits throughout the community.

How have your experiences shaped how you teach?

I've reflected back at my past education and I realized that there just was very little attention paid to how people learn, and how that should inform how people teach. As a scientist, I don't think education had ever really been approached objectively in that way. Even at teaching colleges, you may be teaching a lot of courses, but there's only so much time in the day; you have little time to really think about how you're approaching things and even less to assess whether it's actually impacting how students learn. There's some really good colleagues at Smith College across the sciences and humanities, and especially in the education department where there are so many learning scientists. So, I went to these colleagues and learning scientists to learn about learning, and that was important in shaping some of my ideas in pedagogy. Yet I did not need any guidance to know that, in biology, merging research with teaching was going to be essential. The course-based research approach in laboratory teaching was a philosophy that I started right away in 2005 when I joined the faculty at Smith College. To me, if my students are to be successful, they need to learn how to do research. That also comes into the realm of trying to make science more inclusive, for everybody. Starting to increase the opportunities of how we approach our teaching in a way that infuses these research skills and experiences in real ways has been super-important. My art, my way of seeing things, also influences how I approach teaching. An extreme example of this is my seminar course called,

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'the science of superheroes', in which we use superheroes as a mechanism to engage first-year students from different college divisions in science. We get them to learn some science by trying to hypothesize and manipulate what we understand about biology, chemistry and physics to explain those superpowers. It's a visual product that has art and writing in it, to create a legitimate module that can be used by high school students to learn about that science. Many of my approaches have students produce products that ultimately serve a secondary purpose of helping to educate others, whether it's the recorded and disseminated BioWeb conferences, the documentaries or these superhero scholastics. I have learned that broadening the end purpose of a given assessment can be a 'game-changer' in driving student motivation.

How did you first get involved in outreach activities?

My early interest in potentially teaching in high schools gave me a capacity to have it on the radar. I think it's really important because there's an appalling level of inequities in our education system, which are not going to be fixed in our lifetime. That lack of access to gaining that kind of understanding is negatively impacting our society and our lives in ways that are unmeasurable. Scientists are in a privileged position of having both experience and knowledge that so many never get to see. I strongly feel that scientists need to step up and share what we know, share our excitement, share objectivity and help cut through all of the noise that is confusing everybody to make better decisions for our world.

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I developed my first significant outreach program, called 'Student Scientists', when I applied for Career Award with the NSF, because when you apply for such a grant, the NSF have a requirement for significant 'broader impacts', within which you can propose to do things like outreach. Student Scientists is a three-tier, week-long curriculum that begins with observation, then progresses to guided experimentation and finally has the potential to offer more independent student investigations, all using the zebrafish model system. My program uniquely focuses on getting teachers trained to tailor and deliver this curriculum; we provide the zebrafish embryos, infrastructure, and some microscopes and equipment, and they carry out the curriculum. Unfortunately, it had to shut down during the pandemic, but I'm looking forward to that restarting again in the coming years. In response to the pandemic, I've also created the Online Developmental Biology Teaching Forum using Zoom to bring the developmental biology community of teachers together and help provide an opportunity to support each other through this very challenging period of teaching. Moving forward, I am excited to continue these forums and other modes of engagement to grow and strengthen our community.

You have co-authored the Developmental Biology textbook with Scott Gilbert. How did that come about?

I remember when I was a graduate student, I had lunch with Scott Gilbert, who had come to give a talk. From that moment we just knew each other but later, by going to meetings and because both of us were members of the education committee with the SDB, we got to interact quite a bit. He started to see the kinds of approaches and ways that I was teaching and liked how I was doing things. He asked me to come have a meeting with him and the editors at Sinauer. The idea of writing a textbook was just daunting, but the idea that I could produce a product that might influence how others teach in a way that really improves the learning experience for students won me over. I'm just so thankful and privileged to have had the opportunity to be part of this amazing textbook that Scott started. He created a foundation and a community around developmental biology, and his contributions deserve so much credit. I am equally thankful for how amazingly accepting Scott and the editors have been regarding all of my ideas that have helped to rapidly evolve the last two editions. So, despite the enormous undertaking that crafting this textbook requires, the process and collaboration with Scott has been an honest joy.

Finally, is there anything that our readers would be surprised to learn about you?

Probably one of the more surprising facts is that I have faced challenges with reading and writing my whole life; I bet folks might not suspect that the author of a textbook has those sorts of difficulties. Ironically, I firmly believe that these types of challenges over my life have helped me to become a more empathetic professor and someone who has been more open to novel strategies to help all my students. As a fun pastime, I also love sand sculpting – you'll even find a couple of my sand sculptures pictured in the textbook. Someday, I also have an interest in writing and illustrating a graphic novel centered around the superhero, who would of course be powered by the principles of developmental biology.

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