

Q & A

**Cassandra
G. Extavour**

Cassandra Extavour is the Timken Professor of Organismic and Evolutionary Biology and of Molecular and Cellular Biology at Harvard University, as well as a Howard Hughes Medical Institute Investigator. Her lab studies the evolution of the genetic mechanisms employed during early animal embryogenesis to specify cell fate, development, and differentiation.

What turned you on to biology in the first place? The thing that made me interested in biology was behavioral neuroscience. In high school, even though this term was not yet in my vocabulary, and I didn't yet understand how scientific research could be pursued as a profession, I wanted to understand how the human brain worked. I was curious about how chemical reactions in the human brain drove humans to the often-terrible behavior that has characterized our species throughout our cultural history. That interest is the reason why I began studying biological sciences for my undergraduate degree at the University of Toronto.

What drew you to your specific field of research? I became interested in developmental genetics by chance. The first opportunity I had to do research in a lab was during the summer after my third year of university, when I was invited to join the lab of Joseph Culotti at the Samuel Lunenfeld Research Institute at the University of Toronto. During that summer, my research project was to assist graduate student Antonio Colavita in mapping axon guidance mutants that he had isolated in a mutagenesis screen. I learned the application of Mendelian genetics to *Caenorhabditis elegans* genetic screens, and I loved it.

If you had to choose a different field of biology, what would it be? If as an undergraduate student I had learned about theoretical population genetics, I think that is the field of research I would have become interested in as a graduate student. However, I didn't really learn much about population genetics — either in application or in

theory — until I was a postdoc. By then, it seemed to me perhaps a little bit too late to get into it full time, but learning about this other approach to the evolutionary process came at a crucial time for me and was central to my decision to continue to pursue evolutionary developmental genetics. When I first began my postdoc in 'evo-devo', I quickly became disappointed at what I perceived to be the absence of a clear, predictive, and quantitative framework for understanding what degrees of evolutionary change were to be expected in traits such as gene expression patterns or cellular growth dynamics during morphogenesis. I was — perhaps naively — shocked and disappointed to find that there were no real null expectations in the field. We were all just doing our best to perform comparisons and then speculating on what the evolutionary meaning of the comparisons might be. Reading about population genetics gave me hope that, at least for some elements of the evolutionary process, it could be possible to generate predictive quantitative frameworks to understand them.

Who were your key early influences?

On a personal level, my strongest influences have always been my parents and my siblings. On a scientific level, my doctoral advisor Antonio Garcia-Bellido was a pivotal scientific influence. His depth and rigor of thought and his fearlessness in pursuing ideas — experimental or theoretical — even in the face of significant opposition or incredulity from some of his peers at the time were inspirational to me.

What is the best advice that you have been given?

One of the best pieces of advice I've ever received was from my doctoral advisor, Antonio Garcia-Bellido. When I decided that I wanted to work on the germ line, he said "Cassandra! To do this work, you have to *breathe* the germline, *eat* the germ line, *drink* the germ line, *immerse yourself* in the germ line!" I interpreted his message to mean that I must work on the problem I had chosen as intensely as I could. His advice to all of us that studied with him was that we must follow our instincts with rigorous experimentation, even and especially if our instincts were not reflected in ideas that appeared popular



or fashionable in current scientific literature. I believe that he wanted us to understand that, if we were spending too much of our energy focusing on what the rest of the field was doing, then we would by definition be siphoning off some of our energy away from our own work. Our responsibility was to do our work as well as we were capable of doing it, and if we dedicated anything less than our full capacity our work would not be as good as we could potentially make it.

If you had not become a scientist, what would you have become? My professional goal was always to be a full-time professional musician. Had I not become captivated as strongly as I was by science, I would have pursued this childhood dream. Even through to the end of my doctoral thesis, I was very seriously considering leaving science for music. However, in the end, I wanted to keep science in my life. So, I chose to pursue science full time and music part time.

What has been your biggest mistake?

I try very hard not to have regrets, and I believe that every mistake you make is an opportunity to learn to do something differently in the future. Things that seem to be mistakes in a given moment later often turn out to be blessings in disguise. Having said that, one of the things I regret the most in life is a decision I made when I finished high school. I decided not to audition for

the Conservatory of Music to pursue music full time because I was afraid that I wouldn't get in, as I hadn't had the extensive private training that I was sure most of my competitors would have had. That made me nervous enough to not even try. I regret that decision not because of the decision itself but because the reason I made the decision was that I was afraid to fail. Since then, I can say that I have tried very hard never to make fear of failure the reason that I don't do something. I think it's very important to try everything that you are interested in because if you don't try you'll never know the outcome.

What is your favorite conference? My favorite conference is the *Drosophila* Genetics meeting, which happens every two years in Kolymbari in Crete, Greece. I love this meeting because it has no concurrent sessions, every single attendee speaks, and almost every attendee presents new, exciting, unpublished work. There's an excellent balance of time spent listening to colleagues talking about their work and unstructured time where we can have informal conversations with colleagues that inevitably also enhance our work and the community.

In what ways do inclusion and diversity influence your work or the scientific community in general? Inevitably, I'm influenced by these elements of culture in a very personal way because traditionally there have not been very many Black women who are professional scientific researchers in any field of research — and definitely not in evolutionary biology, developmental biology, and genetics. So, for most of my training and professional career, I've been the only or one of a very small number of other Black scientists, or female scientists, let alone Black female scientists. This perspective, based on my experience, makes me always remember that new colleagues, including prospective new members of my own lab, may also be experiencing their own version of newness, isolation, trepidation, or sometimes even exclusion. It's important to remember that each person comes with a unique personal history that is greatly influenced by the history of who has been allowed to participate in science up until that point in time. So, I try to make it clear as

I operate in the professional sphere that it's important to listen with open minds to different people's experiences and influences and not assume that one's own experiences can be translated to those of other people.

Do you feel a push toward more applied science? I don't feel personally or professionally pushed to pursue applied science any more than we already do. But what I do feel is a strong sense of importance to justify the work that we do to the funders who we hope will choose to fund our research. Unless one is independently wealthy, in this profession one must convince some organization to fund one's work. The onus is on us, the researchers, to explain to the funders why they should be spending their money on what we would like to study, as opposed to any of the other competing applications they may have received or any other type of activity that they might like to support with their funds. I think that it is appropriate that researchers be required to explain and justify the work that we would like to do, beyond simply saying "this is interesting to me personally." In the case of public funding, we need to explain to the taxpayers who provide these funds why it is worth spending their money on the research that we find so interesting.

What do you think is the big problem to be solved next in your field? In the field of comparative evolutionary developmental genetics, a key thing that I believe holds us back from making progress is the lack of null hypotheses. Our field is extremely good at making increasingly nuanced, quantitative, and comparative measurements of various phenotypes across organisms. The field is also getting better at resolving — with increased statistical precision — evolutionary relationships between organisms. So, we have fantastic frameworks for how organisms are related, and we have massive datasets of complex characters. What we don't have are good estimations of the rates of evolutionary change that are to be expected in different lineages for a given trait. Without these null expectations, it's very hard for us to make conclusions about the evolutionary dynamics of traits, whether those traits are primary sequences, morphologies, omics

patterns, or 3D chromatin architecture. We don't know how we would expect any of those traits to change over a given evolutionary relationship, and it's very hard for us to make strong statements about the evolutionary dynamics of these things over long distances.

Which aspect of science, your field or in general, do you wish the general public knew more about? I think it would help all of us if the general public understood more about the scientific process and what distinguishes science from other cultural pursuits. To my mind, what sets science apart from other ways of knowing about the world is the scientific process: documentation, reproducibility, controls, and testing alternative hypotheses. I wish that science education were stronger so that the general public understood that, when scientists interpret data and reach conclusions, they're doing so under a framework that should include at least attempts to eliminate alternative hypotheses to explain observations. This is different from taking a collection of observations and simply proposing a hypothesis that you could imagine to be true but then not proceeding to try to falsify your hypothesis.

Do you believe that there is a need for more crosstalk between biological disciplines? Yes. Incorporating different perspectives into our thinking leads to more creative and novel solutions and insights. This can include opening our research to new disciplines, but if we can't speak the language of other disciplines this can be hard. There's often a language barrier between disciplines, reinforced if we insist on using specialized jargon even when speaking to broad audiences. So, one thing that helps us — just as in other areas of culture — is being exposed to new thinking and ideas by learning more than one language in science.

DECLARATION OF INTERESTS

The author declares no competing interests.

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