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INTERVIEW

Transitions in development – an interview with Rajendhran Rajakumar

Rajendhran Rajakumar is a cross-appointed Assistant Professor in the Department of Biology and Department of Cellular and Molecular Medicine at the University of Ottawa, Canada. Rajendhran's lab uses multiple integrative approaches to understand how environmental factors act on evolution and development (eco-evo-devo) and how this leads to the evolution of biodiversity. We spoke to Rajee over Teams to learn more about his passion for emerging and model systems, most notably ants, and the importance of serendipity in research.

When did you first become interested in science?

My father was an orthopaedic surgeon and family physician, and my mom was a nurse, so I grew up with medicine in my environment. When I was around nine years old, two events solidified that I wanted to do biology. First, I saw Jurassic Park, which I'm sure inspired many famous palaeontologists today as well as molecular biologists who became interested in DNA because of that movie. Both fields have a lot of fascinating things in common, including understanding evolution, inheritance, descent by modification, etc. I was one of those inspired by DNA to be a molecular biologist. Shortly after, I went to the American Museum of Natural History in New York. Again, I could have been inspired to pursue palaeontology, because of all of the beautiful fossils, but DNA was everywhere because of movies like Jurassic Park and I was still hooked! In high school, biology was my best subject by far and I went to Concordia University in Montreal to do molecular biology as an undergrad. I wanted research experience and Ehab Abouheif had just started his lab at McGill University, which was nearby. I had no idea what to expect about lab research environments at that time; the lab (brand new) was empty, except for shelves filled with Tupperware boxes. Ehab took a box off the shelf, opened it up and, lo and behold, there was this entire microcosm – this little society – of ants walking around inside. My mind was blown. That afternoon, we talked about his lab and his research vision, which is when I first learned about developmental biology and eco-evo-devo. I immediately wanted to get involved in research and applied to the grad program there.

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What did you work on during your PhD?

Half of my PhD thesis was studying how ant castes develop and evolve. We showed how a very complex phenotype, the super soldier caste, which exists in a handful of ant species, has independently evolved through an example of parallel evolution through similar developmental mechanisms. We showed that rather than similar phenotypes independently evolving through *de novo* mechanisms, in fact, ancestral development potential can be retained and reactivated by, for example, environmental inductive processes, and eventually potentially selected upon. My thesis went towards understanding the developmental basis of caste evolution at the level of hormones, gene regulatory networks, epigenetics, and various other mechanistic levels of molecular regulation (Rajakumar et al., 2012).

Your brother, Arjuna, is also a research scientist in the field. Have you influenced each other's careers?

My brother initially worked on cancer (glioblastoma) for his Master's at the Montreal Neurological Institute and then on the metabolic basis of cancers, also at McGill University. He needed a new lab environment and Ehab's lab was proliferative at that time. I suggested he should join because it would be the perfect environment to cater to his very diverse interests. As I went on to my first postdoc, he joined the lab as a PhD student. So not only is he in science, and did a PhD in biology, but he did it in a lab where I did my PhD! He was coming into the evo-devo world with an incredible biomedical perspective. It was so interesting to see the novel ideas he was able to generate, and he contributed to a major paper of mine (Rajakumar et al., 2018), which is something I never expected to happen. He's currently in Ruth Lehmann's lab at the Whitehead Institute, continuing his work studying oogenesis from ants to flies. I can't wait for him to start his lab!

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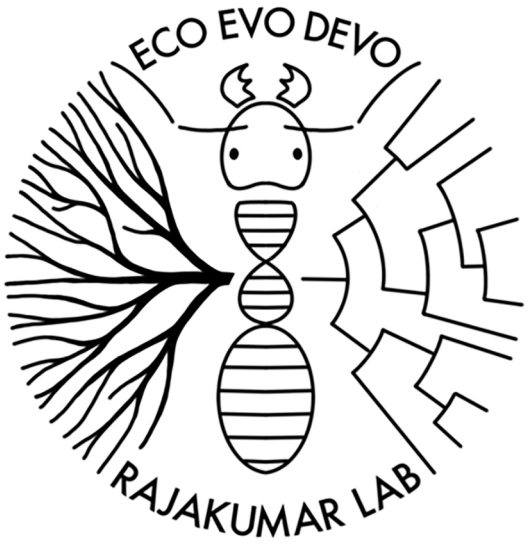

The Rajakumar lab logo. Credit: Erica Vong.

What influenced your decision to move to the University of Florida, USA, for your postdoc with Marty Cohn?

I wanted to test how broad ancestral developmental potential is and ask how it can be reactivated and whether it can be manipulated experimentally to bring back 'lost' traits. I leapt into the vertebrate world and went to Marty Cohn's lab, which is known for many things, including the loss of complex phenotypes, such as limbs in snakes or genitalia in birds, for example. I learned about the entire realm of vertebrate developmental biology and evo-devo, which allowed me to fully appreciate people like Lewis Wolpert, Cheryll Tickle, Denis Duboule, Stephen Jay Gould, Pere Alberch, Brian Hall and Richard Owen. As a person with a background in invertebrates, it was like this literature was untapped, and it opened my eyes. There are so many common ideas and concepts that have been explored in these different lineages, but not much crosstalk. Reflecting on that led Thomas Sanger and me to write on the importance of thinking about the organism as central to evo-devo research (Sanger and Rajakumar, 2019).

How was the transition from Canada to Florida?

I hadn't visited Florida before I moved to Gainesville in the fall of September 2014. I moved from Montreal, a big city with a New York fast-paced lifestyle, so I spent the first month in this stress detox. I got to experience Southern hospitality and Southern charm firsthand, and I was in the best shape of my life biking to work. I felt at home once I finally adjusted to that slower pace, with my wife Marina and our first son Anthony (the first three letters of his name tell you a bit about our influences in naming him!). It was a great experience!

What were your postdoc projects?

When you open up any freezer in the Cohn lab it's like a zoo of embryos – which one to study?! First, I started learning how to work with chick, which was amazing experience to get into the vertebrate development world. Chickens don't have external genitalia, but they do have transient development of the structure. My first idea was to try to reactivate that process of external genitalia development and make a chicken more like a duck, which links back to my earlier ideas inspired by ants on the retention of developmental potential. I also wrote a postdoctoral fellowship proposal to study limb digit loss and re-evolution in lizards. But, in the end, I fell in love with cartilaginous fish, sharks and skates, because they are such amazing systems to work with. They have vestigial development of bone in their axial skeleton – something I had no idea about initially – and I ended up studying bone development in these species. The lab was a great environment, in which I was exposed to many other vertebrate organisms, which was great for being creative in your thinking about broad macro-evo-devo questions.

Why did you decide to do a second postdoc with Norbert Perrimon at Harvard Medical School, USA?

During my graduate studies working with an emerging model organism, I read the model organism literature. For the insect world, like ants for example, you're standing on the shoulders of giants – that of *Drosophila melanogaster*. I was still working with ants in the backdrop and one breakthrough that was emerging was this rudimentary organ, the rudimentary wing imaginal disc that develops in wingless castes of ants (e.g. soldiers), and that could non-autonomously influence other tissues (in this case caste identity and head allometry) and integrate the social environment through interorgan signalling (Rajakumar et al., 2018). The Perrimon lab is known for its foundational work in flies and on interorgan signalling and I wanted to go to one of the best places in the world, to study it in the fly and develop a model organism to complement the emerging model – very much inspired by my experience in the Cohn lab.

My second postdoc was awesome. What Athens was to philosophy, that area around the Charles River, MA, is to science. It was hard to adjust to going back to the urban lifestyle, but it was so inspiring, humbling and incredible to be part of that community. It was also getting difficult to live so far away from family and Canada. Our second son, Theodore, was just born. My wife is a doctor and Boston is a whole lot closer to Montreal and her work.

How did your visiting fellowship at the Konrad Lorenz Institute (KLI), Austria, come about and what was that experience like for you?

While being inspired by Norbert in the value of community building and leadership in one's field, and by the beauty of model organism systems in the Perrimon lab, I realised there's a whole other side of me that's very conceptual and theoretical. The Konrad Lorenz Institute for Evolution and Cognition Research in Klosterneuburg, Austria, is an incredible place where people go for workshops and to develop their thinking. I did a short stay postdoctoral fellowship to further develop this idea of ancestral development potentials. While there, I saw some of my heroes – Eva Jablonka, Michael Levin, Detlef Arendt and Gerd Muller – thinking about, for example, the origins of macroevolution and cognition.

At what point did you start looking for independent positions?

One recommendation is to start applying a year or two before you're in an optimal position because it takes time for you to develop your ideas – you shouldn't be working on your cover letters and research statements just before the application season. Shoot for the stars and apply to incredible places, just a handful at first, because it pushes you to write your research statement in a way that you're trying to attract the attention of the biggest and the greatest – to think outside the box and communicate how incredible your system can be for your future research. I started applying towards the end of my first postdoc and I *really* went for it during my second postdoc. I applied to places that I thought would be a fantastic environment considering my family and research. I always wanted to return

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to Canada; I applied broadly and I had fantastic interview opportunities. I wouldn't have done as well in that season without those preliminary attempts.

What attracted you to start your group at the University of Ottawa?

There are so many great things about Ottawa and the University: it's a couple of hours away from where my wife and I grew up in Montreal, it's a 'Goldilocks city' of not too big, not too small, and it's a dream to be at a top-notch research institute. The Biology Department is incredible, with amazing people working in comparative physiology, cell and molecular biology, ecology, and evolution. I was swept off my feet in terms of the collegiality that the department offered. I was in med faculties during my postdocs and I wanted to continue that so I was cross-appointed in the Faculty of Medicine in 2021. It's a beautiful balance.

How was the transition to becoming a group leader?

I was hired pre-pandemic, I started during the pandemic and the first class I taught in-person was developmental biology in fall 2021. I built that course up from scratch using, of course, the textbook by Micheal Barresi and Scott Gilbert – there's no better textbook in my opinion! The most impact was when I first stood in front of that class, even more than seeing my name for the first time on my office door. It was a third-year class of about 60 students (180 now!) and I remember asking the students, 'for how many of you here is this your first class, in person, at university?' Everyone raised their hand. The class was silent. It was a daunting feeling at first, but, when people looked around, we realised we were all in this together. That was the beginning of the journey.

How have you approached hiring new team members and mentorship?

The first class I taught was an honours seminar online in the fall of 2020. The topic was molecular biology, but I hijacked it to be developmental genetics and evo-devo. Of the 23 students in the class, around eight of them applied to my lab, and three of them became my first graduate students. I would advise early career researchers to put as much effort as they can into their classes. They're beautiful recruitment grounds for amazing students, who will inspire you with their questions, ideas and different perspectives, that can potentially be brought to your lab. It's important to think about how and who you recruit, and to make sure that people already in the lab are involved. For example, graduate students also interview honours students wanting to join the lab, so graduate students play a direct role in the process of building the team. I very much value and appreciate having a harmonious lab that provides an environment for students to train, learn, and evolve their thinking in a constructive and supportive manner.

I love to mentor. I first learned as a graduate student, having undergraduates work with me and my projects, which continued when I was a postdoc as well. I try to continue that mentality. For example, honours students are teamed up with graduate students to work on projects together, so that honours students can contribute to something larger than a short-term honours project. There's a constant level of mentorship and mentor/mentee relationships. I also encourage people to develop a mentorship network – to get advice from people with different life experiences.

Can you summarise the research themes of your lab?

We're exploring questions at different levels of biology. There's a beautiful connection from molecules, to cells, to tissues, to the formation of organs and how they communicate with each other to form an entire body plan of an animal, and then, how individuals interact with each other – from cells to societies. I love that integrative approach to biology using emerging models and model organisms. Eco-evo-devo is at the heart of the lab, ants are the inspiration and flies are a beautiful model organism to complement emerging organisms to test mechanistic ideas at higher resolution. There are people in the lab who like 'organism/trait first, mechanism second' projects; for example, the evo-devo of different appendages. Then, there's the other aspect, people who prefer 'mechanism first' and are interested specifically in a type of epigenetic regulation or gene regulatory network, and how those impact the organism. I find those axes complement each other well. Inspired by how the Perrimon lab contributes to the *Drosophila* community and how Ehab helped pioneer eco-evo-devo as a field, the long-term goal I want to achieve is to continue to build a community of individuals who do integrative work with ants and social insects more generally.

What are the challenges and opportunities associated with working with a variety of 'emerging model organisms'?

It's about forming bridges. For ants, and social insects more generally, there are organism-centric communities studying animal behaviour, ecology, chemical communication, evolution, etc. that you can interact with. At the same time, you can be equally involved in discipline-driven societies – learning about cutting-edge techniques, tools and approaches in model organisms and trying to pioneer them in emerging models.

How important is fieldwork to your science? What does it involve?

I realised in Ehab's lab that there are three ways of exploring. First, scholarship: diving deep into the literature. It doesn't matter what decade or even what language, as a graduate student I was reading things in French and translating from German. Scholarship is important to generate amazing ideas; to breathe new life into the disciplines and to help generate questions. Second, tinkering: having fun in the lab doing experimental biology. The third way of exploring is going into the field and seeing the questions that nature provides us – like Indiana Jones exploring. It helps you think outside the box; it gets you thinking about natural history, and the flora and fauna around the organism you're studying. There's a quote from a paper that had a major impact on me: 'the story of any species chosen at random is an epic, filled with mysteries and surprises that will engage biologists for generations to come' (Tschinkel and Wilson, 2014).

Many do not realise that lots of us in developmental biology do fieldwork to collect our samples. For communities working on model organisms, like flies, you can order (or make) transgenic lines from stock centres – that's a mature state of a community that has been established. But if we want to work on these emerging organisms, to do *in vivo* experimental biology, we need to go out in the field and try to collect different species that are relevant to the questions we're trying to answer. It is a practical reason, we have no choice!

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But there's also something very beautiful about fieldwork; students have so much fun doing it. It's a great time to bond, generate ideas and discuss. As a developmental biologist, you generate all these different phenotypes, variations on a theme of some trait, and it's very important to see the biological relevance of that variation. It's grounding to help you see, in a new light and in a natural context, the significance of the experimental biology you're doing in the lab. It's a fantastic part of research.

You are an Associate Editor/Editorial Board Member at BMC Biology and JEZ-B. Why did you decide to get involved in science publishing and how do you see your role?

Ehab is the Editor-in-Chief of JEZ-B, a journal that I've loved for years, and he provided me with an opportunity to be part of the editorial board. Then, BMC Biology was searching for people to become involved in the journal as Associate Editors – academics who play a vital part in selecting papers and handling the review process. As a reviewer, I know how important that process is to the scientific endeavour. I applied because I was interested in seeing the good, the bad and the ugly of the publication process. I wanted to be a positive force in promoting good practice and to be at the frontier of seeing the latest research.

Do you have any advice for early career researchers?

As development biologists, we have to be inspired by each other's work and support each other – to explore unchartered territories together. Through my journey I've learned about the beauty of serendipity: expect the unexpected and be open-minded. Let the data speak for itself even if it is surprising. Take a moment to step back and think about alternative explanations and hypotheses. If we already know what to expect of our data, we're not doing it right! Serendipity might come and surprise you – be ready.

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

During graduate school, half of my thesis was studying a key hormone, juvenile hormone, and how manipulating it could reactivate an ancient super soldier caste from tens of millions of years ago. When that work came out, it went viral in the media with analogies to the super soldier serum that made Captain America. Then, the second major part of my thesis was studying epigenetics in size variation right as the Ant-Man movie was coming out about a superhero that can change size. So, my research was inadvertently making the scientific basis for the Avengers! Theodore, my son, is in love with Spider-Man. Maybe he'll keep it in the family and one day he'll reveal the scientific basis for Spider-Man.

Rajendhran Rajakumar was interviewed by Alex Eve, Senior Editor at Development. This piece has been edited and condensed with approval from the interviewee.

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