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INTERVIEW

An interview with Joshua Gendron

Joshua Gendron is Associate Professor of Molecular, Cellular and Developmental Biology at Yale University, USA. His research focuses on understanding how protein degradation systems regulate timing mechanisms and environment sensing in plants. Joshua joined the team at Development as a Guest Editor for the journal's Special Issue: Metabolic and Nutritional Control of Development and Regeneration. We met with him over Teams to learn more about why he decided to get involved, his research and his career path.

Could you take me back to that moment when you first became interested in science?

I knew from very young that I was interested in science because I liked exploring nature. I especially liked aquatic environments. There were all these little creeks around my house where I could find tadpoles to scoop up and watch them turn into frogs. In college, I was on track to become a park ranger, not a scientist. I wanted to work in the Tahoe National Forest, collecting fungus from trees or something, but there were a couple of moments in college that really changed how I thought about things. I took my first genetics class and I absolutely loved it! I still keep in touch with my genetics professor from that class, Professor Stuart Brody, at University of California San Diego (UCSD). Now I teach genetics at Yale. Then, at the end of college, I took a lab course, which happened to be taught by five of the world's best plant biologists. One of them, Joanne Chory (Salk Institute for Biological Studies), offered me a position in her lab, so I spent a few months there at the end of my undergraduate and then a year as a technician. While I was there, Joanne explained to me how a PhD program works, and she convinced me to apply to graduate school and helped me get in. It was a big turning point because I declined a park ranger job near San Diego and went to Stanford for graduate school instead.

What influenced your decision to go to Stanford and join Zhi-Yong Wang's lab?

I was applying to all different universities and Zhi-Yong, the postdoc that I was working with in Joanne's lab, was applying to faculty positions at the same time. He got an offer at the Carnegie Institution, which is on the Stanford campus, and I got into Stanford. I worked with him as a technician for the summer before I started graduate school and got the lab started; then I continued working on the same subject, brassinosteroids, that we'd worked on in Joanne's lab. It was a big help because I had two years of experience with the conceptual knowledge of the topic. I was able to jump right into the projects and get started quickly.

You must have been one of the first hires for his group?

I was the first. It was a great experience because I had his full attention and saw what it's like to start a new lab. It was also hard because everything was moving very quickly. At that time, the brassinosteroid field just exploded; between 2000 and 2010 the field connected the whole signalling pathway, from receptor to transcription factors – it was amazing – but it was competitive. Zhi-Yong was always good at getting papers out quickly though; I appreciated that about him.

Can you tell me a bit more about what you were working on?

In Joanne's lab, Zhi-Yong and I worked on BZR1, which is one of the transcription factors in the brassinosteroid signalling pathway. At that time, it was just a protein sequence, we didn't know it was a transcription factor. We published a paper about cloning it and describing its physiological role in brassinosteroid regulated growth (Wang et al., 2002), but we didn't know the biochemical function. It was the very early days of protein sequence analysis and, if you look at those papers, my little brother is an author on them. He had some computer background and found a small sequence that looked like a DNA-binding domain, which we tested. Once we showed BZR1 was a classic DNA-binding transcription factor, things moved quickly and we revealed how BZR1 controls feedback regulation of the brassinosterioid signalling pathway. We published that paper in Science, describing the biochemical function (He and Gendron et al., 2005). From there, I kept working on BZR1 and noticed that *BZR1* mutants had floral organ separation defects. We collaborated with Kathryn Barton's lab to show that improper regulation of BZR1 disrupts organ and boundary formation (Gendron et al., 2012a). It was fun because it was just something that I had noticed while growing the plants and it led to my first my first experience of studying organogenesis.

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You then moved back to UCSD to join Steve Kay's group. What was it about the lab that attracted you initially?

I had some restrictions; my wife is a cell biologist working in animal cells, so we had to go somewhere that had opportunities for both of us. She had some potential places in Boston, but that wasn't right for me. San Diego has excellent labs in plant and animal biology, so we decided to go there. So I interviewed with Steve Kay and talked to the people in Steve's lab, and I realised that the clock was similar to the brassinosteroid pathway: it's all oscillatory feedback loops. It was like we were speaking the same language and I felt like it was going to be a good place for me scientifically. That was important because I wanted to make sure that, if I was going to spend the rest of my life studying that topic, I was interested in it. The other important part was that the lab was a very friendly group of people and we'd go out for coffee every day at 15:00 to talk about life and not about science!

What did you work on while you were there?

I went there to try to figure out the function of *TOC1*. I showed that TOC1 has the potential to interact with DNA and act as a transcriptional repressor (Gendron et al., 2012b), which is very similar to what I did with BZR1. It led to the idea that the plant clock wasn't that similar to the human clock and that we were missing other components, which were subsequently found by other groups.

But I knew that I didn't want to work on the core clock forever because it's a very competitive field. I wanted to work on related mechanisms and I became interested in protein degradation. We knew that TOC1 was regulated by an E3 ligase and I thought there must be other E3s that regulate the clock. Although I knew a lot about the clock, I didn't know as much about studying E3 ligases, so I spent a year in Eric Bennett's lab (he's a great ubiquitin biologist and friend from graduate school). I learned about the ubiquitin proteasome system, and he helped me come up with some clever techniques for studying the ubiquitin proteasome system in plants. I took those things with me to get started at Yale.

How was your experience moving to the East Coast to start your own group?

It was great, but there were a lot of challenges that I didn't expect. I didn't realise how much actual time it took to do everything. In my first year, I was preparing lectures at one o'clock in the morning for the next day, and I had new graduate students and committee assignments – that part was challenging. But the science part seemed to happen without too much difficulty. I had smart, motivated students and postdocs at the beginning, who were willing to buy into a non-traditional trajectory where it wasn't clear what exactly we were going to do. I do remember that I thought it might be a challenge to hand over the reins of doing experiments to the students – maybe it wouldn't be as fun. But I remember the first time my first graduate student, Ann Feke, came to my office, and I could tell that she was very excited about something. She plopped down a piece of paper, which showed a clear result from an experiment supporting the hypothesis that she had come up with. I felt happier than if I had done it myself because this person came to my lab, they trusted me and I taught them the system, but then they were able to design an experiment, do it and show it to me. It was very rewarding to see somebody go through the process of becoming a scientist right in front of my eyes.

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Do you think your PhD experience prepared you for what it was going to be like setting up a lab?

For sure, I give credit to that experience of helping Zhi-Yong start his lab from scratch. Also, when I was with Steve, we moved from UCSD to the University of Southern California, which was like starting a new lab in some ways. The other person I should give credit to is my wife. We started our academic positions at the same time and we actually moved into the same shared lab space and office at the beginning. She was so organised and on top of everything. It was great working together with somebody who was going through the same process.

Were there any skills that you didn't feel prepared for at the time?

I had one mentorship style when I started but it wasn't suitable for everybody. I realised that I have to have 10 different mentorship styles to be an effective mentor! Over time, I've learned that each person comes with a set of skills, but everybody has something that they need to learn. It's important to quickly identify what their skills are and make sure that they have the opportunity to use them and then make sure that you supplement those other places where they need some help.

What are the main themes of your research now?

Our central focus has always been daily and seasonal timing mechanisms, including the circadian clock and photoperiod measurement systems. Initially, we were working at the intersection of the circadian clock and protein degradation. The clock is a dynamic system: every 24 h the gene needs to be activated, transcribed, post-transcriptionally regulated, translated and post-translationally modified; then, finally, the protein is degraded. Every eukaryotic clock requires the E3 ubiquitin ligase system to mediate degradation of clock proteins, but in plants, the clock and the E3 ligase system are much more complicated genetically. We thought that there was this area that nobody had explored effectively and we started looking for E3 ligases that regulate the clock.

We're also interested in how the clock uses E3 ligases to regulate downstream biological processes. We looked for E3 ligases that are transcribed with daily and diurnal rhythms, and used different genetic and biochemical techniques to understand their function. We have a standard pipeline: we take a F-box gene and make dominant-negative mutants, knock it out, etc. Then, we look at the transcription of the gene using luciferase technology to track the rhythms. We made one of the first reporters that reports on seasons, so we can tell whether a plant 'thinks' it's winter or summer (Liu et al., 2021), rather than just what time of day it is, which is what a clock reporter does. We pulled on this thread, and it unravelled into this much larger problem: how metabolic networks control seasonal gene expression. In fact, there's a metabolic network that can measure day length as a function of photosynthetic duration rather than light duration. It's been exciting to find new day-length measurement systems in plants in a totally tangential way.

Your lab bridges the fields of metabolism, environmental control and circadian rhythms. Do you think it's useful for young scientists to have that interdisciplinary approach?

It's useful, but it can also be hard. The clock is this ultra-complicated machine, and photosynthesis is an ultra-complicated sensing system, and we know they intersect somewhere to give seasonal measurement. It's difficult to approach questions touching on multiple fields. The people in the lab must be very exploratory

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and not afraid to go after any biological question. It's scary, in some sense, because, unlike other fields they are not linear systems. But these intersections of fields are where new discoveries can be made.

Do you have many collaborators?

I've had collaborators on the protein degradation part of our work. We designed a reverse genetic strategy to overcome redundancy in the E3 ubiquitin ligase gene family, and it can help people working on protein degradation in their labs. I've also been collaborating with people who are experts in seasonal flowering time and I recently wrote a review with Dorothy Staiger, an expert in that field (Gendron and Staiger, 2023). The one thing that I'm less comfortable with is the metabolism side, which I came into from the side, so I'm trying to connect with the experts on that side.

What goal would you like to achieve during your career?

I want to continue to understand daily and seasonal timing mechanisms in plants. We've developed bioinformatics approaches to understand how many genes are controlled by seasons and there are probably many seasonal timing systems that are unstudied. We now know that there are several ways plants measure day lengths: absolute day lengths, photosynthetic periods, the duration of blue light or red light, or some other signal. In the long run, I'd like to understand these more comprehensively. I think this is important because plants are using daylength to predict things like seasonal temperature or water availability, but climate change is rapidly untethering these signals. So I think our work will help understand how plants are going to respond to climate change.

You recently joined the team at Development as a Guest Editor for the Special Issue: Metabolic and Nutritional Control of Development and Regeneration. Why did you decide to get involved?

There are two reasons: one, I wanted to learn something new. I enjoy research that approaches classical questions from different angles, perhaps using modern techniques. I hope I get to see something that might inspire my own thinking. Two, I enjoy reading science and writing. As an Editor, I hope I have the chance to read papers, give feedback and hear the opinions of the editors, as well as see a little bit of how Development works behind the scenes.

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In your view, what excites you about the field right now and how do you see the field developing in the next few years?

In plant biology, there was a period when people split into their individual fields but now many people are realising there is a central link, which is fundamental metabolism. It's been exciting to see many fields return to one core idea. Mass spectrometry technologies are getting better and easier to use, but we're still using older techniques for the visualisation of metabolites. It will be a big deal when we can track metabolite movement *in vivo* more effectively. Also, single-cell technologies are being expanded into the metabolite realm so not only are you getting a sense of the genes (the DNA, RNA and protein) but as things become more precise, you're also going to have a sense of what metabolites are in different tissues and cell types.

Do you think science outreach and engagement is important?

I run two outreach programs. One is the Green Café (https://greencafe.yale.edu/) with Marsh Botanical Garden at Yale. We have a monthly presentation series on any plant topic, bringing in scientists to share their passion for science and plants without the use of PowerPoint. It's mandatory that speakers have some type of taste, touch and smell component. For example, we've done talks on coffee, chocolate, miracle berries, tea and popcorn. A lot of people from Yale will come but also people from the community, local garden clubs, kids from schools or local college students.

The other program I've participated in is Passage, a work integration program here at Yale that helps students with emotional disorders or autism spectrum disorders from public schools get into college. One of the teachers approached me and asked if they could do lab work, which is perfect – everybody can grow *Arabidopsis*. For the last 9 years or so, I've had students who have autism or health impairments work in the lab for about a year before they move on to college. It's been really rewarding because it gives people in the lab a chance to mentor others, and it gives us a chance to work with people who may not be well-represented in science. The students have gone on to do science degrees or become science-related professionals.

Finally, what would Development readers be surprised to find out about you?

I'm not that surprising! I have plant-related hobbies: bonsai with my kids, landscaping. Also, I still skateboard, even though I'm 45 years old.

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