© 2020. Published by The Company of Biologists Ltd | Development (2020) 147, dev191650. doi:10.1242/dev.191650

INTERVIEW

An interview with Irene Miguel-Aliaga

Katherine Brown*,‡

Irene Miguel-Aliaga is Professor of Genetics and Physiology at Imperial College London, and Section Chair and Programme Leader at the Medical Research Council London Institute of Medical Sciences (LMS). Her laboratory is interested in metabolism, organ plasticity and 'continued development', using mainly *Drosophila* to explore how and why adult organs change in size or function in response to environmental or internal challenges. Irene recently joined the Development team as an Associate Editor, focussing on the field of metabolism in developmental and stem cell biology. We caught up with Irene at her lab in London to find out more about her background and work – and her perspective on this emerging area of developmental biology.

Let's start at the beginning – what first got you interested in science?

I wasn't one of these kids who knew they wanted to be a scientist when I was really young. I always liked animals – I guess I found nature very exotic because I grew up in a very urban environment in Barcelona. As I got older, it was mainly reading that got me into science – I was a bit of a bookworm. I was inspired by the adventures of primatologists such as Jane Goodall or Dian Fossey, the poetry of Carl Sagan's Cosmos, and the fun and surreal cocktail of invention, engineering and sociology of some of Boris Vian's novels. So I went on to do biochemistry as an undergrad in Barcelona, and there I got very interested in molecular biology and developmental biology.

You came to the UK from Spain for your PhD – what prompted your decision to leave your home country at that early stage in your career and how did you find it?

I'd like to say that I really wanted to do a PhD and Oxford was the best place for me to go, and in hindsight that's true, but actually it was really that I wanted to live abroad for a year and do something useful while experiencing another country. So I applied for various things, and one of them was a La Caixa scholarship that was for one year's research abroad. Originally, I was only going for one year, but when I started in Kay Davies' lab in Oxford, it so happened that she had funding for a PhD and asked me if I wanted to take it; I said 'sure'! And I never went back.

I was always an anglophile growing up: I was into British indie music and The Red Wedge (a left-wing music collective that tried to engage young people in politics). I was even attracted by the weather – growing up in sunny Barcelona, the idea of rain and fog was amazing! So I really wanted to come to the UK and there wasn't much of a culture shock when I came here. The bigger issue was the language – I'd learned English at school but when you come to the UK you realise that the English you've been taught isn't really the same as the English people speak! So it took a couple of years to adjust to that. And I'm still here, so clearly it was a good decision.

In your PhD, you used a range of model systems: *C. elegans*, cell culture and *Drosophila*. Since then, you've worked almost exclusively with *Drosophila* – though you're also doing some mouse work these days. Why the fly?

When I started my PhD, Kay was exploring the idea of establishing invertebrate models for human disease. She'd been working on neurodegeneration for many years but was keen on leveraging flies and worms, and I was the guinea pig for that project. I really liked working with flies and have stuck with them ever since. For what we're doing now, I find flies really powerful: temporal and spatial control of gene expression or protein function are key to distinguishing cause from effect in inter-organ signalling, and flies are arguably the most versatile system for this kind of approach.

You started out in your PhD and postdoc working on neural development, but now have a strong focus on physiology and metabolism. How did that transition come about?

As a postdoc in Stefan Thor's lab, I was looking into how neurons become different from one another, trying to understand the transcription factor networks that determine cell identity. I identified neurons that innervate the gut and I remember thinking at the time that we knew very little about them and I was interested in finding out more – initially from a developmental perspective. I then did a second postdoc with Alex Gould, and the general interest of the

*Executive Editor, Development

‡Author for correspondence (katherine.brown@biologists.com)

K.B., 0000-0001-9110-8276

Development (2020) 147, dev191650. doi:10.1242/dev.191650

lab there was more about metabolism and physiology, so I started thinking about these neurons more from a physiological perspective – what are they actually doing? And this was really the question that I wanted to address when I started my own lab.

Studying these neurons also made us realise that the intestine is very plastic, so we became more broadly interested in the bidirectional crosstalk between the neurons and the gut tissue, and in the crosstalk between development and physiology. You make an organ during development but that's not the end of the process. This organ communicates with others in the body, and receives input from the environment (such as nutrient status), and these inputs change the organ – so the developmental processes continue into adulthood. I find the intersection between developmental biology and physiology very interesting – and we need to break down the barrier between these fields.

Some of your recent work has looked at the impact of sexual identity on stem cell behaviour and animal physiology. Can you tell us a bit more about this work – and do you think that male and female cells are more different than we've previously appreciated?

Absolutely – I think we've ignored these differences for many years. In terms of our work, initially we found that the stem cells of the gut 'know' intrinsically whether they're male or female – based on their sex chromosomes – and this affects their behaviour: the female cells divide more often than the male cells. What was striking is that this phenomenon is adult reversible – we could masculinise or feminise the cells in the adult in a cell-intrinsic way and change their cell division pattern. This sexual dimorphism is important physiologically: proliferation-prone female stem cells allow the female intestine to re-size during reproduction. But it also makes the female cells more vulnerable to tumorigenic insult, so there's a trade-off between the built-in plasticity and the risk of tumorigenesis.

More recently we've also been doing some work that points to extrinsic regulation of sexual identity. Historically, it has been assumed that, in *Drosophila* and other invertebrates, sex determination is a cell-intrinsic process. But I think now there's evidence that, in both vertebrates and invertebrates, there are also extrinsic factors that contribute to sex identity of cells. So a cell may be integrating information both from its own chromosomes and from external signals like hormones or – as we've shown – a cytokine that relays 'maleness' from the male gonad to the gut. The crosstalk between the gut and the gonad happens in a portion of the gut that's next to the male gonad, so this raises the possibility that the relative position of internal organs matters – that there's some logic in the spatial arrangement of organs within the body wall cavity that helps to define organ physiology. In the case of the cytokine signalling from the male gonad to the gut, this induces a sex-specific difference in metabolism so that the male gut sends citrate back to the gonad to regulate spermatogenesis. I find this a really intriguing example of bidirectional crosstalk that depends on spatial organisation, and we're very interested in understanding more broadly the different ways (hormonal, neuronal, metabolic and so on) in which inter-organ crosstalk can be spatially confined.

You recently joined Development as an Associate Editor – to handle papers on metabolism in developmental and stem cell biology. Can you tell us why you decided to get involved and what your role entails?

There were two reasons why I was keen to get involved when James invited me to join the team. One is that Development is a journal that I've read since I was a PhD student and have always respected. I really value the fact that it's a community journal that gives its profits to the community – I've benefited personally from the funding The Company of Biologists provides for meetings – so now I have the opportunity to give something back and that's really great. And then the second reason is that I just find this area of metabolism and development fascinating as an emerging field, and I think I'll really enjoy reading and handling papers on this topic.

In terms of what the role entails, I will be handling manuscripts in the metabolism field in the same way that other editors on the journal work. But I also see my role as promoting Development to researchers working in the metabolism field and trying to grow this area in the journal. So I'd encourage anyone with a story they think might be suitable for the journal to consider submitting, and to get in touch if they want to discuss the paper further!

What kinds of research in this area do you find particularly exciting right now?

I think there are two things I'd say here. The first is the idea that metabolites can be instructive during development – that cell fate transitions or organ formation can be dictated by a metabolic change. 10 years ago, if you pulled a metabolic gene out of a screen, you'd think it was some boring housekeeping gene and you wouldn't look at it any more. But we're now beginning to learn that all these processes we used to think of as 'housekeeping' differ between cell types and are instructive for development. So the idea that there are specific metabolic transitions and particular metabolites that affect developmental events is really fascinating, but we know very little about it. There's a lot still to understand both about the mechanisms by which metabolic changes regulate development – through epigenetic modifications, signalling and perhaps other routes we've not thought about yet – and about the functional consequences of those changes.

Second, I'm very interested in the idea of continuing development throughout life: developmental biology isn't the same as embryology – it doesn't end when the animal is born. There is a lot of organ remodelling after birth and all the way through adult life, involving both adult progenitors and their postmitotic progeny. I think much of this will be dictated by external or systemic inputs – nutrition, reproductive state and so on – so there are many possibilities for interaction between nutritional state, metabolism and developmental processes that we still have to learn about.

Metabolism is much more dynamic than had previously been recognised – both across space and time – and we don't have all the tools we need to look at this, particularly not at the 'omic' scale

Are there tools or resources that we need to develop to really help push this field forwards?

One major issue we have in the field is annotation of metabolites, especially in non-mammalian species. We still know relatively little about what metabolism looks like in some of these systems, and we tend to make inferences based on what we know in mammals. But there may be differences between, for example, *Drosophila* and mammals. More generally, I think there's increasing recognition that – contrary to what I believed at the end of my undergrad – our knowledge of all these metabolic

Development (2020) 147, dev191650. doi:10.1242/dev.191650

pathways is incomplete and there may be things happening that aren't in the text books.

Another thing is that metabolism is much more dynamic than had previously been recognised – both across space and time – and we don't have all the tools we need to look at this, particularly not at the 'omic' scale. Some of the developments in imaging mass spectrometry – to visualise metabolites with spatial resolution – are really exciting and are rapidly improving, but this is still very challenging in small organisms like *Drosophila*. We can circumvent this for individual metabolites using genetically encoded sensors, but you can only do that in a targeted way. Ideally we'd love to be able to do metabolomics with spatio-temporal resolution but we're not there yet.

Finally, it's really challenging to dissect out direct versus indirect effects of manipulating metabolic pathways. So not only do we need to focus on both loss- and gain-of-function approaches, but I think we probably need to spend more time just looking at and documenting what's happening under normal conditions, which can be as revealing as genetic manipulations.

If you want to do something about diversity and inclusion…you need to capture kids from under-represented minorities early

You've done quite a lot of public engagement over the course of your career. Why do you think it's important to reach out beyond the scientific community, and what do you get out of these activities?

It definitely works both ways. Scientists aren't the only people that can engage with the public on scientific matters, but we are really qualified to do so – so it makes sense for us to get involved. I find it very enjoyable to see that you might be able to motivate people to get interested in science – hopefully the next generation of scientists. And if you want to do something about diversity and inclusion, which I'm quite passionate about, then outreach events for young people are important. You need to capture kids from under-represented minorities early to encourage and empower them to stay engaged with science while they're still at school.

And for me, I've learned a lot about presenting and communicating my work more clearly from engaging with people that know nothing about it – you know that your jargon won't work, and you have to extract what really matters rather than getting distracted by the details. When you talk to someone who doesn't know anything about your area, you really have to think about why you're doing what you are doing – and that's something you don't always spend much time on.

In 2018, you were awarded a Suffrage Science Women in Science award. What are these awards, and what did it mean to you to receive it?

These awards were founded in 2011 by Mandy Fisher here at the LMS but have since become international. They're awarded to women for their scientific achievement but also for their ability to inspire others. What's nice is that you become part of a network: when you get the award, you receive an heirloom – inspired both by science and the suffragette movement – and you keep it for 2 years and then pass it on to someone that you find inspiring. So you are part of a pedigree of women that all become connected.

More generally, what do you think are the challenges facing women and under-represented minorities in science at the moment?

I think the main challenge is their environment. A major limitation for women and under-represented minorities is that they feel like aliens in an environment where there are few of them, and this can lead to marginalisation. Especially as I become more senior, I find more and more that I go to meetings where I'm the only woman, or the only person who doesn't have white hair, so inevitably you feel a bit like you don't belong.

I also worry that there's an excessive focus on mentoring, leadership and confidence-building for women. Although well intentioned, these can make you feel like there's some kind of deficiency with the way you are, and actually there's nothing wrong with women as they are. Instead, we need to broaden our definition of a leader and of success to ensure that it is not too narrow-minded, and is more encompassing of different approaches, personalities and lifestyles.

The other issue I see is that there are different expectations placed on men, women and under-represented minorities, which may result in differential support. For example, I have been often asked whether my family is OK with me working long hours and travelling lots, and so on. Differences in the environment that female and underrepresented scientists experience can make them doubt their ability (and desire) to succeed. So, going back to 'confidence-building for female scientists', the widely held view that female scientists are 'lacking in confidence' is over-simplistic: they may also be under more scrutiny, or think more about how to juggle their work and home responsibilities and keep everyone happy – which is arguably a good thing!

What would be your advice to young researchers starting out in your field today?

This is difficult, because everyone is different and would probably benefit from different advice. But I guess that if there's a common thread it's that you should really try to enjoy yourself and have some fun with your work. And if you don't, maybe you should consider other careers. And the enjoyment you get is of course about both the environment and culture of the place you're working in, and about the topic you're studying. I'm lucky – I really enjoy what I do, but it is tough, and if I didn't get that sense of fun and enjoyment, why would I want to go through all the hardship?

Finally, is there anything that people would be surprised to find out about you?

I guess maybe that there's lots of things I'm really bad at – but really enjoy! I'm a lousy writer, a lousy driver (I failed my test several times!) and a lousy saxophone player – I play for my kids but I'm no good at it any more. So I may have had some scientific success, but this goes to show that trade-offs are ubiquitous beyond development and physiology!