© 2023. Published by The Company of Biologists Ltd | Development (2023) 150, dev202441. doi:10.1242/dev.202441

INTERVIEW

An interview with Jonathan Slack

Jonathan Slack is Emeritus Professor at the University of Bath. His research interests have included early development of the *Xenopus* embryo, regeneration of limbs and tails, and attempts to reprogramme other cell types to β cells. In September 2023, Jonathan was awarded the 2023 British Society for Developmental Biology Wolpert Medal, which recognizes an outstanding individual who has made major contributions to the teaching and communication of developmental biology in the UK. We chatted to Jonathan at the European Developmental Biology Congress, where he was presented with the medal, to find out more about his career and his experience writing textbooks and the 'A Very Short Introduction' books on stem cells and genes.

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

Like many others, I was always interested in science from a child. My father was an industrial chemist and I used to read his old chemistry textbooks for fun. I had my fossil collection, knew the major stellar constellations and was good at science at school.

You did your PhD with Ulrich E. Loening at the University of Edinburgh. What did you work on and how was that experience?

My first degree, at Oxford, was in biochemistry. I was interested in development and felt that it would be good to learn how to work with nucleic acids. Ulrich was well known for studies on ribosomal RNA so I did my PhD on this. This was the pre-cloning era of molecular biology and the work was more chemistry than development. I found it rather dull, although Ulrich did teach me to be very organised, clean and tidy when doing experiments.

You then joined Lewis Wolpert's group in London as a postdoc. Can you tell us more about the work you did during that time?

Towards the end of my PhD, I had decided that I did not want to go on working on ribosomal RNA. I attended a lecture by Lewis, given in Edinburgh, and was very impressed by the ability to gain interesting developmental information from some simple grafts combined with model building. So I applied for an MRC Training fellowship to switch direction, and I spent two years in his lab at the Middlesex Hospital Medical School. At the time, most of the lab worked on chick limb development, but I fell in love with the colony of axolotls that lived there, and ended up doing experiments on limb bud determination in axolotl embryos. This involved creating very beautiful double posterior duplicated limbs. Lewis had enormous enthusiasm about all scientific problems and, among other things, he taught me to put the right spin on the work for publication.

You set up your own research group at Mill Hill, London, in the late 1970s, moved to Oxford in 1985 and eventually to the University of Bath in 1995. What did your group focus on?

The Mill Hill institute was a small satellite institute of the then Imperial Cancer Research Fund (ICRF; now part of Cancer Research UK). It had recently acquired a new director, John Cairns, of DNA replication fame. At the time (1976) he believed that almost nothing useful was known about cancer and that developmental biology might offer a way in. He took a gamble by appointing several rather young developmental biologists, including me. In those days there was much less competition than today. You could do a few grafts, accompany the results with a bit of theoretical speculation and publish it in Nature! I continued working on the axolotl limb, focusing on the regeneration of duplicated limbs. I also started up a project on early development. This had arisen from my study of the pre-second world war German embryological literature. I was particularly interested by papers of Yamada, which seemed to show that there was a gradient of something controlling the dorsoventral patterning of the mesoderm in the embryo at the gastrula/early neurula stage.

I didn't really have a 'group' at the time, just one postdoc and one technician. But I was able to publish several papers in what are now regarded as 'flashy' journals and so got tenure at the ICRF at the rather young age of 31. Notable results were the demonstration that there was indeed a dorsoventral signal in the mesoderm of the early amphibian embryo, and that duplicated axolotl limbs showed 'gradient like' behaviour when they regenerated. I also found that the putative 'positional information' underlying pattern regeneration was stable for at least 1 year.

After tenure, I set off on a high-risk, and ultimately unsuccessful, project to discover the glycoproteins responsible for positional

Jonathan Slack's contact details: Department of Life Sciences, University of Bath, Bath BA2 7AY, UK.
E-mail: bssjmws@bath.ac.uk

Development (2023) 150, dev202441. doi:10.1242/dev.202441

information using 2D gels. I was joined by a new postdoc, Jim Smith, to whom I gave the project of repeating Spemann's organiser experiment, but using *Xenopus*, and tracking the fates of graft and host with the newly discovered injectable lineage labels. The paper on this is now a 'JEEM classic'.

Shortly after this, the lease on our building ran out. The ICRF established a new Developmental Biology Unit (DBU) in Oxford, headed by Richard Gardner, to which some of us went. The DBU functioned from 1985-1996, which turned out to be the real 'golden age' of modern developmental biology. In this period, I was able to establish a small group of five or six people and achieved quite a lot in understanding the early development of *Xenopus*. We constructed an accurate fate map using the new injectable cell lineage labels, established the existence of three primary signals controlling formation of the body plan and found that FGF (fibroblast growth factor) mimicked one of the signals. Later, we established that FGFs in the early embryo have several roles, but probably the most important is acting as a whole-body posteriorising signal. Much of this turned out to apply not only to *Xenopus*, but also to zebrafish, chick and mouse.

In 1995, you moved your lab to the University of Bath. What prompted the move and what did your lab work on?

Towards the end of my time at the DBU, I was feeling that early development was becoming quite well understood and that the future lay with organogenesis, particularly using all the new mouse transgenic and knockout lines. I became interested in the development of the pancreas, and set out to learn some basic mouse techniques to investigate it. Unfortunately, at this stage the ICRF ran out of money and closed the DBU. I could have moved to the central London labs, but I did not wish to commute into London, so looked round for another job. I was fortunate to end up at the University of Bath, which enabled me to set up a small developmental biology programme, with labs working on *Xenopus*, mouse and zebrafish. Because of moving to a university, I had to get grants, and I couldn't get a big grant to work on the pancreas, on which I had no previous track record, so the *Xenopus* work continued alongside the pancreas work. At Bath we continued the study of FGFs and their role in *Xenopus* development, and started a new project on the regeneration of the tadpole tail. This ran for about 12 years; we showed that each tissue in the tail regenerates itself, that the muscle came from muscle satellite cells rather than from myofibres, and that Wnt, FGF and Notch signalling were necessary for regeneration. At Bath, I also met David Tosh, who was interested in liver metabolism and development, and had come across the phenomenon of pancreas-to-liver transdifferentiation in copper-deficient rats. This got us interested in the possibility of doing the reverse: reprogramming liver cells to pancreas, and thereby β cells, by overexpressing appropriate transcription factors. This turned out to be difficult, but we eventually achieved some success many years later, in the Minnesota Stem Cell Institute, using a three-gene cocktail in immunodeficient mice.

In 2007 your lab moved to the University of Minnesota – what influenced this decision?

By then I had been head of a large department in Bath for 6 years. I had stepped down from this and I didn't want to be a dean because this involves wall-to-wall committee meetings every day. Moreover, by this time I felt that developmental biology had reached maturity and I was becoming more interested in the applied spinoff: what we call stem cell biology. The University of Minnesota had an opening for a director of their Stem Cell Institute, so I went there.

It was a very interesting time, not least because induced pluripotent stem cells (iPSCs) had just been discovered. As indicated above, I was able to progress work on the reprogramming of liver cells to insulin-secreting cells, and also to start a new project on *Xenopus* limb regeneration, which was later taken into mice by my postdoc Gufa Lin. I also learned a lot about stem cells!

Apart from doing research, you have written several books. Have you always been interested in writing? What prompted you to write your first book 'From Egg to Embryo'?

Yes, I have a background in school and student journalism, and have always found writing easy. In the early 1980s, molecular biologists were becoming interested in developmental problems. But because of my exposure to experimental embryology, I felt they were looking at things in the wrong way, for example focusing on DNA sequences needed for globin gene expression, instead of asking how the body pattern was generated. 'From Egg to Embryo' (Slack, 1983) was a potted guide to experimental embryology for molecular biologists. It also emphasized the importance of theory and model building for understanding developmental phenomena.

You also wrote the textbook 'Essential Developmental Biology', first published in 2001 and now in its fourth edition. How was your experience writing a textbook?

By the late 1990s I felt that modern (molecular-genetic) developmental biology was approaching maturity. This does not mean it is finished, just that many of the main questions have been answered and the main explanatory concepts are generally accepted. This means that it is possible for different people to agree on what should be in a textbook. Before then, there were textbooks of developmental biology, but they varied a lot in the topics they covered and the mechanisms they highlighted. So 'Essential Developmental Biology' (Slack, 2001) was written as a brief guide to the whole of animal development, not just early development, and at an undergraduate rather than a research monograph level. It was intended to be more concise and student-friendly than most other existing developmental biology textbooks. Perhaps inevitably, pressure from the publishers have meant that each edition is bigger and more costly than the one before, although I obviously think it is the best of the available textbooks!

With the field moving quickly, how do you decide when and what to update in each edition?

Usually, the publisher asks for a new edition. I prefer not to do them too often as it is a lot of work, comparable to writing the original edition. I am now retired, but I've continued to monitor the literature. I note down anything I think looks interesting and keep the citation on EndNote and the PDF in my files. If I'm writing a chapter on a specific topic, I would go to my PDFs, read a recent review, track down recent relevant papers and make handwritten notes until it's in my head. Then I'll just write the chapter with reference to my notes. I do find writing comes quite easily.

You co-authored the latest edition of 'Essential Developmental Biology' with Leslie Dale. How has the writing experience changed with another person on board?

Les was my postdoc at Mill Hill and the DBU and I have always got on well with him. He had been professorial Head of Teaching for Anatomy and Developmental Biology at University College London, so had a unique feel for the level of detail appropriate for

Development (2023) 150, dev202441. doi:10.1242/dev.202441

students. We divided up the chapters and critiqued each other's text; it all went very smoothly!

Textbooks contain many visual contents. How do you decide what images and diagrams to include in a textbook?

For the line drawings in the textbooks, I've worked with a brilliant illustrator called Debbie Maizels, of 'Zoobotanica', who specializes in biological images. I would rough out something in pencil and send it to her, then she would draw it in colour to professional standards.

Published images of specimens are trickier. I would say about 15 years ago you could pretty much take what you liked out of the literature, reproduce it and give credit for where it came from, but you wouldn't expect to have to pay any money for it. In the latest edition of 'Essential Developmental Biology' (Slack and Dale, 2022), although many of the images were used in the previous edition, we didn't have the permission to use them again, so we were being asked for hundreds of US dollars for pictures already in the book. We couldn't afford it, so I had to spend a great deal of time finding substitutes.

You wrote 'A very short introduction' books on 'Stem Cells' and 'Genes'. How did you approach writing the 'A Very Short Introduction' books compared with textbooks?

It is very rewarding. These books are intended for the educated lay reader who is interested in the subject and wants a brief and comprehensible guide. To write at this level you really need to understand the material and you need to be able to pick out key topics and anticipate blocks to understanding, which are often invisible to the specialist. Also, there is more impact. These titles have sold many more copies than the grand total of citations for my research work.

For the Stem Cells book (Slack, 2021), I wanted to clarify some of the misinformation out there. Most people who are non-specialists think that stem cells are magic cells – if you have something wrong with you, you can inject some stem cells and you will get better. In the book I had to explain that isn't the case. I also explained the difference between pluripotent stem cells and tissue-specific stem cells, and wrote about the principal clinical applications of stem cells.

For the Genes book (Slack, 2023), it could potentially cover the whole of biology, but I had to get it into only a limited number of pages. Before writing the book, I was very struck that the word 'gene' means different things to different people – molecular biologists consider a gene to be a sequence of DNA encoding a protein. But in other areas of biology, when people talk about genes for certain traits they are thinking of polymorphisms: i.e. differences between individuals at the same genetic locus. In evolutionary theory or sociobiology a 'gene' may be an entirely hypothetical determinant for some trait. I thought that these were important distinctions that people should understand, so I made the centrepiece of the book the concept of the gene and what different meanings the word 'gene' can have. In the second edition, I updated and made a few changes, such as squeezing in the Denisovan DNA, because I thought that was pretty cool!

You have recently received the 2023 Wolpert Medal from the BSDB, which recognises your contributions to science communication and education. What does this award mean to you?

I am delighted to have this side of my work recognised by the award. It is nice for the community to have some awards for teaching and communication, as well as for research.

What is your opinion about the relevance of printed textbooks in this day and age, where information is so readily available online?

Across the board, the hard copy book refuses to die! It is true that we all find a lot of information on the internet these days, but I find it most useful for specific nuggets of data: the biochemical function of a protein or the molecular identity of a mutation. For subject structure and explanation, I think the book remains best, although nowadays it can usefully be provided as an e-book accessible online to the whole institution, rather than as a few copies in the library.

Where do you think the field of developmental and stem cell biology will be in 10 years?

People are finally getting their teeth into the problem of developmental timing, so I hope we see a big breakthrough in that area in the next few years. At some stage there is bound to be a huge public row about human 'embryoids': embryos made from iPSCs that can develop to term if implanted. The people who work on this keep saying it is all about studying human development, but once the public gets to hear of such technology, I expect them to demand its use for reproduction.

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

I have been a Morris dancer since 1987. For the benefit of foreign readers, Morris dancing is a form of English traditional dance usually performed outdoors in groups of six, and often using sticks, bells and hankies. The music is very vigorous and uplifting. People laugh at it, but it is good fun to do. I have been a member of several teams, including one in Minnesota. As well as dancing for a male team, I now play the melodeon for a ladies' team, and also in pub music sessions.

Jonathan Slack was interviewed by Joyce Yu, Online Editor at Development. This piece has been edited and condensed with approval from the interviewee.

References

Slack, J. M. W. (1983). *From Egg to Embryo*. Cambridge: Cambridge University Press.
Slack, J. M. W. (2001). *Essential Developmental Biology*. Oxford: Blackwell Science.
Slack, J. M. W. and Dale, L. (2022). *Essential Developmental Biology*, 4th edn. Hoboken, NJ: Wiley-Blackwell.
Slack, J. M. W. (2021). *Stem Cells: A Very Short Introduction*, 2nd edn. Oxford: Oxford University Press.
Slack, J. M. W. (2023). *Genes: A Very Short Introduction*, 2nd edn. Oxford: Oxford University Press.