

BSDB

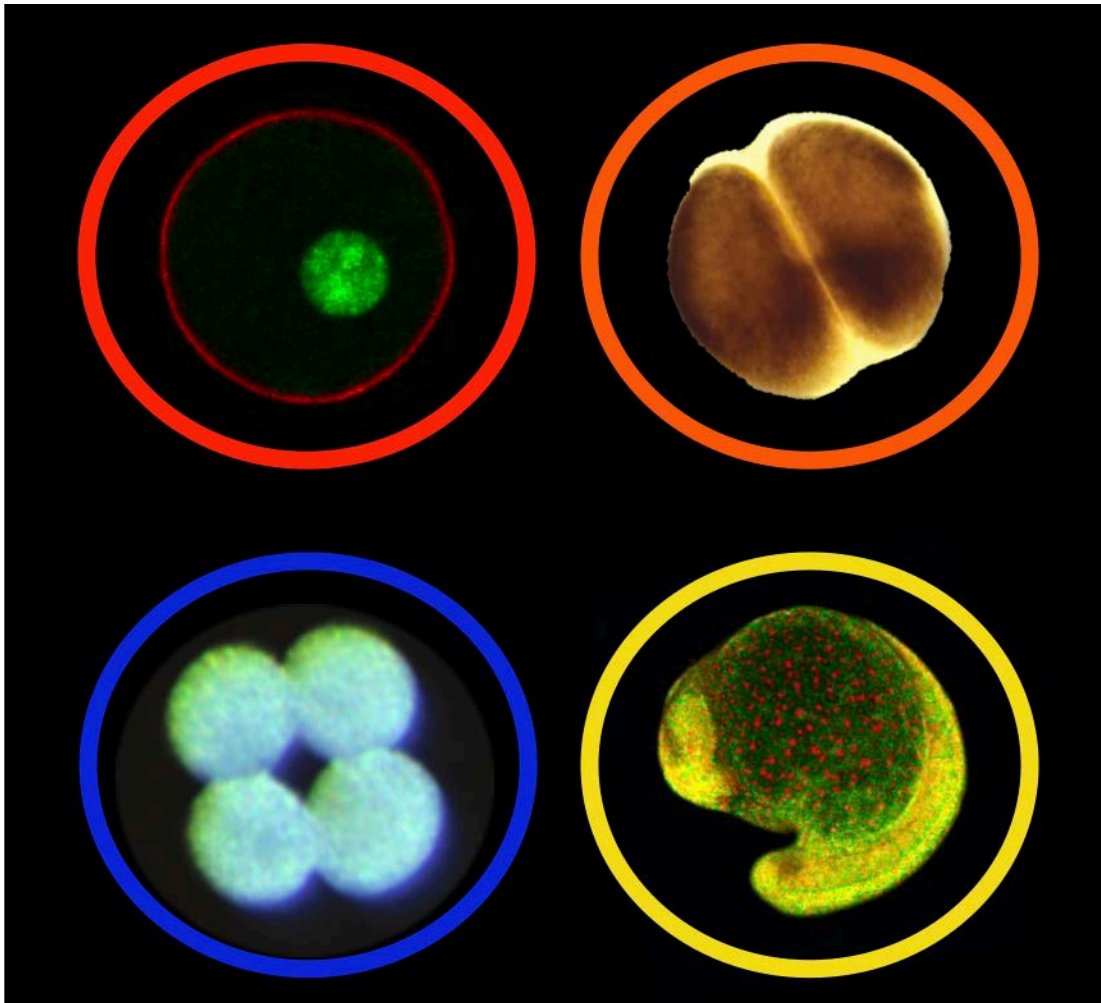
Newsletter

British Society for Developmental Biology

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"The slogan on the 2019 EDBC conference website sits next to an image of neural crest cells migrating, and reads "...moving forward together", and I think this will continue to be reflected in the next meeting to be held in a major European city, in the UK."

Hello everyone, and welcome to the 2020 BSDB newsletter. The aim of these newsletters is to provide a re-cap of society activities over the preceding year, and to continue to build on the **BSDB archive**. This was set-up by our previous communications officer, Andreas Prokop, and makes very interesting reading for those who wish to know more about the history of the society, and of developmental biology as a discipline.

One of the main events of 2019 was the revitalization of the European Developmental Biology Congress (EDBC), hosted in Alicante. It was a very good meeting and was great to see many BSDB members were able to make it. It also offers an opportunity for committee members from European developmental societies to get together, and the discussions were very fruitful. We are very happy to say that it will be hosted within the UK in 2023 and the BSDB will be playing an important role in organizing the next EDBC. The slogan on the 2019 EDBC conference website sits next to an image of neural crest cells migrating, and reads "...moving forward together", and I think

this will continue to be reflected in the next meeting to be held in a major European city, in the UK.

In 1986, the Portuguese Nobel laureate, José Saramago released a novel entitled "A Jangada de Pedra", later released as "The Stone Raft" in English. In it, a story is told where the entire Iberian continent splits off from the European mainland and begins to float off into the North Atlantic Ocean. While some of the people on our island prepare to kit out the Royal Yacht Britannia with new steam engines and a giant lasso over Big Ben, my prediction is that we will still not be shifted all that far with even the greatest of tugboats. As we all know, science benefits the most when divisive walls are broken down, and diversity is always at the core of our interests. Unfortunately, it is also an activity that is at the whim of geopolitical decisions in terms of its funding and hiring structure. This, however, is not true of our scientific societies or the choices we as a community make in sharing and communicating our work. Rest assured that the BSDB is always looking for new ways to improve and increase these

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“Everyone has a responsibility in doing what they can to instigate positive change in their research communities, and in doing so we can exercise inherent skills for which we have been trained as research scientists.”

“It is up to each one of us to use our skills to find solutions that will benefit our teaching and research environments by making them more accessible, diverse and engaged.”

“With so much turmoil around us, it is always helpful to hear from others of how their teaching and research experiences can continue to provide energy and inspiration during challenging times. Huge thanks to the Node and Company of Biologists for spearheading eBSDB and other initiatives that keep us moving while sitting still.”

interactions, and we are always interested in ideas from our membership.

Efforts to increase diversity in academia must run at all levels, within and across borders. Inequality in the representation of people from diverse social, ethnic and economic backgrounds is a continuing problem that is symptomatic of issues surrounding institutional racism, social inequality and bias at the core of our institutions. Everyone has a responsibility in doing what they can to instigate positive change in their research communities, and in doing so we can exercise inherent skills for which we have been trained as research scientists.

1. **Collect data** and do research into how widening participation programmes operate in your environment. Expose yourself to new opinions and first-hand experiences of bias through reading and listening to articles and other sources of information.
2. **Share information** with your colleagues and be open about what you have learnt, even if this feels uncomfortable. If you have found an interesting article/book/podcast/website/video that has changed your viewpoint in a positive way, share it: it will likely impact others in your surroundings too.
3. **Communicate** your research findings to the appropriate institution or group in order to facilitate real change. Contribute to or advocate for existing schemes that you think make a positive impact on widening participation in academia. Where there are gaps in your research communities and institutions, call them out and suggest positive

ways forward based on your research findings.

This is a problem that we all share. It is up to each one of us to use our skills to find solutions that will benefit our teaching and research environments by making them more accessible, diverse and engaged. As communications officer for the BSDB, I aim to use our society to help disseminate and share information about useful initiatives and valuable information for us to continually take action towards widening participation in developmental biology research and teaching. Please keep an eye on website for relevant links and reading material.

We are all struggling to cope with the pressures of working from home and managing the return of researchers to their experiments where possible. However, this strain proves more difficult for some than others and often in ways that aren't easy to detect from the outside. I would encourage you all to keep an eye out for colleagues who might be struggling, we benefit greatly from a strong and positive developmental biology community in the UK and its times like these that test our limits. While it was unfortunate that this year's Spring meeting was cancelled, it was encouraging to see so many of us rapidly engage in online activities. With so much turmoil around us, it is always helpful to hear from others of how their teaching and research experiences can continue to provide energy and inspiration during challenging times. Huge thanks to the Node and Company of Biologists for spearheading eBSDB and other initiatives that keep us moving while sitting still. Please check out their recent announcements in this newsletter.

Benjamin Steventon

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Chair's welcome note by Paul Martin



"Ottoline and I served on the BSDB committee together as young 'uns in the 90s, and if you'd asked me then if she would ever be the Chair, I would have said yes, probably.... but surely not me too!"

"We need to continue enthusing the next generation of young folk who want to ask fascinating and important questions in all of our lovely model organisms."

"...your Society is run by a very conscientious, hard working bunch of folk that largely span the model organisms as well as all of our developmental biology theme areas, and we have fairly good geographical coverage too."

For those of you who don't know, I have taken over the role of Chair of the BSDB from Ottoline Leyser and this is the first of our newsletters where I need to write my Chair's report. Ottoline and I served on the BSDB committee together as young 'uns in the 90s, and if you'd asked me then if she would ever be the Chair, I would have said yes, probably.... but surely not me too! But I am also at heart a developmental biologist and I still love experimenting on various embryo models. I began as a chick embryologist with Julian Lewis but now my lab work on *Drosophila* and zebrafish and a little with mouse embryos, and recently we've even begun doing things with *Arabidopsis* seedlings. We study wound healing and cancer and I like to think of our approach as being "in vivo cell biology of disease".....but frankly, the questions we ask about cell and tissue movements and how cells talk to each other are still, at their core, developmental biology inspired questions.

The next five years for our community will be interesting and could even be a bit of a roller coaster ride. At the moment several things that effect how we do our science are not completely stable. The UK is sadly out of the EU but we were recently part of a fantastic European Developmental Biology Congress in Alicante and we are the hosts for the next meeting in 2023, although we haven't yet figured out where in the UK this will be. Our European colleagues are mostly pretty jealous of how generously our field is funded by the MRC, Wellcome Trust and other charities who are all generally sympathetic to our cause (although there have been some recent hiccoughs); and, of course, the fabulous Company of Biologists (CoB) remain huge supporters of UK cell and developmental biology. Our discipline is constantly morphing and encompasses several very trendy fields including stem cell biology, regenerative medicine and tissue morphogenesis, and while Plan S is a bit of a scary unknown, there are a

good range of classy journals that are outlets for our work. We need to continue enthusing the next generation of young folk who want to ask fascinating and important questions in all of our lovely model organisms. A colleague of mine in Bristol, Helen Weavers, and I, have just taken on a mathematician to model wound healing in fly pupae for his PhD, and he can't get over how beautiful his first movies are. All who do developmental biology must remind ourselves how lucky we are to be working with such aesthetically pleasing raw materials. And those who teach 3rd year undergraduate developmental biology courses, thanks, and please keep inspiring our future stars.

When Ottoline mentioned to me that I might replace her as BSDB Chair, she said that the BSDB committee is wonderful....and they do seem to be. I've only chaired one committee meeting so far but I can report to you that your Society is run by a very conscientious, hard working bunch of folk that largely span the model organisms as well as all of our developmental biology theme areas, and we have fairly good geographical coverage too. To those of you coming to our **annual Spring meeting in Warwick** please come to our AGM and meet the committee and see (and influence) how we operate. This year we will need to take on two or three new committee members and so any of you feeling community spirited please offer yourselves up. Another reason to come to the AGM is that Jim Smith (who was Chair of the BSDB when Ottoline and I were first on the committee), has agreed to come speak to us with his Wellcome Trust hat on and talk us through his thoughts about directions for our community and answer questions from the floor.

I am keen to be a good ambassador for our community during the time I am Chair of the BSDB. Tell me if you have concerns about the field and/or if you have thoughts about what needs doing.

Introducing the new BSDB committee members



Tom Bennett, University of Leeds
<https://tombennettlab.org/>

“...the majority of his work has focussed on the question of how plants are able to coordinate the growth and development of distinct organs in both space and time, and over long distances (up to 120 metres in some trees).”



“His new group at Manchester is now investigating how newborn neurons repolarise following apical abscission, and how this repolarisation leads to initiation and maintenance of axon extension in response to signals from the surrounding tissues.”

Tom is a plant developmental biologist, currently leading a research group at the University of Leeds. He has worked on a variety of developmental systems, including the patterning of the root cap, a small but wonderful tissue that Darwin compared to “the brain of one of the lower animals” (rather unflatteringly for all concerned). However, the majority of his work has focussed on the question of how plants are able to coordinate the growth and development of distinct organs in both space and time, and over long distances (up to 120 metres in some trees). Plants have plastic and continuous development, which acts as both a response and solution to the environmental conditions the plant finds itself in. The plant must carefully balance its investment in the growth different organ types (roots, shoots, leaves, etc.) to acquire resources from both the soil and the air, in order to keep growing and ultimately reproduce. The ability to coordinate growth in space and time is thus absolutely key to the development of plants, but to achieve this plants use a staggeringly small number of signalling molecules, which makes it very difficult to understand how any specificity is achieved. Tom’s research is thus aimed at understanding how complex developmental patterns can emerge from such a simple communication system.

Raman Das, University of Manchester

Raman Das is an MRC Career Development Fellow at the University of Manchester. He did his PhD with Stuart Wilson and Marysia Placzek at the University of Sheffield, where he developed a system to perform RNAi-mediated knockdown of gene function in chick embryos. He then applied this system to carry out a screen for cadherin gene function in the developing spinal cord. His PhD was followed by postdoctoral training with Kate Storey at the University of Dundee, where he developed innovative methods to perform live imaging of neuronal differentiation in the developing chick spinal cord. This resulted in the discovery of apical abscission, which mediates acute loss of cell polarity in differentiating neurons, allowing them to delaminate from the neuroepithelium. His new group at Manchester is now investigating how newborn neurons repolarise following apical abscission, and how this repolarisation leads to initiation and maintenance of axon extension in response to signals from the surrounding tissues.

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Meeting Officer's report by Sally Lowell



"There was even an online version of the legendary BSDB party in which developmental biologists across the land danced in their kitchens to the sounds of our collaboratively-built playlist. It was a lot of fun."

"...this year we introduced BSDB Childcare Grants to provide flexible financial support to enable people with caring responsibilities to attend BSDB meetings, including attendance at remote meetings."

We had a fantastic Spring Meeting planned for this March so it was with heavy hearts that we announced that the meeting would be cancelled because of Covid-19. Our spirits were soon lifted by an email from the team at Company of Biologists & Development proposing some innovative ideas to maintain at least some aspects of the meeting online. And so was eBSDB born. We are very grateful to Katherine Brown, Seema Greewal, Alex Eve & James Briscoe of Development, Mate Palfy of PreLights, and especial big enormous thanks to Aidan Maartens of The Node. They all helped us to pull together an interactive and fun collection of events at VERY short notice, including online discussion of posters, mini-talks & tweetorials, medal announcements made with the help of our Chair's rather lovely dog, and an image competition. There was even an online version of the legendary BSDB party in which developmental biologists across the land danced in their kitchens to the sounds of our collaboratively-built playlist. It was a lot of fun.

We also owe a big thanks to the people who worked so hard to put the original meeting programme together: Clare Baker and Tanya Whitfield from BSDB, Stefan Hoppler and Aziz Aboobaker from GenSoc, and Postgrad Reps, Jessica Forsyth (BSDB) and Emily Baker (GenSoc). We are delighted that almost all the speakers have agreed to speak at next years Spring meeting. It remains to be seen what format that meeting will take....

Even before Covid we had been thinking hard about how we might adapt our conferences to be more sustainable in response to the climate emergency. Covid has of course accelerated those

discussions. We are, for example, exploring hybrid models for conferences that preserve social interactions but cut down as much as possible on air travel. I'm always happy to get feedback from BSDB members on these matters so please feel free to email me at meetings@bsdb.org with thoughts or suggestions about the future of BSDB meetings.

Our Autumn meeting this year was to be a rather special joint meeting with our pals at the International Society for Differentiation on the topic of "Deciphering Cellular Decision-Making Across Scales". This has now been postponed for TWO YEARS to 2022 because we did not want to compete with the ISDB, which is planned to take place in October 2021 in Portugal.

Peering into the more distant future, I see we'll be back with the BSCB for a joint Spring meeting in 2022. I'm also pleased to announce that in 2023 the BSDB will be hosting the next meeting of the European Congress for Developmental Biology. Plans for the format of these future meetings, and plans for our other Autumn meetings, are all currently up in the air for obvious reasons but we'll let you know when our plans become clearer.

And finally... this year we introduced BSDB Childcare Grants to provide flexible financial support to enable people with caring responsibilities to attend BSDB meetings, including attendance at remote meetings. We've also adapted our usual conference grants so that they can now be used for costs associated with attending remote conferences. Please check out the "Grants" section of our website for more info on all our funding schemes.

Graduate Representative's report by Jessica Forsyth

"Our main focus for the meeting was organising an interactive, informal careers workshop to offer our members the chance to speak to people inside and outside of academia and find out how they ended up where they were today."

"Each table leader gave a single, key piece of advice to the room, these varied from how to manage the work life balance to following what you're interested in. This session was a pleasure to organise and help run, from meeting the table leaders to speaking with attendees about what they took from the session."

In 2018 I was elected as the Graduate Rep for the BSDB, so this means I'm about to complete my second year as rep for this society! I have no idea where the time has gone, but I have thoroughly enjoyed helping organise events for the spring meetings along with maintaining our social media and am looking forward to the upcoming year!

Last year was Charlotte and I's first year helping organise the student led events at the Spring meeting and we co-organised these along with the BSCB representatives- Gautam Dey and Joyce Yu. It was fantastic working alongside them and a brilliant way to ease ourselves into the craziness that ultimately ensues with organising events.

Our main focus for the meeting was organising an interactive, informal careers workshop to offer our members the chance to speak to people inside and outside of academia and find out how they ended up where they were today. We can't thank our table leaders enough, with such a broad representation from different fields of work, the event really inspired me and others and showed the huge diversity of

careers developmental biology can lead to. The session was concluded by a quick-fire advice talk. Each table leader gave a single, key piece of advice to the room, these varied from how to manage the work life balance to following what you're interested in. This session was a pleasure to organise and help run, from meeting the table leaders to speaking with attendees about what they took from the session. Thanks to everyone for attending and making this such a valuable experience for all.

The Sunday evening of last year's meeting brought us the return of the Student Social Pub Quiz. The balloon sculptures were all fantastic (despite not all being the tallest!) and the debates during the music round would rival even the most heated of lab meetings! I think watching people agonise over the songs and the link between them was even more fun than participating in the quiz. Well done to our winners and commiserations to the losers- I mean lucky winners of BSDB wooden spoons!



'Quick-fire' advice session at the end of the Careers Workshop from our fantastic table leaders representing various career paths.



Last place prizes from the BSDB Student Social.

With such a great start into our roles as reps for the BSDB, we have been working on our website (www.bsdbpostgrads.com), and making sure there's plenty of resources available for you. It has had a complete makeover and we still want more

"If you want to be featured on our website, either tweet us (@bsdbgradstudent), direct message us on Instagram (bsdb.graduates) or contact us through our webpage."

"Due to ongoing events we had to diversify how we delivered the workshop and held our first online Twitter careers workshop (great opportunity to have a constant supply of tea during the 'conference')!"

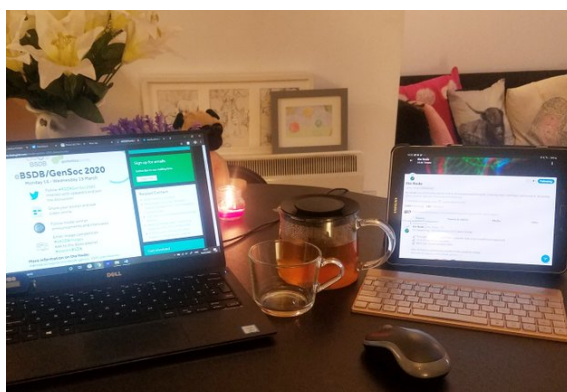
images to show off our members' work. If you want to be featured on our website, either tweet us (@bsdbgradstudent), direct message us on Instagram (bsdb.graduates) or contact us through our webpage.



Website makeover

This leads me nicely onto our newly created Instagram account. We want to be able to share all of your beautiful confocal images, images from conferences, and proud poster pictures! Follow us on Instagram and tag us in your pictures (we may even repost them or use them on our website)!

This year we were due to host the Spring Meeting with GenSoc and so we



Setup for the #eBSDB meeting, constant tea supply at the ready!

had been working with the reps from GenSoc to organise another Careers Workshop with new table leaders representing different career paths. Due to ongoing events we had to diversify how we delivered the workshop and held our first online Twitter careers workshop (great opportunity to have a constant supply of tea during the 'conference')! We showcased some of our fantastic table leaders ranging from editors at popular journals to early career researchers who chose to leave academia and pursue their research elsewhere.

We also held our first ever careers poll. Anyone on the #eBSDBcareer hashtag could vote- meaning we got a fantastic range of votes. First we asked what is the most important skill obtained during a PhD. Over 50% of you said *perseverance* was the most important. We also asked what people thought the most important skill was for securing a job inside of academia. This was far closer with votes for all options: knowledge of the field (44.4%), practical skills (11.1%), people/leadership skills (22.2%) and presentation skills (22.2%). Finally we asked the same question but for securing a job outside of academia, surprisingly no-one said that knowledge of the field was the most important skill- showing you don't need to be an expert in the field before perusing your chosen career, you keep on learning!

Although the Spring Meeting wasn't quite as we had planned, we had a great time putting together the bios of our fantastic table leaders and seeing all the #eBSDB tweets coming in. Thanks to everyone who helped this happen and kept our 'meeting' feeling as busy as normal!

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"I am pleased to be writing my first report as Treasurer and know that I have big shoes to fill, since Prof. Chris Thompson maintained the finances exceptionally during his term."

"...our Society's income exceeded our expenditure by almost £9,000. This figure is positive for several reasons, the main one being that in 2019 we did not host an autumn BSDB meeting in the UK. Instead, the European Congress for Developmental Biology took place in Alicante, further strengthening our UK-European ties."

"Our own expenditure on travel grants (£42,570) was higher than the income the Society received from its membership (£35,145), and was possible because our investments continue to perform well, thus allowing us to provide increased funding in our core areas."

I am pleased to be writing my first report as Treasurer and know that I have big shoes to fill, since Prof. Chris Thompson maintained the finances exceptionally during his term.

The Society remains vibrant with 1321 verified members at the end of July 2019, meaning a steady maintenance of our membership, despite the challenging environment for securing funding for recruitment of students and postdocs to labs in the UK and worldwide. This membership consists of around 871 full and 450 student members. The financial situation of the Society remains in good shape and this has allowed us to continue our activities to promote developmental biology, described below.

Report on the financial year 2018-19

As shown in the accompanying provisional accounts for the Society for the period August 2018 - July 2019, this last year has seen us invest heavily in activities supporting the community. Despite this, our Society's income exceeded our expenditure by almost £9,000. This figure is positive for several reasons, the main one being that in 2019 we did not host an autumn BSDB meeting in the UK. Instead, the European Congress for Developmental Biology took place in Alicante, further strengthening our UK-European ties. Therefore we did not invest up front in set-up costs, as we normally would for our autumn meeting. Instead, we contributed an additional £8,000 in travel grants to this meeting, which are billed in the next financial year. Additionally, Company of Biologists (CoB) Principal Investigator grants are not synchronised with our financial year, but the remaining amount has all been allocated.

The Society awarded 67 travel

grants to allow student and postdoc members to attend the BSDB Spring meeting 2019 in Warwick (£33,115) as well as travel to the autumn 2018 meeting (19 awards, £8,000). In addition, due to the support of the CoB PI Grants, we were able to open up funding, allowing us to award 9 grants to PIs for the spring meeting. This enabled PIs with little funding, or with a primary focus in teaching developmental biology, to attend our flagship meeting. A further 13 CoB PI grants were awarded for international conferences (total £14,300) and the remaining funds were allocated by the end of the calendar year. In addition, we are continuing to award the Dennis Summerbell Award to recognise a talented postdoctoral scientist in developmental biology, providing support for travel to, and registration for the autumn meeting.

Our own expenditure on travel grants (£42,570) was higher than the income the Society received from its membership (£35,145), and was possible because our investments continue to perform well, thus allowing us to provide increased funding in our core areas.

The sum received from the Company of Biologists is essential for the running of the Society. The block grant (£35,000) helps us to support the running costs of meetings in spring and autumn, and Gurdon CoB Summer Studentships. In order to remain competitive and to ensure we attract the best students, these studentships were again funded at a slightly higher rate (£16,000 total). We also receive £37,500 to spend on CoB/BSDB travel awards to help towards the costs of our members' attendance/travel to overseas meetings. In total, 71 CoB/BSDB travel awards were made in 2018-19 (£36,695), reflecting the high demand, with awards granted to all eligible applicants. Finally, we were

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"...the Society continues to have a healthy reserve, allowing us to cope with unforeseen events, such as a pandemic, that led to the cancellation of our spring 2020 meeting and can result in general financial instability, which is likely to affect future return on our investments."

also grateful to receive a dedicated award (£5,000) to support travel to practical and training courses, which was awarded across 6 eligible applicants to attend courses in the USA, Japan and Europe. These have proven very popular, and have allowed us to fund travel at a higher amount than normal, which is necessary given the normally prohibitive costs of these courses.

Future Plans

Although from the accounts it appears that our income was greater than expenditure, this was planned for and approved by the committee (see above). Furthermore, the Society reserves have actually risen slightly during the reporting period, due to the continued good performance of our investments. It should be noted that our ability to maintain such a healthy balance on current expenditure is also due to the great efforts of our committee members and conference organisers, who strive to raise income via sponsorship and keep costs under control. Consequently, we received some return from the autumn meeting in 2017, as well as from the spring 2018 meeting. As a result, the Society continues to have a healthy reserve, allowing us to cope with unforeseen events, such as a pandemic, that led to the cancellation of our spring 2020 meeting and can result in general financial instability, which is likely to affect future return on our investments. Our overall solid financial health means that we will continue to invest in new activities and can do this without any significant threat to the core business of the Society.

In light of the financial buoyancy of the Society we are continuing to promote developmental biology in the UK. We will continue to award undergraduate bursaries to attract students into developmental biology laboratories over the summer vacation with the aim of setting them on track for future PhDs. Previous sources of funding for these sorts of

activities have come under severe strain and there is a fear that fewer undergraduates are considering developmental biology as a career option. In honour of the achievements of our pre-eminent UK developmental biologist, these bursaries are named Gurdon CoB Summer Studentships. Secondly, to ensure that our meetings remain successful and continue to attract top scientists from around the world, we have allowed for an increased investment in our meetings of £30,000 over the next 5 years. This will enable us to keep the cost of the meetings down (and thus promote attendance), whilst ensuring that we can meet increasing travel costs for speakers.

Company of Biologists Block

Grant: We will use the Society Block Grant to allow us to run the Society's activities, to subsidise our successful spring and autumn meetings, and to award graduate student prizes. This allows the Society to use its own funds to finance travel grants mainly for our younger members to attend BSDB meetings. Our spring and autumn meetings continue to be popular and we are grateful for the CoB funding, which allows us to cover speaker expenses and other administrative costs, and so keep down the registration costs to encourage wider participation from less well funded research groups. Last year our spring and autumn meetings depended on support from CoB and our projected costs for next year include £25,000 for meetings and £16,000 for our summer studentship scheme.

Company of Biologists Travel

Grants: The CoB has generously provided an additional grant that we administer to allow the provision of awards to our members to travel to overseas meetings and courses or on laboratory visits (£37,500). Demand for these awards remains high as outlined earlier. At present, we award grants which cover around 40% of the costs requested per applicant, with applicants covering

remaining costs from other sources. These awards have enabled young scientists to attend a wide range of meetings and courses. We receive very positive feedback from the grant recipients and demand remains at a high level. All awardees are strongly encouraged to acknowledge CoB support at these meetings in talks or posters. We are also excited that the CoB PI Support Grants (£20,000) and Practical Course Grants (£5,000) are being fully utilised, that allow us to dedicate greater levels of

funding for PI travel and training. In this tough funding climate, we can only see this demand rising. Furthermore, we have seen an increase in the number of applications for expensive residential practical courses, a sign of the integration of new methodologies and interdisciplinary nature of developmental biology research. We are therefore happy to administer these awards in 2019-20, as we see them as fundamental for continuing the success of developmental biology research in the UK.

The Waddington Medal 2019



"Here we introduce the 2019 winner Kate Storey who won the 2019 Waddington medal for her outstanding work in understanding the fundamental processes that control neural differentiation in vertebrate development."

"...Kate has been able to gain substantial insights into the fundamental and conserved processes that regulate vertebrate neurogenesis. Her work has pioneered innovative live imaging approaches for monitoring behaviour and signalling of individual cells within developing tissues."

The **Waddington Medal** is the only national award in Developmental Biology. It honours outstanding research performance as well as services to the subject community. The medal is awarded annually at the BSDB Spring Meeting, where the recipient presents the Waddington Medal Lecture. Here we introduce the 2019 winner Kate Storey who won the 2019 Waddington medal for her outstanding work in understanding the fundamental processes that control neural differentiation in vertebrate development.



Kate was first introduced to the core questions of developmental biology at the University of Sussex. She then started her research career as a graduate student in Cambridge where she already showed originality of thought and direction with an independent project on the neural development of the earthworm. This interest in understanding how a simple nervous system forms was pursued further supported with a Harkness fellowship in Berkeley, California, where she investigated leech development. On returning to UK, Kate switched to studying the development of the vertebrate nervous system where, over

the years, she has made a string of exciting and important discoveries. This work has gained her international recognition in the field of developmental neurobiology and it is this, together with her many contributions to the developmental biology community, that has led to her being awarded the 2019 Waddington medal from the BSDB.

Kate Storey is now the head of the Division of Cell & Developmental Biology and Chair of Neural Development, in the School of Life Sciences, at the University of Dundee in Scotland. She investigates cellular and molecular mechanisms regulating neural differentiation in chick and mouse embryos as well as in mouse and human embryonic stem cells. By combining the advantages of each of these experimental systems, Kate has been able to gain substantial insights into the fundamental and conserved processes that regulate vertebrate neurogenesis. Her work has pioneered innovative live imaging approaches for monitoring behaviour and signalling of individual cells within developing tissues. These approaches have led to discovery of a new form of cell sub-division, named apical abscission, as well as providing insights into cell signalling dynamics that underpin asymmetric cell division. Not only is this work an excellent example of what can be learnt from observing cell biology within its normal context *in vivo*, it also pointed to new mechanism by which signalling is regulated during differentiation. Understanding how the dynamics of neuronal specification and

"Her discoveries have led to a programme of work that highlights the very best of developmental biology and continues to be an inspiration for young researchers entering the field."

"Kate is seen as a leader in the field and has been prominent in promoting developmental biology in the UK and beyond."

"In addition to her scientific achievements, Kate is known for her contributions to promoting science to a wider audience world-wide through a unique collaborative project with her sister Helen, a fashion designer. In this project, key developmental processes served as inspiration for designing textiles and dresses to chronicle the emerging human embryo."

differentiation is controlled during early development is a continued theme in Kate's work.

Her earlier work showed that an interplay between FGF, Wnt and Retinoic Acid signalling is a fundamental signalling switch regulating the onset of neural differentiation. More recent findings have now linked a component of this, FGF/ERK signalling, to molecular machinery directing chromatin accessibility at neural genes. A further essential aspect of this discovery is in the provision of a mechanism by which the timing of neural differentiation can be coordinated with the progressive generation of somites within the paraxial mesoderm. Such work emphasises the ways in which developmental biologists can learn from studying processes from the sub-cellular level, through to the tissue and whole embryo level. Her discoveries have led to a programme of work that highlights the very best of developmental biology and continues to be an inspiration for young researchers entering the field.

Kate is seen as a leader in the field and has been prominent in promoting developmental biology in the UK and beyond. In Scotland, as Head of the Cell and Developmental Division of the University of Dundee since 2010, she has supported developmental biologists at different times in their careers. She has co-organized many scientific meetings including the first chick community wide meeting in 2007, the 2006 BSDB Autumn meeting on signal transduction mechanisms in development and, significantly, an EMBO workshop on spinal cord development that brought the field together for the first time in Sitges (Spain) in 2014. She has organised the Joint meeting of British, Spanish and Portuguese Societies for Developmental Biology 2015; and this year she co-chaired the Academy of Medical Sciences first international meeting on Neural Development in Oxford. Kate has in addition played an important role in the development of the field over the past ten years as a director of The Company of Biologists in particular by initiating and overseeing a series of

interdisciplinary workshops on cell and developmental biology.

Kate was elected to the Royal Society of Edinburgh in 2012 and awarded the MRC Suffrage Science Heirloom Award 2014. She was elected to EMBO membership in 2016 and to the Academy of Medical Sciences 2017. In addition to her scientific achievements, Kate is known for her contributions to promoting science to a wider audience world-wide through a unique collaborative project with her sister Helen, a fashion designer. In this project, key developmental processes served as inspiration for designing textiles and dresses to chronicle the emerging human embryo. The resulting exhibition **"Primitive Streak"** has been seen by over 3 million people. The exhibition was one of eight major achievements identified in The Wellcome Trust's celebration of its first 75 years, being one of the best examples of The Trust's contribution to science communication.

Selected papers:

Kasioulis I., Das, R.M., and Storey, K.G. (2017) Inter-dependent apical microtubule and actin dynamics orchestrate centrosome retention and neuronal delamination. *eLife* 2017;6:e26215.

This paper uncovers novel cytoskeletal architecture that characterises apical neuroepithelial cells. The study demonstrates how this is generated and shows that it is required for neuronal delamination.

Das, R.M. and Storey, K.G. (2014) Apical abscission alters cell polarity and dismantles the primary cilium during neurogenesis. *Science* 343, 200-204

This work identifies a new form of cell sub-division, apical abscission, which takes place as neurons are born and detach from the ventricular surface. This is mediated by downregulation of N-cadherin and actino-myosin contraction and involves loss of apical membrane

and regulated dismantling of the primary cilium. Apical abscission may represent a new mechanism for regulating cell signaling during differentiation: loss of ciliary membrane possessing the hallmarks of active Shh signaling suggests that apical abscission curtails signaling through this pathway.

Patel, N.S., Rhinn, M., Semprich, C I., Halley, P.A., Dollé P., Bickmore W.A., and Storey, K.G. (2013) FGF signalling regulates chromatin organisation during neural differentiation via mechanisms that can be uncoupled from transcription *PLoS Genet.* 2013, 9:e1003614

This paper shows that FGF signalling promotes chromatin compaction at neural genes in the mouse embryo and that this regulation of chromatin accessibility can be uncoupled from mechanisms that direct transcription.

Das, R.M. and Storey, K.G. (2012) Mitotic spindle orientation can direct cell fate and bias Notch activity in chick neural tube. *EMBO Reports* 13(5): 448-54

This paper shows that apico-basally-orientated cell-division generates an apical daughter that becomes a neuron and a basal daughter that elevates Notch activity and divides again in the chick neural tube. The work links asymmetric division to Notch signalling dynamics and identifies a new neuronal differentiation step in which apical cells commencing neuronal differentiation rapidly lose apical complex proteins.

Olivera-Martinez I, Harada H, Halley PA, Storey KG (2012) Loss of FGF-Dependent Mesoderm Identity and Rise of Endogenous Retinoid Signalling Determine Cessation of Body Axis Elongation. *PLoS Biol* 10(10): e1001415 doi:10.1371/journal.pbio.1001415

This paper provides a mechanism for cessation of body axis elongation in the chick. It reveals a sudden and discrete loss of FGF-dependent mesoderm identity gene brachyury in the late tailbud and shows that this is due to breakdown of oppositional signalling between FGF and retinoid pathways.

Delfino-Machín, M., Lunn, J.S., Breitkreuz, D.N., Akai, J. and Storey, K.G. (2005) Specification and maintenance of the spinal cord stem zone. *Development* 132, 4273-83.

Characterizes the stem zone (now known as the Caudal Lateral Epiblast, CLE) of the chick embryo and shows that cells here express both neural and mesodermal genes. The work demonstrates the requirement (but not sufficiency) for FGF signalling for the induction and maintenance of stem zone (CLE) and the differential regulation of Hox genes in the elongating body axis.

Diez del Corral, R., Olivera-Martinez, I., Goriely, A., Gale, E., Maden, M., and Storey, K (2003) Opposing FGF and Retinoid pathways control ventral neural patterning, neuronal differentiation and segmentation during body axis extension. *Neuron* 40, 65-79.

This work describes the discovery of an oppositional signalling switch between FGF and retinoic acid that controls differentiation onset in the body axis. FGF represses differentiation, while retinoic acid attenuates Fgf8 in neuroepithelium and paraxial mesoderm, where it controls somite size, and is further required for neuronal differentiation and expression of key ventral patterning genes.

Acknowledgements: *B.Steventon would like to thank Kate Storey for her contributions to this text, and Alfonso Martinez Arias and Cheryll Tickle for helpful information and thoughts taken from their nomination text.*

The BSDB gratefully acknowledges the continuing financial support of The Company of Biologists Ltd (CoB).

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The Waddington Medal 2020



"We are very pleased to announce that this year's Waddington medal winner is Professor Dame Ottoline Leyser DBE FRS."

"We are also very pleased with the recent news that Ottoline will now be Chief Executive of the UKRI. Congratulations Ottoline, we wish you all the best in this new role!"

"Ottoline's work has resulted in huge advances in our knowledge of hormone action during the control of branching in plant development. Notable contributions include being among the first to exploit the advantages of Arabidopsis as a model species to study hormone action."

The **Waddington Medal** is the only national award in Developmental Biology. It honours outstanding research performance as well as services to the subject community. The medal is awarded annually at the BSDB Spring Meeting, where the recipient presents the Waddington Medal Lecture.



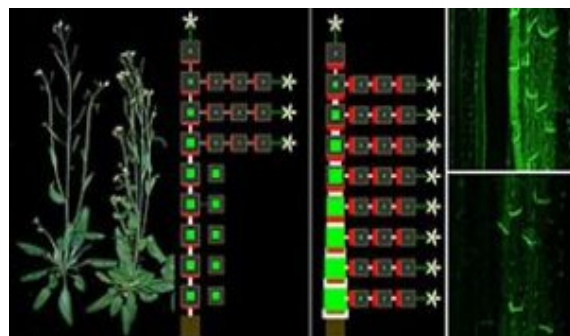
We are very pleased to announce that this year's Waddington medal winner is Professor Dame Ottoline Leyser DBE FRS. After having served on the BSDB committee and then as treasurer (1999-2009), and only recently having stepped down as our chair, her efforts in supporting our community are well known. This prize will add to a number of Ottoline's awards that include listing in the 2017 New Year Honours list as DBE for her services to plant science, science in society and equality and diversity in the sciences. She has also been awarded the Society of Experimental Biology's President's Medal (2000), the Royal Society Rosalind Franklin Award (2007), the International Plant Growth Substance Association's Silver Medal (2010), the UK Genetics Society Medal (2016) and the EMBO Women in Science Award (2017). She is also a fellow of the Royal Society, an foreign associate of the US National Academy of Sciences, a member of EMBO and the Leopoldina. So, we are very pleased to be able to add the 2020 Waddington medal to this list, in recognition of her contributions to UK Developmental Biology research and our community.

We are also very pleased with the recent news that Ottoline will now be Chief Executive of the UKRI. Congratulations Ottoline, we wish you all the best in this new role!

Ottoline's career began as an undergraduate and then PhD student in the Department of Genetics at the University of Cambridge. She then travelled to Indiana University as part of her post-doctoral research before establishing her lab through a lectureship at the University of York in 1994. In 2011 she was instrumental in establishing the Sainsbury lab in Cambridge, where she is now director.

"Ottoline's current research programme remains refreshing and exciting, embracing computational modelling, quantitative traits and selective breeding to give an integrated systems view of the regulation of plant form". Tanya Whitfield and Nick Monk, University of Sheffield.

Ottoline's work has resulted in huge advances in our knowledge of hormone action during the control of branching in plant development. Notable contributions include being among the first to exploit the advantages of *Arabidopsis* as a model species to study hormone action. In doing so, she revealed the mechanism by which the classical plant hormone auxin acts, having identified the auxin receptor in collaboration with Mark Estelle. In addition, she has done pioneering work in understanding the function of MAX genes in controlling branching. Her work exemplifies how a creative application of inter-disciplinary approaches, experimental embryology and genetics can be combined together to understand the fundamental principles of development. In doing so, it represents the very best of developmental biology



“She has also been a great advocate for Science, Women, and developmental biology in the political arena as well as for the general public”. Claudio Stern (University College London) and Enrico Coen (John Innes Centre).”

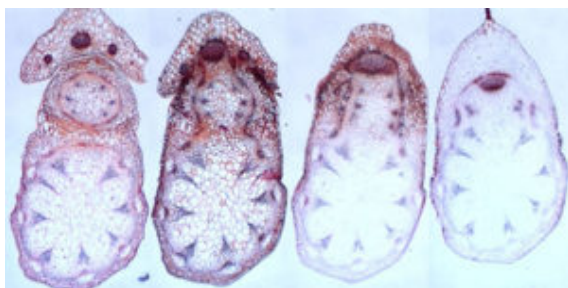
“Ottoline continues to make substantial contributions to both teaching and research aspects of the Developmental biology community. Recent examples include serving on the Editorial Board of Development, sitting on the Nuffield council on Bioethics, and being a Member of Council of the Royal Society.”

and communicates clearly the excitement that can be derived from research in our subject.

“She has also been a great advocate for Science, Women, and developmental biology in the political arena as well as for the general public”. Claudio Stern (University College London) and Enrico Coen (John Innes Centre).

Alongside her research career, Ottoline has driven many initiatives for improve equality and diversity in the Sciences. One of her best-known contributions has been the publication of her booklet “*Mothers in Science: 64 ways to have it all*”. Her approach here was to lead by example, and has proven to be very effective. We encourage our members to read recent interviews with Ottoline that can be found in **Development** and the **Royal Society of Biology**.

“When I was pregnant with twins and trying to run my newly-formed research group I came across Ottoline’s little book “*Mothers In Science*”. It was so important to me, and is just one example of the many things that Ottoline has done that have been important to so many people.” Sally Lowell, University of Edinburgh.



Ottoline continues to make substantial contributions to both teaching and research aspects of the Developmental biology community. Recent examples include serving on the Editorial Board of Development, sitting on the Nuffield council on Bioethics, and being a Member of Council of the Royal Society. She has been co-Editor in Chief for Current Opinion Plant Biology. Ottoline is also a committed teacher of developmental biology, and is the joint author of the textbook Mechanisms in Plant Development (Leyser and Day, 2003, Blackwell Science Ltd).

Selected papers:

Leyser HM, Lincoln CA, Timpte C, Lammer D, Turner J, Estelle M (1993). *Arabidopsis* auxin-resistance gene *AXR1* encodes a protein related to ubiquitin-activating enzyme E1. *Nature* 364:161-4.

Rouse D, Mackay P, Stirnberg P, Estelle M, Leyser O (1998). Changes in auxin response from mutations in an *AUX/IAA* gene. *Science* 279:1371-3.

Sabatini, S; Beis, D; Wolkenfelt, H; et al. (1999). An auxin-dependent distal organizer of pattern and polarity in the *Arabidopsis* root. *Cell*. 99: 463-472.

Gray, WM; Kepinski, S; Rouse, D; et al. (2001). Auxin regulates SCFTIR1-dependent degradation of *AUX/IAA* proteins. *Nature* 414: 271-276.

Stirnberg P, van De Sande K, Leyser HM (2002). *MAX1* and *MAX2* control lateral shoot branching in *Arabidopsis*. *Development* 129:1131-41.

Sorefan, K; Booker, J; Haurogne, K; et al. *MAX4* and *RMS1* are orthologous dioxygenase-like genes that regulate shoot branching in *Arabidopsis* and pea. (2003). *Genes & Development*. 17: 1469-1474.

Booker, J; Auldrige, M; Wills, S; et al. (2004). *MAX3/CCD7* is a carotenoid cleavage dioxygenase required for the synthesis of a novel plant signaling molecule. *Current Biology*. 14:1232-1238.

Kepinski S, Leyser O (2005). The *Arabidopsis* F-box protein *TIR1* is an auxin receptor. *Nature* 435:446-51.

Shinohara N, Taylor C, Leyser O (2013). Strigolactone can promote or inhibit shoot branching by triggering rapid depletion of the auxin efflux protein *PIN1* from the plasma membrane. *PLoS Biol*. 11:e1001474.

Acknowledgements: B.Steventon would like to thank Tanya Whitfield, Nick Monk, Claudio Stern and Enrico Coen for their contributions to this text.

The Cheryll Tickle Medal 2019



"This fostered a long-standing interest in morphogenesis, which became the focus of her independent research group when awarded a Wellcome Trust Career Development Award in 1998, hosted in the Department of Genetics, Cambridge".

"...Bénédicte's group often pioneers new methodologies to follow developmental processes quantitatively, and at multiple scales."

In 2016, the BSDB introduced the Cheryll Tickle Medal, which is being awarded annually to a mid-career, female scientist for her outstanding achievements in the field of Developmental Biology. The BSDB is proud to announce the 2019 awardee Bénédicte Sanson.



After a PhD in Paris on the molecular mechanisms of mRNA processing in phage, Bénédicte Sanson switched to *Drosophila* developmental genetics for a postdoc in Cambridge at the MRC-LMB. During her four-year postdoc with Jean-Paul Vincent (1994-1998), she investigated key aspects of Wingless signalling (the homologue of vertebrate Wnt-1) in development. Through this work, she became aware that the mechanisms underlying cell sorting at compartmental boundaries remained elusive. This fostered a long-standing interest in morphogenesis, which became the focus of her independent research group when awarded a Wellcome Trust Career Development Award in 1998, hosted in the Department of Genetics, Cambridge. Since then, Bénédicte has built up an internationally recognized research group, obtaining a Lectureship in 2009, then a Readership in 2018, in the Department of Physiology, Development and Neuroscience. In 2011 and then in 2017, she was awarded a Wellcome Trust Investigator Award to work on the mechanisms of cell sorting and collective cell movement *in vivo*.

Bénédicte has made key contributions to the field of developmental signaling, including demonstrating that the adhesion and signaling activities of

Armadillo (the homologue of vertebrate Beta-catenin) are separable (Sanson et al., 1996) and elucidating novel signaling regulations at the parasegmental organizer in *Drosophila* embryos (Desbordes and Sanson, 2003; Sanson, 2001; Sanson et al., 1999). More recently, the work of her group has focused on understanding the fundamental processes driving tissue morphogenesis during development. Their work on tissue-scale forces showed that an extrinsic axial force extends the main body axis in *Drosophila* embryos, acting in parallel to actomyosin-dependent polarized cell intercalations (Butler et al., 2009). Next, they identified the source of this extrinsic force as caused by the invagination of the endoderm at the posterior of the embryo (Lye et al., 2015). Their work on cell sorting demonstrated that actomyosin-based mechanical "barriers" stop cells from invading adjacent compartments, pioneering CALI on GFP in *Drosophila* embryos to inactivate Myosin II subcellularly (Monier et al., 2010). They further showed that actomyosin-based barriers also order cells during axis extension (Tetley et al., 2016). Recently, the work of her group has shed light onto how actomyosin-driven tension can orientate cell divisions at compartmental boundaries (Scarpa et al., 2018). They also investigated how epithelial folding and actomyosin-enrichment are coupled downstream of Wingless signaling at boundaries (Urbano et al., 2018).

Underlying all of this work is a clear understanding that morphogenesis is dependent on both genetic and physical inputs. As a consequence, Bénédicte's group often pioneers new methodologies to follow developmental processes quantitatively, and at multiple scales. Their approaches include computational methods to automatically track cell behaviours in real time, for thousands of cells; light sheet imaging (SPIM) to analyse morphogenetic events at the scale of the whole embryo; and laser cuts to probe and manipulate

"In addition to her research contributions, Bénédicte has taught in a range of molecular and developmental genetics courses. Since her appointment in 2009, a significant fraction of her teaching for the University of Cambridge has been for the first year course in Veterinary Anatomy..."

"Other contributions include the active support of postdoctoral careers, both through a previous appointment at the Wellcome Trust to evaluate candidates for early career fellowships, and as Postdoc Committee Chair for her Department."

tissue tension. By combining such imaging and computational techniques, the lab continues to investigate how cell intrinsic and extrinsic forces integrate to shape developing tissues. Recently, Bénédicte's group started developing computational models in collaboration with physicists and mathematicians, to explore the more mechanical aspects of morphogenesis.

In addition to her research contributions, Bénédicte has taught in a range of molecular and developmental genetics courses. Since her appointment in 2009, a significant fraction of her teaching for the University of Cambridge has been for the first year course in Veterinary Anatomy, contributing to the practical element of the course, where the students dissect the different organs and tissues. Other contributions include the active support of postdoctoral careers, both through a previous appointment at the Wellcome Trust to evaluate candidates for early career fellowships, and as Postdoc Committee Chair for her Department.

Selected papers:

Butler, L. C., Blanchard, G. B., Kabla, A. J., Lawrence, N. J., Welchman, D. P., Mahadevan, L., Adams, R. J. and Sanson, B. (2009). Cell shape changes indicate a role for extrinsic tensile forces in *Drosophila* germ-band extension. *Nat Cell Biol* **11**, 859-864.

Desbordes, S. and Sanson, B. (2003). The glypican Dally-like is required for Hedgehog signalling in the embryonic epidermis of *Drosophila*. *Development* **130**, 6245-6255.

Lye, C. M., Blanchard, G. B., Naylor, H. W., Muresan, L., Huisken, J., Adams, R. J. and Sanson, B. (2015). Mechanical Coupling between Endoderm Invagination and Axis Extension in *Drosophila*. *PLoS Biol* **13**, e1002292.

Monier, B., Pelissier-Monier, A., Brand, A. H. and Sanson, B. (2010). An actomyosin-based barrier inhibits cell mixing at compartmental boundaries in

Drosophila embryos. *Nat Cell Biol* **12**, 60-65.

Sanson, B. (2001). Generating patterns from fields of cells. Examples from *Drosophila* segmentation. *EMBO Rep* **2**, 1083-1088.

Sanson, B., Alexandre, C., Fascetti, N. and Vincent, J. P. (1999). Engrailed and hedgehog make the range of Wingless asymmetric in *Drosophila* embryos. *Cell* **98**, 207-216.

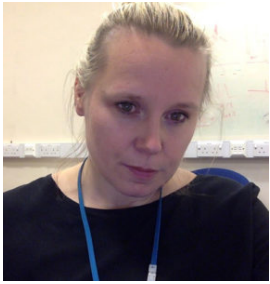
Sanson, B., White, P. and Vincent, J. P. (1996). Uncoupling cadherin-based adhesion from wingless signalling in *Drosophila*. *Nature* **383**, 627-630.

Scarpa, E., Finet, C., Blanchard, G. B. and Sanson, B. (2018). Actomyosin-Driven Tension at Compartmental Boundaries Orients Cell Division Independently of Cell Geometry In Vivo. *Dev Cell* **47**, 727-740 e726.

Tetley, R. J., Blanchard, G. B., Fletcher, A. G., Adams, R. J. and Sanson, B. (2016). Unipolar distributions of junctional Myosin II identify cell stripe boundaries that drive cell intercalation throughout *Drosophila* axis extension. *Elife* **5**, e12094.

Urbano, J. M., Naylor, H. W., Scarpa, E., Muresan, L. and Sanson, B. (2018). Suppression of epithelial folding at actomyosin-enriched compartment boundaries downstream of Wingless signalling in *Drosophila*. *Development* **145**.

The Cheryll Tickle Medal 2020



"Her keen interest in emerging technologies and the development of novel molecular biology tools allowed her to consistently stay at the forefront of regulatory genomics in developmental biology."

"Tatjana is extremely dedicated to carrying out her research meticulously and strives to broaden the range of technologies employed..."

In 2016, the BSDB introduced the Cheryll Tickle Medal, which is being awarded annually to a mid-career, female scientist for her outstanding achievements in the field of Developmental Biology. The BSDB is proud to announce the 2020 awardee, Tatjana Sauka-Spengler.



Originally from Bosnia and Herzegovina, Tatjana completed her undergraduate studies in Physics at the University of Sarajevo and soon after sought asylum from the Bosnian War in Czech Republic, where she became a High School teacher at the Gymnazium of Pardubice (1992-93). Having obtained her first graduate degree in Solid State Physics at the University of Paris (1999), Tatjana was selected for the "Interface Physics-Biology" Graduate programme and after discovering a passion for developmental biology at the MBL Embryology Course in Woods Hole, she pursued a second PhD in Biology in the group of Sylvie Mazan at the University of Paris, with whom she worked to elucidate the conserved gene regulatory mechanisms of gastrulation (1-3). She then went on to work as a postdoctoral researcher in the group of Marianne Bronner at the California Institute of Technology. There, she pioneered experimental approaches to study gene regulation *in vivo* using avian embryos (4,5). In parallel, she developed methodologies to for the study the genomics of the sea lamprey, *Petromyzon marinus* (6,7). Tatjana spearheaded the establishment of a system in the Bronner lab to efficiently produce sea lamprey embryos throughout the summer, which became so successful that it still attracts

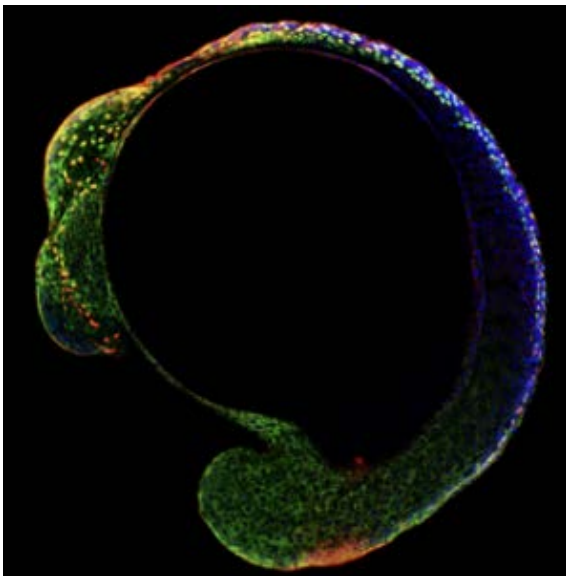
researchers from all over the world for the "lamprey season" in Caltech. This enabled Tatjana to pioneer molecular biology approaches in lampreys, including loss-of-function experiments and the development of enhancer reporter assays. This early work laid the foundation for her subsequent contributions to illuminate the evolution of vertebrates, through the window of comparative studies of neural crest gene regulatory networks (reviewed in (8)).



In 2012 she became a group leader in the MRC Weatherall Institute of Molecular Medicine (WIMM) at the University of Oxford, where she was awarded the prestigious Lister Institute Research Prize (2013) and the March of Dimes Basil O'Connor Research Award (2013). Her keen interest in emerging technologies and the development of novel molecular biology tools allowed her to consistently stay at the forefront of regulatory genomics in developmental biology. Indeed, Tatjana pioneered enhancer screens to identify thousands of cell-type specific cis-regulatory elements in avian and zebrafish embryos, which together with single cell genomics allow for the reverse engineering of entire gene regulatory networks (9). Tatjana is extremely dedicated to carrying out her research meticulously and strives to broaden the

range of technologies employed (i.e. Cut-and-Run-sequencing, machine learning approaches to next generation sequencing analysis) in order to break the boundaries of research in her field. Now an Associate Professor for Genome Biology at the University of Oxford generously supported by the Wellcome Trust Senior Research Fellowship (2019), the Sauka-Spengler lab uses the neural crest, the enteric nervous system and the zebrafish heart epicardium to explore the dynamics of gene regulatory networks in development, regeneration, disease and evolution (9-17).

What further distinguishes Tatjana as a Cheryll Tickle awardee is her passion and dedication to the fostering of young talent in the field developmental biology. This stretches beyond the mentoring of her own group, and breadth of support we have received in her nominations for the award is a true testament to her contributions to the developmental biology community in the UK. There is no better way to understand this than through the words of the many people who have benefitted from her knowledge and energy since establishing her lab in 2012. I'll therefore leave you with the following quotes, that do so well to emphasize how deserving she is of this award.



"As her mentees, we believe Tatjana's unique mentorship style is her most outstanding characteristic, and the achievements she seems to be most proud of are those of the people she mentored. Indeed, her first graduate students, postdoctoral fellows and advisees are now establishing their labs (i.e., Betancur lab in UCSF, Hockman lab, Uni. of Cape Town, Simoes-Costa lab in Cornell Uni., Strobl-Mazzulla lab in IIB-INTECH, Argentina). Testament to this, in 2018 she was awarded the RDM Award for Excellent

Supervision (University of Oxford)". Chloe E. Tubman and Ivan L. Candido-Ferreira, DPhil candidates, University of Oxford.

"Tatjana is an inspirational role model for trainees and in particular for female scientists, for whom she provides guidance on balancing work and home life and inspires the confidence and direction to pursue individual goals". Prof. Paul Riley, University of Oxford

"Simply put, Tatjana is an outstanding supervisor and mentor, not only to the people directly working with her, but also to any other junior scientist that approaches her for guidance". Dr. Filipa Simões, University of Oxford.

"With her relentless energy and enthusiasm for excellent science combined with extensive knowledge and capacity to inspire, she has been a fantastic mentor. She sees the positive side of every situation and always provides a resolution, whether it be an experimental problem, writer's block or personal matters". Dr. Ruth Williams, University of Oxford.

"During our long-term collaboration Tatjana has hosted and supervised a number of my PhD students and post-doctoral fellows in her lab at the WIMM and trained them in maximising use of the zebrafish model to study heart development and regeneration. She has individually tutored my group members in bioinformatics to analyse RNA-Seq and ATAC-Seq datasets and modified gene editing approaches, which has been invaluable for the next stages of their research careers". Prof. Paul Riley, University of Oxford.

"Tatjana very readily welcomes visiting scientists to her laboratory. She also generously shares her expertise and knowledge with collaborators. For example, she has applied her in vivo biotinylation approach in zebrafish (10,18), which enables the isolation of specific cell populations by affinity purification, to characterize the neutrophil response to mycobacterium infection (19). With colleagues she applied this approach to characterize different epicardial subpopulations (17), and has discovered how macrophages contribute to cardiac regeneration (16)". Prof. Andrea Munsterberg, UEA

Biography adapted from Chloe E. Tubman and Ivan L. Candido-Ferreira, DPhil candidates, University of Oxford. Additional input and editing provided by Tatjana Sauka-Spengler.

Selected papers:

1. Sauka-Spengler, T., B. Baratte, M. Lepage, and S. Mazan, *Characterization of Brachyury genes in the dogfish S. canicula and the lamprey L. fluviatilis. Insights into gastrulation in a chondrichthyan*. Dev Biol, 2003. **263**(2): p. 296-307.
2. Sauka-Spengler, T., B. Baratte, L. Shi, and S. Mazan, *Structure and expression of an Otx5-related gene in the dogfish Scyliorhinus canicula: evidence for a conserved role of Otx5 and Crx genes in the specification of photoreceptors*. Dev Genes Evol, 2001. **211**(11): p. 533-44.
3. Sauka-Spengler, T., A. Germot, D.L. Shi, and S. Mazan, *Expression patterns of an Otx2 and an Otx5 orthologue in the urodele Pleurodeles waltl: implications on the evolutionary relationships between the balancers and cement gland in amphibians*. Dev Genes Evol, 2002. **212**(8): p. 380-7.
4. Betancur, P., M. Bronner-Fraser, and T. Sauka-Spengler, *Genomic code for Sox10 activation reveals a key regulatory enhancer for cranial neural crest*. Proc Natl Acad Sci U S A, 2010. **107**(8): p. 3570-5.
5. Sauka-Spengler, T. and M. Barembaum, *Gain- and loss-of-function approaches in the chick embryo*. Methods Cell Biol, 2008. **87**: p. 237-56.
6. Nikitina, N., M. Bronner-Fraser, and T. Sauka-Spengler, *The sea lamprey Petromyzon marinus: a model for evolutionary and developmental biology*. Cold Spring Harb Protoc, 2009. **2009**(1): p. pdb emo113.
7. Sauka-Spengler, T., D. Meulemans, M. Jones, and M. Bronner-Fraser, *Ancient evolutionary origin of the neural crest gene regulatory network*. Dev Cell, 2007. **13**(3): p. 405-20.
8. Sauka-Spengler, T. and M. Bronner-Fraser, *A gene regulatory network orchestrates neural crest formation*. Nat Rev Mol Cell Biol, 2008. **9**(7): p. 557-68.
9. Williams, R.M., et al., *Reconstruction of the Global Neural Crest Gene Regulatory Network In Vivo*. Dev Cell, 2019. **51**(2): p. 255-276 e7.
10. Trinh, L.A., V. Chong-Morrison, D. Gavriouchkina, T. Hochgreb-Hagele, U. Senanayake, S.E. Fraser, and T. Sauka-Spengler, *Biotagging of Specific Cell Populations in Zebrafish Reveals Gene Regulatory Logic Encoded in the Nuclear Transcriptome*. Cell Rep, 2017. **19**(2): p. 425-440.
11. Williams, R.M., U. Senanayake, M. Artibani, G. Taylor, D. Wells, A.A. Ahmed, and T. Sauka-Spengler, *Genome and epigenome engineering CRISPR toolkit for in vivo modulation of cis-regulatory interactions and gene expression in the chicken embryo*. Development, 2018. **145**(4).
12. Kenyon, A., D. Gavriouchkina, J. Zorman, V. Chong-Morrison, G. Napolitani, V. Cerundolo, and T. Sauka-Spengler, *Generation of a double binary transgenic zebrafish model to study myeloid gene regulation in response to oncogene activation in melanocytes*. Dis Model Mech, 2018. **11**(4).
13. Lukoseviciute, M., et al., *From Pioneer to Repressor: Bimodal foxd3 Activity Dynamically Remodels Neural Crest Regulatory Landscape In Vivo*. Dev Cell, 2018. **47**(5): p. 608-628 e6.
14. Hockman, D., et al., *A genome-wide assessment of the ancestral neural crest gene regulatory network*. Nat Commun, 2019. **10**(1): p. 4689.
15. Ling, I.T.C. and T. Sauka-Spengler, *Early chromatin shaping predetermines multipotent vagal neural crest into neural, neuronal and mesenchymal lineages*. Nat Cell Biol, 2019. **21**(12): p. 1504-1517.
16. Simoes, F.C., et al., *Macrophages directly contribute collagen to scar formation during zebrafish heart regeneration and mouse heart repair*. Nat Commun, 2020. **11**(1): p. 600.
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The Beddington Medal 2019

"David has been awarded the Beddington medal for his exceptional work performed during his 3-year MRC-funded PhD at the University of Edinburgh with Prof Jamie Davies and Dr Peter Hohenstein (2015-2018): The thesis is titled 'Mechanisms of kidney vascularisation and the roles of macrophages in renal organogenesis'."

"He is now a post-doctoral fellow at the UK Dementia Research Institute (University of Edinburgh; 2019-present), continuing research in macrophage biology under the supervision of Prof Josef Priller. His current focus is on brain macrophages (microglia) in development, neurodegeneration, and aging."

The **Beddington Medal** is the BSDB's major commendation to promising young biologists, awarded for the best PhD thesis in Developmental Biology defended in the year previous to the award. **Rosa Beddington** was one of the greatest talents and inspirational leaders in the field of developmental biology. Rosa made an enormous contribution to the field in general and to the BSDB in particular, so it seemed entirely appropriate that the Society should establish a lasting memorial to her. The design of the medal, mice on a stylised DNA helix, is from artwork by Rosa herself. We would like to congratulate the 2019 winner of the Beddington Medal, David Munro, and would like to take this opportunity to give a brief overview of his career and the PhD project that was awarded the Beddington medal.

Jim Smith introduced the 2019 Beddington medal with heartfelt memories of Rosa Beddington and her time at the NIMR. Please read more of his thoughts [here](#).



"The really impressive thing about David's work is that he did not come to my lab to fit in with an existing line of research but created one of his own". Jamie Davies, University of Edinburgh.

David received his undergraduate degree in Sport and Exercise Science at the University of Stirling (2010-2014). With this, he achieved a first-class honours degree and the prize for the best overall performance throughout a physiology related degree (British Physiological Society Undergraduate Prize). His dissertation project

investigated associations between *ADRB2* mutations (an adrenaline receptor gene in humans) and athlete status/athletic ability measurements. Subsequently, he was awarded a University of Stirling Head of School Summer Bursary Award to remain in Stirling during the summer of 2014 and investigate the relationship between transcribed ultra-conserved regions of RNA (T-UCRs) and the development of diet-induced insulin resistance in humans (*Summer 2014*). He then moved to the University of Edinburgh for his MSc by Research in Biomedical Sciences (2014-2015). Again, he received a distinction and was awarded the Class Prize for best student. During this time, he studied the physiology of S-acylation the regulation of skeletal muscle energy expenditure by an obesity-associated phospholipase as part of two research placements.

David has been awarded the Beddington medal for his exceptional work performed during his 3-year MRC-funded PhD at the University of Edinburgh with Prof Jamie Davies and Dr Peter Hohenstein (2015-2018): The thesis is titled 'Mechanisms of kidney vascularisation and the roles of macrophages in renal organogenesis'. During his PhD, he gave several oral and poster presentations at national and international conferences, supervised students (including a Gurdon Summer Studentship Awardee), established numerous international collaborations, was awarded travel grants (including a BSDB Conference Grant), and reviewed manuscripts for leading journals (including *Cell Reports*, *Angiogenesis*, and *Scientific Reports*). He is now a post-doctoral fellow at the UK Dementia Research Institute (University of Edinburgh; 2019- present), continuing research in macrophage biology under the supervision of Prof Josef Priller. His current focus is on brain macrophages (microglia) in development, neurodegeneration, and aging.

Thesis description

Kidneys are specialised organs that clean the blood, removing waste while retaining what is useful. This requires a complex vasculature, and its formation as a foetus develops is poorly understood. I started my PhD research by using advanced microscopy techniques to visualise how blood vessels form in three-dimensions in the mouse kidney. In doing so, I identified when and from where the first blood vessels enter the kidney, and how blood vessels pattern at the edge of the kidney throughout development.

Blood vessels can form through angiogenesis (branching of new vessels from pre-existing ones) and/or vasculogenesis (assembly of new vessels from the coalescence of endothelial precursor cells). It has long been thought that a combination of both processes occurs during kidney vascularisation; however, my thesis work indicates that this concept may not be correct. My data instead suggest that kidney vascularization relies on growth and remodelling of pre-existing vessels (angiogenesis) and does not depend on vasculogenesis at any point (**Publications 1 and 5 in CV**). When assessing the entire 3D vascular tree of the kidney, isolated endothelial cells were never observed at any developmental age. Instead, all vessels, including the newly forming ones, were connected to pre-existing vessels that could be traced to the major circulatory vessels.

I then focused on the blood vessels at the edge of the kidney, which I found to consistently and accurately pattern around a special collection of cells – the cap mesenchyme. The cap mesenchyme contains cells that eventually become the cleaning tubes of the kidney, the nephrons. This cell population undergoes rounds of splitting at the kidney's periphery. As this happens, I demonstrated that blood vessels migrate through the newly opened regions between the separating cap mesenchymal populations (**Publication 1 in CV**). This occurs in cycles throughout development and is likely to be vital for the oxygenation of the kidney's outer region, the site where important processes such as nephron formation take place.

I determined that a signalling molecule, semaphorin-3f, and its receptor, neuropilin-2, were expressed in a pattern consistent with them having roles in this cyclical patterning of blood vessels; however, using mouse models where the genes for these molecules were deleted, I established that they were not vital for this process (**Publication 2 in CV**).

I next shifted my research focus towards a

specialised cell type known as the macrophage (macro = big; phage = eater) in the developing kidney (**Publication 3 in CV**). Macrophages are immune cells best known for clearing foreign and damaged cells. These cells have vital roles during animal development, but little is known about their specific functions during kidney development.

Macrophages arrived in the mouse kidney early during its development, where they were required to clear away misplaced cells to 'set-the-stage' for early kidney development (**Publication 6 in CV, under review**). Throughout later development, most macrophages wrapped around blood vessels and I demonstrated their ability to eat endothelial cells (which usually line the blood vessels) and red blood cells (which are carried within them) within the kidney. I also established that kidney macrophages produced many molecules linked to blood vessel development, and so I examined the consequences of macrophage-loss on blood vessel formation. Blood vessels normally form continuous networks in the kidney; however, when macrophages were depleted (by blocking a macrophage-survival signalling pathway), connections between renal blood vessels were reduced (**Publication 6 in CV**).

Publications

1. **Munro DAD**, Hohenstein P, Davies JA. 2017. Cycles of vascular plexus formation within the nephrogenic zone of the developing kidney. *Scientific Reports*. 7: 3273.
2. **Munro DAD**, Hohenstein P, Coate TM, Davies JA. 2017. Refuting the hypothesis that semaphorin-3f/neuropilin-2 guide endothelial patterning around the cap mesenchyme in the developing kidney. *Developmental Dynamics*. 246:1047-1056.
3. **Munro DAD**, Hughes J. 2017. The Origins and Functions of Tissue-Resident Macrophages in Kidney Development. *Frontiers in Physiology*. 8:837. (Review)
4. Mills CG, Lawrence ML, **Munro DAD**, El-Hendawi M, Mullins JJ, Davies JA. 2017. Asymmetric BMP4 signalling improves the realism of kidney organoids. *Scientific Reports*. 7:14824.
5. **Munro DAD**, Davies JA. 2018. Vascularizing the kidney in the embryo and organoid: questioning assumptions about renal vasculogenesis. *Journal of the American Society of Nephrology*. (Perspectives article).
6. **Munro DAD**, et al. Macrophages restrict the nephrogenic field and promote endothelial connections during kidney development. *eLife* 2019;8:e43271 DOI: [10.7554/eLife.43271](https://doi.org/10.7554/eLife.43271)

The Beddington Medal 2020

"Alongside his clinical work, Wajid has maintained a strong interest in research. His interests lie in the early development of mammalian embryos and how this relates to the challenging congenital anomalies he faces in his neonatal and paediatric patients."

"...his foundations in three alternate disciplines (medicine, computer science and embryology) has enabled him to produce a PhD thesis of exceptionally high quality, for which he is deserving of the 2020 BSDB Beddington award."

The **Beddington Medal** is the BSDB's major commendation to promising young biologists, awarded for the best PhD thesis in Developmental Biology defended in the year previous to the award. **Rosa Beddington** was one of the greatest talents and inspirational leaders in the field of developmental biology. Rosa made an enormous contribution to the field in general and to the BSDB in particular, so it seemed entirely appropriate that the Society should establish a lasting memorial to her. The design of the medal, mice on a stylised DNA helix, is from artwork by Rosa herself.



Wajid Jawaid is a national trainee in Paediatric Surgery in the London Deanery currently based at Addenbrooke's hospital in Cambridge. Alongside his clinical work, Wajid has maintained a strong interest in research. His interests lie in the early development of mammalian embryos and how this relates to the challenging congenital anomalies he faces in his neonatal and paediatric patients. Wajid's PhD work has identified novel pathways by studying murine gastrulation and early organogenesis at a single cell level. This has required him to develop molecular approaches together with the development of novel computational methods.

While working as a practising paediatric surgeon, Wajid was inspired to take on a PhD in 2014 under the supervision of Prof. Berthold Göttgens and Prof. Jenny Nichols at the Wellcome-MRC Stem Cell Institute, University of Cambridge. Here, he learnt how defects in the early lineage specification events of

mammalian embryos can explain many of the tragic infant deformities that he was faced with in his clinic. In preparation for his PhD, he had previously undertaken an MPhil in Computational Biology at the Department of Mathematics and Applied Physics at the University of Cambridge, for which he was awarded a distinction. Thus, it is easy to see how his foundations in three alternate disciplines (medicine, computer science and embryology) has enabled him to produce a PhD thesis of exceptionally high quality, for which he is deserving of the 2020 BSDB Beddington award.

Wajid contributed to eight papers during his PhD, two of which were as first author. For his co-first author publication in 2016, Wajid pioneered a novel approach to investigate mesoderm formation by generating the first single cell transcriptome analysis of early mouse gastrulae. He found that *Tal1*, a transcription factor initially believed to be required to pause nascent mesoderm in an uncommitted state, is not essential for diverting cells exiting the primitive streak from precocious cardiac development. Wajid's contribution to this study included dissection of early postimplantation mouse embryos (E6.5), as well as processing and analysis of the scRNAseq data. For his co-first author paper of 2018, a more ambitious RNAseq data set was generated from embryos of a range of stages to enable a deeper understanding of cell fate decisions during gastrulation to be garnered. Wajid masterminded and organised the timed mating for embryo production, and recruited the dissection team, since this large-scale undertaking required rapid collection of single cells.

In addition to his work in the lab, he used his expanding computational skills to contribute extensively to the bioinformatics analysis. Wajid generated an interactive web tool and personally instructed members and associates of the gastrulation consortium on its operation. This ambitious study

“Wajid is now established in Cambridge as a paediatric surgeon, and has established a career plan with his head of department to return to developmental biology as a surgeon scientist later this year, a very rare breed of individuals who combine an active career in surgery with research at the bench.”

“I am comforted to know that sick children will benefit from the depth of knowledge and dexterity Wajid acquired during his PhD that will ensure the best possible treatment for them at the hands of a genuinely compassionate and competent individual”.

contributed novel understanding of how somatic cell types may be ordered and, crucially, revealed a role for leukotriene induction, via Alox5 and its cofactor, Alox5a, in specification of erythromyeloid progenitors from haemogenic endothelium precursors. Wajid then returned to the lab to employ an *in vitro* assay using embryonic stem cells to demonstrate a role for leukotriene in driving blood formation.

Outside of these major contributions of his PhD work, Wajid collaborated extensively and is a co-author on multiple studies. These include a project with Shlomit Edri and Alfonso Martinez Arias to explore the transcriptomic signature marking neuromesodermal progenitors in aggregates of mouse embryonic stem cells allowed to develop in 3D culture, or gastruloids. He also worked with mouse embryos to study the role of Nanog during gastrulation together with a visiting PhD student, Julio Sainz de Aja. In addition, he contributed to a larger group of researchers who together performed dynamic single cell RNAseq analysis of mouse embryos during gastrulation.

Wajid is now established in Cambridge as a paediatric surgeon, and has established a career plan with his head of department to return to developmental biology as a surgeon scientist later this year, a very rare breed of individuals who combine an active career in surgery with research at the bench.

Finally I leave you with some thoughts on Wajid from our 2017 Cheryll Tickle award winner- Prof. Jenny Nichols:

“I am comforted to know that sick children will benefit from the depth of knowledge and dexterity Wajid acquired during his PhD that will ensure the best possible treatment for them at the hands of a genuinely compassionate and competent individual”.

“It was always a pleasure for me to work at the bench alongside Wajid; his enthusiasm, wit and generally sunny disposition, even at antisocial times of night, made the experiments a lot of fun,

and I knew I could rely on his reagents and high standards to ensure a meaningful (and publishable) outcome. Wajid’s participation in various projects was also in demand further afield”.

Selected papers:

Ibarra-Soria X*, Jawaidd W*, Pijuan-Sala B, Ladopoulos V, Scialdone A, Jörg DJ et al. Defining murine organogenesis at single-cell resolution reveals a role for the leukotriene pathway in regulating blood progenitor formation. *Nat Cell Biol.* 2018 Feb;20(2):127-134

Scialdone A*, Tanaka Y*, Jawaidd W*, Moignard V*, Wilson NK, Macaulay IC et al. Resolving early mesoderm diversification through single-cell expression profiling. *Nature.* 2016 Jul 14;535(7611):289-293

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Edri S, Hayward P, Jawaidd W, Martinez Arias A. Neuro-mesodermal progenitors (NMPs): a comparative study between pluripotent stem cells and embryo-derived populations. *Development.* 2019 Jun 24;146(12)

Belluschi S, Calderbank EF, Ciaurro V, Pijuan-Sala B, Santoro A, Mende Net al. Myelo-lymphoid lineage restriction occurs in the human haematopoietic stem cell compartment before lymphoid-primed multipotent progenitors. *Nat Comm.* 2018 Oct:9

Moignard V, Woodhouse S, Haghverdi L, Lilly AJ, Tanaka Y, Wilkinson AC et al. Decoding the regulatory network of early blood development from single-cell gene expression measurements. *Nat Biotechnol.* 2015 Mar;33(3):269- 76

Updates from the Company of Biologists – FocalPlane



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FOR IMMEDIATE RELEASE

The Company of Biologists and Journal of Cell Science launch FocalPlane, a new microscopy community site

FocalPlane is a trusted online meeting place to connect people, products, resources and information from the microscopy community.

Cambridge, UK, 1 July 2020 - Microscopy is a discipline that unites biologists across all areas of research. A frequently cited difficulty is the gap in knowledge sharing between microscopy experts and non-experts. Technical language can make the field feel exclusive and intimidating for those wanting to make use of current microscopy techniques. In response, The Company of Biologists and Journal of Cell Science have created a new community resource. FocalPlane is a community website for microscopists and biologists alike to share microscopy news, events and resources.

A Scientific Advisory Board has been appointed to support the site alongside its own dedicated Community Manager. Each of the five Advisory Board members bring their own microscopy specialism, making FocalPlane a centre of expertise. “We’ve been looking forward to creating this resource for a long time, to bring the biological research community [together] with the optical microscopy development community,” says Advisory Board member, Professor Ricardo Henriques (University College London, UK).

The community site is free to access and users can register for a free account to post their own contribution. FocalPlane will host news, interviews, opinions, tools, job listings and events to help promote interactions and foster connections. “We encourage you to make the site part of your online routine, and look forward to many interactions with you all,” says Sharon Ahmad, Executive Editor, Journal of Cell Science.

FocalPlane is the third community site launched by The Company of Biologists, following in the successful footsteps of the Node and preLights. The Node, now in its tenth year, serves the developmental biology community, whereas preLights is a preprint highlighting service featuring a team of over 200 early-career researchers.

Journal of Cell Science, which hosts the FocalPlane site, has a long history of publishing papers relating to microscopy. The journal was established in 1853 as ‘Quarterly Journal of Microscopical Science’ and the archives showcase the evolution of microscopy over time.

About The Company of Biologists

The Company of Biologists is a not-for-profit publishing organisation dedicated to supporting and inspiring the biological community. The Company publishes five specialist peer-reviewed journals: Development, Journal of Cell Science, Journal of Experimental Biology, Disease Models & Mechanisms and Biology Open. It offers further support to the biological community by facilitating scientific meetings, providing travel grants for researchers and supporting research societies.

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Updates from the Company of Biologists – The Node Network



Development

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The Node Network

The journal *Development* and its publisher The Company of Biologists are excited to announce the launch of the Node Network, a global directory of developmental and stem cell biologists.

Scientists often have a hard time finding the right people for professional purposes, whether this be committee and panel members, referees for papers and grants, speakers for conferences and seminar series, or expert sources. Another challenge is for these roles to represent the diversity of their scientific fields, an issue epitomised by male-dominated speaker lists and so-called ‘manels’.

The Node Network aims to address these challenges, helping our users to identify individuals that might not otherwise spring to mind. The Network is entirely inclusive – any member of the developmental and stem cell biology community, at any stage of their career, can join. Members of the Network provide information on scientific field, model organism, place of work and career stage. They can also voluntarily provide details on aspects of diversity such as gender, race/ethnicity, LGBTQ+ identity and disability status. This inclusivity means that the Network can be used solely from a scientific perspective, but can also help those wanting to better promote diversity.

James Briscoe, Editor in Chief of *Development* and senior group leader at the Francis Crick Institute, conceived the idea for the Node Network and has been working with *Development*’s in-house team on the project. He said “I’m excited about the launch of the Node Network. I hope it will become a useful resource for the community and would encourage anyone interested to register and to use the directory. Together we can support our diverse and inclusive field.”

You can find out more about the Network and register to access it at

www.thenode.biologists.com/networkinfo

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Updates from the Company of Biologists – Price Freeze



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FOR RELEASE ON Monday 6 July 2020

The Company of Biologists announces e-journal price freeze for 2021

In recognition of the unprecedented and ongoing challenges facing the library and research communities worldwide, there will be no increase in The Company of Biologists' e-journal prices in 2021.

As a not-for-profit publisher committed to maximising the availability of high-quality biological science research, we are keen to support our authors, readers and library customers as far as possible during these difficult times.

We are therefore freezing fees for e-access to our subscription journals - Development, Journal of Cell Science and Journal of Experimental Biology - until 31 December 2021. This applies to both new and existing customers. Article processing charges (APCs) will also remain at 2020 levels throughout 2021.

In addition, we are waiving 2021 price increases for the two-year Read & Publish Open Access agreements we have signed with national library consortia - Jisc in the UK, IReL in Ireland, and MALMAD in Israel - and with individual institutions.

"Our mission is to support and inspire the biological community, and we want to ensure that the highest quality research continues to be available as widely as possible during these uncertain times and beyond. As a result, we have taken the decision to freeze our e-journal prices in 2021," says Matthew Freeman FRS, Chairman of The Company of Biologists and Head of the Dunn School of Pathology at the University of Oxford.

"We are also supporting the library and research community through our Read & Publish initiative which offers libraries a cost-neutral transition to Open Access with free and unlimited Open Access publishing for corresponding authors."

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[The Company of Biologists](#) is a not-for-profit publishing company dedicated to supporting and inspiring the biological community. We publish five specialist peer-reviewed journals - three hybrid journals (Development, Journal of Cell Science, and Journal of Experimental Biology), and two Open Access journals (Disease Models & Mechanisms, and Biology Open). We also host scientific meetings and workshops, and provide a variety of grants to the scientific community.

Our [Read & Publish Open Access initiative](#) was launched in November 2019, and we have signed national-level consortia agreements with Jisc in the UK, IReL in Ireland, and MALMAD in Israel, as well as with individual institutions.

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BSDB Gurdon Summer Studentship Report (32)

I am Franklin Lo, a 4th year undergraduate student at the University of Edinburgh. My summer internship was carried out in Professor Sir John Gurdon's lab at Gurdon Institute of the University of Cambridge and I was supervised by Professor Sir John Gurdon, Dr Jerome Jullien and Khayam Javed.

The major focus of my internship was to understand the functions of oocyte-specific B4 linker histone during nuclear reprogramming (NT). This maternal factor is abundant in oocytes and eggs, and present also in early embryo until the mid-blastula transition. The injection of somatic cell nuclei into *Xenopus* oocytes has been shown to reverse the restriction of some gene expressions and induce expression of pluripotency genes including *POU5F1* and *SOX2*. This cell division independent process utilises components in the germinal vesicle (GV) of oocytes, and mechanism of reprogramming in NT is thought to be identical to the reprogramming of sperm genome by eggs after fertilisation. Therefore, NT is an excellent approach to gain further insights on the mechanism of nuclear reprogramming in eggs.

B4 is an important component of reprogramming by NT since it substitutes somatic histones in injected somatic cell genome and drives the transcription of pluripotency genes. A recently developed novel antibody-based methodology called Trim-Away enables targeting and degradation of specific proteins in *Xenopus* oocytes including B4 linker histone without any genetic manipulations. The procedure involves the injection of Trim 21 mRNA or protein into the cytoplasm or GV of oocytes, respectively, followed by GV injection of antibody specific to a maternal factor. The rationale of Trim-Away is that the constant region of antibody binding to its target protein interact with Trim 21 protein, which then recruits ubiquitin proteasome that degrades the protein-antibody-Trim21 complex (Fig. 1). By using this technique, we have targeted B4 linker histone to study the effect of its degradation on the efficacy of reprogramming after NT.

To perform these experiments, my first few weeks of the internship was dedicated on practising DNA/mRNA injection into the GV and cytoplasm of oocytes using Drummond microinjector under a light microscope. GV injection was especially a

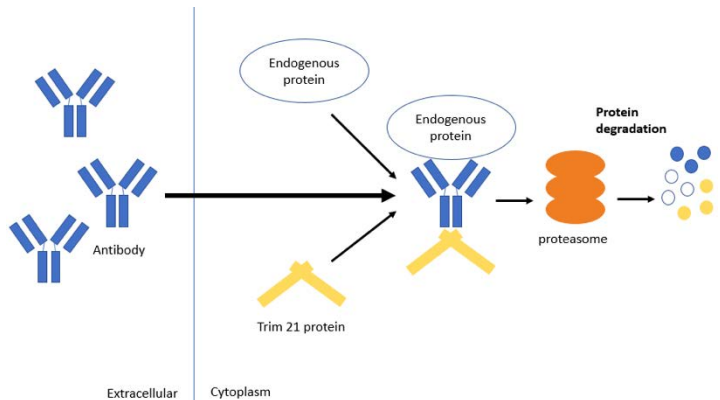


Figure 1: Mechanism of protein degradation by Trim Away. The sophisticated characteristic of this method is its capability to knock down endogenous proteins such as maternal factors efficiently, which is not possible with techniques like gene editing and RNA interference.

tough challenge for me since GV is hidden just underneath the pigmented region of *Xenopus* oocytes. A precise positioning of glass needle against oocytes and controlling the depth to penetrate are of utmost importance for successful GV injection. While my success rate began to hover around 50-60% after few weeks of practice, everyone else can aim the GV at approx. 90% efficiency! Such accuracy is important to run experiments smoothly. Nonetheless, I was compensating my inefficiency of GV injection by both increasing the number of oocytes I inject and co-injecting DNA encoding fluorescent protein which gives an indication of successful injection. Trim-Away is a very useful technique and future attempts may involve targeting different maternal factors to study the mechanism of nuclear reprogramming.

I was also responsible for generating both Trim 21 fused with mCherry and B4 linker histone proteins using bacteria. It started off with cloning of these genes into an appropriate plasmid vectors and transforming it into a BL21 bacteria for protein expression. Protein purification worked but the yield was extremely lower than our prediction. After numerous attempts, we managed to produce a large quantity of these proteins using a strain of bacteria called Rosetta. I still remember the joy of seeing pink bacterial culture as Rosetta strain was highly expressing Trim 21- mCherry (Fig. 2). Unfortunately, my time in the lab was limited and I could not purify these proteins.



Figure 2: Protein expression using Rosetta strain. Trim21-mCherry production (right) turns bacterial culture medium pink while wild type B4 protein (left) production did not change the colour of culture medium.

Having gained experiences to work with oocytes, I also began to work with *Xenopus* embryos which is made by fertilising eggs with sperms extracted from testis. Oocytes and eggs are naturally protected by a jelly-like coating which impede penetration of resulting embryos with a microinjector. But unlike oocytes, de-jellying process of embryos are difficult, and I often killed the embryos by de-jellying excessively. The unusual hot weather in Cambridge also deteriorated the egg quality and heightened the difficulty of working with embryos; researchers working with *Xenopus* often avoid performing important experiments during the summer. The time frame for injection is also shorter in embryos since they divide and develop, hence time window for injection is shorter than oocytes which are static. Despite encountering these challenges, I still found experiments with embryos very exciting as mRNA injected can affect embryo development and produce unique phenotypes.

Despite being a Nobel laureate, professor Gurdon is always humble and active as a researcher - he is very focused and still loves to perform experiments. Everyone, including myself, gains strong motivations to work hard from seeing his working style. His talkative and approachable personality makes him a great researcher even more; he often taught me procedures to work with oocytes and invited me to his tea-time for further discussions.

I was also surprised to see that everyone in the lab is very enthusiastic and keen about learning new information even from outside of their field of interest. This nature must be acting as a strong foundation for them to come up with creative ideas. The experience I had at Gurdon lab was stimulating

and fantastic, I very much appreciate mentorship, patience and kindness from Professor Gurdon, Jerome and Khayam. Working closely with several supervisors enabled me to participate on multiple projects and gain a variety of invaluable experiences.

I would also like to convey my gratitude to other lab members namely, Nigel Garrett, Can Aztekin, Dr Eva Hörmanseder, Dr Ming-Hsuan Wen, Dr Chris Penfold and Dilly Bradford for their immense support and mentorship during the internship.

Finally, I would like to thank BSDB for providing me this opportunity and I strongly recommend students who wish to do a lab internship to apply for this studentship. It offers students to gain hand-on experiences in an exciting lab!

Franklin Lo

BSDB Gurdon Summer Studentship Report (33)

Slightly different to many of the fortunate students supported by the BSDB, I do not come from an especially strong scientific background. Approaching my final year of undergraduate medicine, I wanted to spend the summer studying something not offered by the traditional medical electives. I wanted a better appreciation for the more fundamental cellular processes that underly developmental biology. I wanted some sort of foundation to work from, so I could better understand some of the science that may eventually be translated to medicine in the future. I was also curious, how would I fare out of my natural habitat of wards and surgical theatres; would I take to laboratory work, or spend my 8-weeks fumbling with protocols and pipettes?

I began my internship at Prof Uri Frank's laboratory in the Biomedical Sciences building at NUI Galway. Under the supervision of postdoctoral researcher, Dr Miguel Salinas-Saavedra, I was given a crash course in laboratory techniques, methods to correctly follow protocols and the various rules surrounding the culture and manipulation of *Hydractinia*. During my internship I was expected to develop my practical skills and have an appreciation and understanding of the role of cellular senescence in the reprogramming of *Hydractinia*.

Hydractinia, or 'tiny jellyfish' as my family dubbed them, are a cnidarian model organism that has been employed in development, regeneration, and allrecognition studies. Roughly 8 mm in length

Hydractinia are naturally found on the shells of hermit crabs. Prof Frank's laboratory is the only one in Ireland to study these animals, and one of less than 10 laboratories worldwide. Similar to the freshwater cnidarian *Hydra*, *Hydractinia* have remarkable regenerative capacities. Figure 1 shows a photo of an anotated feeding polyp.



Figure 1: Photograph of a *Hydractinia* feeding polyp. Structures highlighted are the hypostome (green), tentacles (red), Body (blue), stolon (orange) and head (yellow arrow with bracket).

Hydractinia possess a population of adult stem cells, known as interstitial cells or i-cells. These cells are highly proliferative and normally replace cells during tissue homeostasis and regeneration¹. I-cells are anatomically restricted to certain areas in the adult; they are excluded from the intact head (but can migrate to it upon injury). Interestingly, isolated heads that lack i-cells, can nevertheless regenerate a fully functional animal that includes germline competent i-cells.

The mechanisms of conversion from terminally differentiated head cells to stem cells (i.e. i-cells) is currently unknown. This idea fascinated me. The concept also represented an opportunity to study the mechanisms that can destabilize the fate of animal cells in a regenerative, non-malignant context. Preliminary work done in the Prof Frank's laboratory suggests cellular senescence might be a potential trigger that induces dedifferentiation in neighbouring cells. This information lead to lots of reading; I needed a better understanding cellular

senescence and cell cycle limitations before I started practical experiments!

At the start of my internship I tried a number of different experiments centred around cellular senescence in *Hydractinia*. Using the fluorescent probe SPiDER-βGal to detect β-galactosidase activity, we sought to detect potentially senescent cells (a hallmark of senescence is high β-galactosidase activity that can be detected using SPiDER-βGal). Having detected β-galactosidase activity, Dr Salinas-Saavedra sought to optimise a method of performing an in vivo time-lapse on the confocal microscope. I meanwhile conducted some visual morphological studies in which I cut hypostomes and kept them in sea water with 5% cell culture medium, changed at regular intervals, to see the time frame associated with complete regeneration. The ultimate goal was to form fully regenerated polyps from cut hypostomes and go on to prove that these polyps were fully functional and could reproduce sexually. As the time passed we decided that the concentration of the media was too low, and the regime was changed to 10% medium for 1h changed daily. Unfortunately, by day 45 all samples had expired. Fig 2 shows an example of a healthy and an expired sample. Due to my limited time at the lab, optimising the protocol proved to be an impossible task but the experiment will be replicated by the lab, perhaps with shorter daily medium exposure.

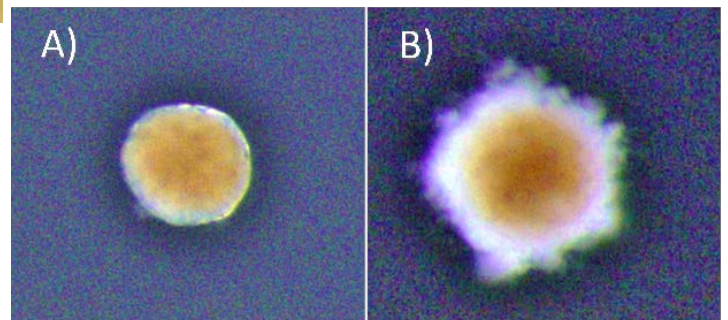


Figure 2: Both photographs are of a hypostome cut from a feeding polyp, kept them in sea water and exposed to 10% medium for 1h changed daily. (A) An example a healthy sample of a hypostome at day 43 post-cut. (B) An expired sample of hypostome at day 45 post-cut.

* Brightness in the photos was increased +40% for viewing purposes.

We also wanted to form a timeline to establish when cell replication occurs in hypostomes of *Hydractinia* at various days post cutting. To do this I conducted a double staining experiment in which I stained for both EdU and Piwi1 protein, using hypostomes at days 0-7 post-cutting along with full polyps to be used as controls. EdU is used to assay DNA synthesis in tissues and to detect cells which have undergone DNA synthesis during time of

incubation. Unfortunately, EdU staining proved to be difficult in my particular case. Initial experiments failed to stain, despite positive results for the antibody and DAPI staining; the latter stains DNA. We hypothesised that I had cut the control polyps too high from the stolon (above the proliferative zone) to see any EdU staining or the EdU protocol simply had not worked. Additional issues presented with poor staining due to tissue contraction.

To try and mitigate this problem I used a new EdU and antibody staining protocol. For this I used feeding polyps cut at the stolon. To combat the contraction issue, I added $MgCl_2$ for 15 minutes incubation prior to fixation to one sample, and sea water to the other as a control. Figure 3 shows an example of a feeding polyp from either sample group stained with DAPI, EdU and Piwi1 viewed under a confocal microscope. Interestingly, although very little change was seen in terms of tissue contraction, EdU staining appeared much stronger in the control sample in comparison to the $MgCl_2$ exposed sample. It would have been interesting to see whether a longer time in $MgCl_2$ would yield a more notable difference in tissue contraction.

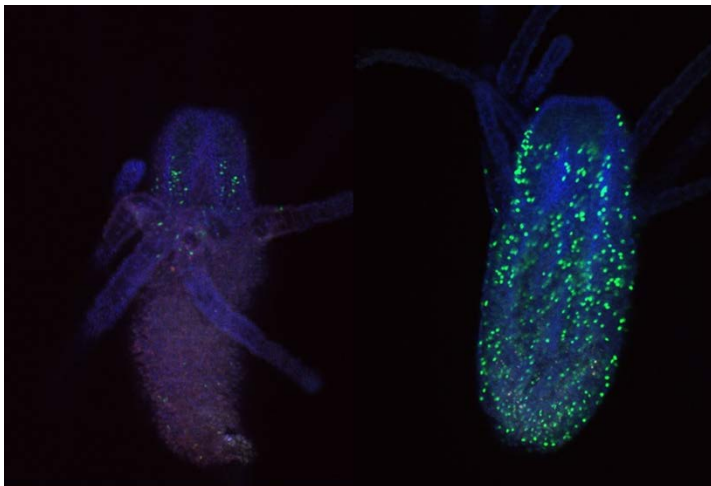


Figure 3: Fluorescent staining comparing hydractinia polyps incubated in $MgCl_2$ prior to fixation on left, to control on right. Blue stain – DAPI; green stain – EdU; red stain; Piwi1.

I also looked closely at the Piwi1 staining. PIWI proteins are a germline marker in *hydractinia*³. Staining for PIWI1 in these polyps enabled me to look at the i-cells; checking their quantity and location. It was apparent that some polyps had been cut too high as the expected i-band was not present. Figure 4 is an example of the separated strands of DAPI, EdU, Piwi1 with the far right coloured image ultimately compiled from each layer overlapping. Given the limited data, more experiments need to be conducted to draw any strong conclusions. Ultimately, I gained very real insight into the challenges faced daily by

researchers and have a new appreciation for the resilience of those conducting experiments.

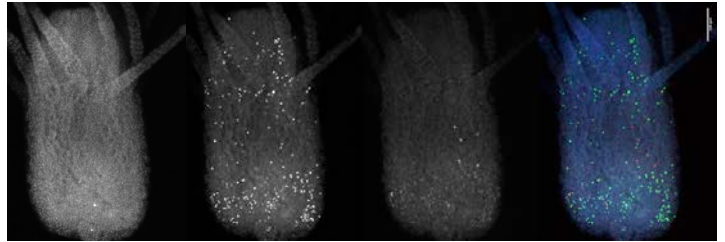


Figure 4: Hydractinia polyp stained with DAPI, EdU, Piwi1 with image compiled of the three strands (far right) viewed under confocal microscope.

The weeks felt very short as I approached the end of my internship. I would like to thank Prof Uri Frank and all of my laboratory colleagues for their endless support and incredible patience. With the support of the BSDB Grant I was able to work as part of a cutting-edge research team, perform independent experiments, participate in weekly meetings and discuss concepts with experienced researchers. I learnt specific methods and better understood protocols. The transferable laboratory skills that I have developed will certainly help me to secure a research position after graduation, and hopefully enrich my medical career. I wish the lab all the best in their endeavours to understand the fundamental questions in regenerative biology.

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Réiltín Ní Theimhneáin

Visualising neural crest induction, migration and differentiation in *Xenopus*

Throughout my undergraduate studies I have become increasingly captivated by the intricacy and elegance of animal development. Especially interesting to me is how processes such as morphogenesis, tissue patterning or cell migration, which can appear incomprehensible, emerge from relatively simple interactions at the molecular level. Observing how a single cell transforms into a complex organism is a unique and thought-provoking experience. I am grateful to the BSDB for the studentship allowing me to explore this field. I would strongly recommend the Gurdon studentship to anyone interested in topics ranging from evolution, epigenetics, cell signalling, cancer, to stem cells and regeneration – all of these processes may be elucidated by taking a developmental point of view.

During the summer studentship I have learnt to work with *Xenopus laevis* embryos and keep track of their development. The aim of my project was to optimise techniques for visualising the neural crest with other tissues relevant to its induction, migration and differentiation. To do this I used two well established techniques in developmental biology: *in situ* hybridisation and immunofluorescence (see Figure 1).

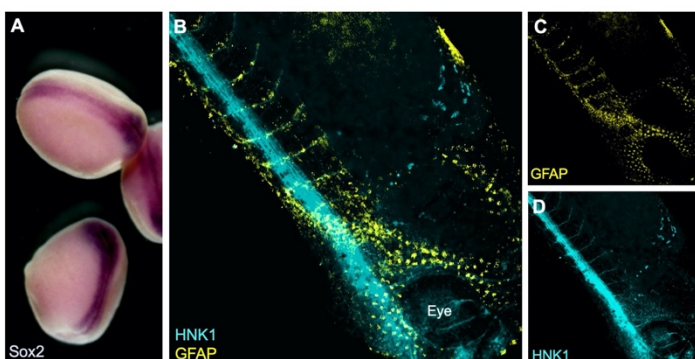


Figure 1: A) Colorimetric *in situ* hybridisation with neural plate marker *Sox2* in late neurula stage *Xenopus* embryos. B-D) Whole-mount fluorescent immunostaining for neuronal marker *HNK1* and glial marker *GFAP* in a tailbud (Neuwkoop and Faber stage 31) embryo.^{+/+}

Why study neural crest cells?

The neural crest is a fascinating population of cells unique to vertebrates, which is induced at the neural plate border and following neurulation delaminates and migrates away from the neural tube. A subset of these cells migrates into head regions where it gives

rise to a variety of tissues including bones, cartilage, as well as neurons. This cranial neural crest also migrates into the branchial (or pharyngeal) arches and contributes in a major part to the craniofacial skeleton. This has undergone major changes during vertebrate evolution. For instance, some of the jaw bones present in our common ancestors with reptiles have given rise to the middle ear bones of mammals (Santagati & Rijli, 2003). A possible explanation for this versatility of the neural crest is that its cells retain multipotency for longer than the three embryonic germ layers, prompting some to consider it a 'fourth germ layer' (Simoes-Costa & Bronner, 2015).

The diversity of neural crest-derived cells, which also includes melanocytes, Schwann cells, meninges or the cornea, makes it an important model of differentiation with a potential for therapeutic applications. It is also a great model for studying cell migration (Szabó & Mayor, 2018) and by proxy epithelial to mesenchymal transition in cancer metastasis. Recent work even attributed the ability to remove cellular debris from early neural tube to migrating neural crest cells, potentially through a macrophage-like mechanism (Zhu, et al., 2019).

Going further with established techniques

I have been testing and optimising techniques to visualise proteins and gene expression that may help elucidate how the neural crest gets induced and how it migrates through the embryo. For example, I have imaged the neural crest with nearby mesoderm, which is required during induction, using a combination of fluorescent *in situ* hybridisation (FISH) and immunostaining. In order to visualise expression of two different genes within the embryo a double *in situ* hybridisation (ISH) can be used. This is especially important in *Xenopus*, as no antibody is known to efficiently and exclusively label the neural crest. Although colorimetric ISH is easier and does not require clearing of the tissues, it doesn't enable exploring the 3D structure by imaging the whole embryo at once. I have used confocal and multiphoton microscopy to analyse the embryos (see Figure 2). Unfortunately, it seems that using two RNA probes at the same time reduces signal intensity and although I have tried to optimise the signal amplification reaction and bleaching to neutralise endogenous peroxidase activity, I have not been able to reduce the background.

One possibility is to delimit the neural crest using an antibody for fibronectin, an extracellular matrix component that encourages neural crest migration. Using double immunostaining (Figure 2B) I was able to confirm migratory neural crest cells express N-

Cadherin near the optic vesicle as fibronectin outlines the neural crest streams (Scarpa, et al., 2015). Towards the end of my summer project, I have also manipulated cell contractility using drug treatments to observe changes in neural crest cell behaviour using several antibodies.

How to get radial: Unlocking the mechanisms for symmetry establishment across plant organs

The development of multicellular organisms depends on correct establishment of symmetry both at the whole-body scale and within individual tissues and organs. Setting up planes of symmetry must rely on communication between distant cells within the organism, presumably via mobile morphogenic signals. Although symmetry in nature has fascinated scientists for centuries, it is only now that molecular data to unravel mechanisms for symmetry establishment are beginning to emerge.

Over the summer, I had the opportunity of conducting a research project at the John Innes Centre (JIC) working under the supervision of Dr Laila Moubayidin, whilst participating in the amazing JIC/TSL/EI International Undergraduate Summer School.

Dr Moubayidin's research looks at identifying a conserved "core machinery" necessary and sufficient to control symmetry establishment across plant organs. She is elucidating the underlying process of symmetry establishment at the cellular, molecular and genetic level. Unlocking the molecular mechanisms that underpin this regulation holds potential for understanding the processes that allow plant organs to reach their perfectly-optimized shape and function.

The project I worked on focused on gynoecium (the plant female reproductive structure) development, using *Arabidopsis thaliana* as a model system. The gynoecium forms in the centre of the flower and it is derived from the fusion of two carpels. The gynoecium includes the ovary, which displays bilateral symmetry, and the style, at its apex, characterized by radial symmetry (Figure 1). The ovary is important for seeds production and the style is important for fertilization.

During its development, the distal end of the gynoecium becomes radially symmetric via a switch from bilateral to radial symmetry. Symmetry transitions are common during embryogenesis in all multicellular organisms. In most cases, the transition is from radial to bilateral symmetry, which is controlled by *Hox* and *decapentaplegic* genes in animals. The *A.thaliana* gynoecium, instead, is the only molecularly documented example of a developing structure that reprograms its development over time to achieve a bilateral-to-radial symmetry transition.

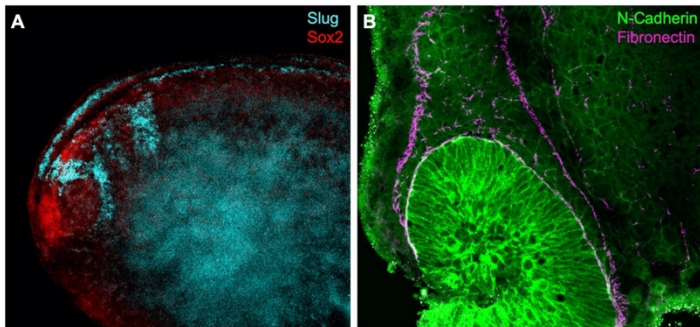


Figure 2: A) Fluorescent in situ hybridisation using RNA probes for *Slug* (neural crest) and *Sox2* (neural plate) in a whole-mount stage 22 *Xenopus* embryo. B) Dissected embryo immunostaining shows N-Cadherin expression in migratory neural crest. Fibronectin outlines the streams of cranial neural crest.

I thank Prof Roberto Mayor for supervising this summer project and Dr Adam Shellard for teaching me methods used in the lab. I have learnt a lot about how research is done and presented my results at a lab meeting in the final week and used this experience to transition from undergraduate study into my PhD.

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Matyas Bubna

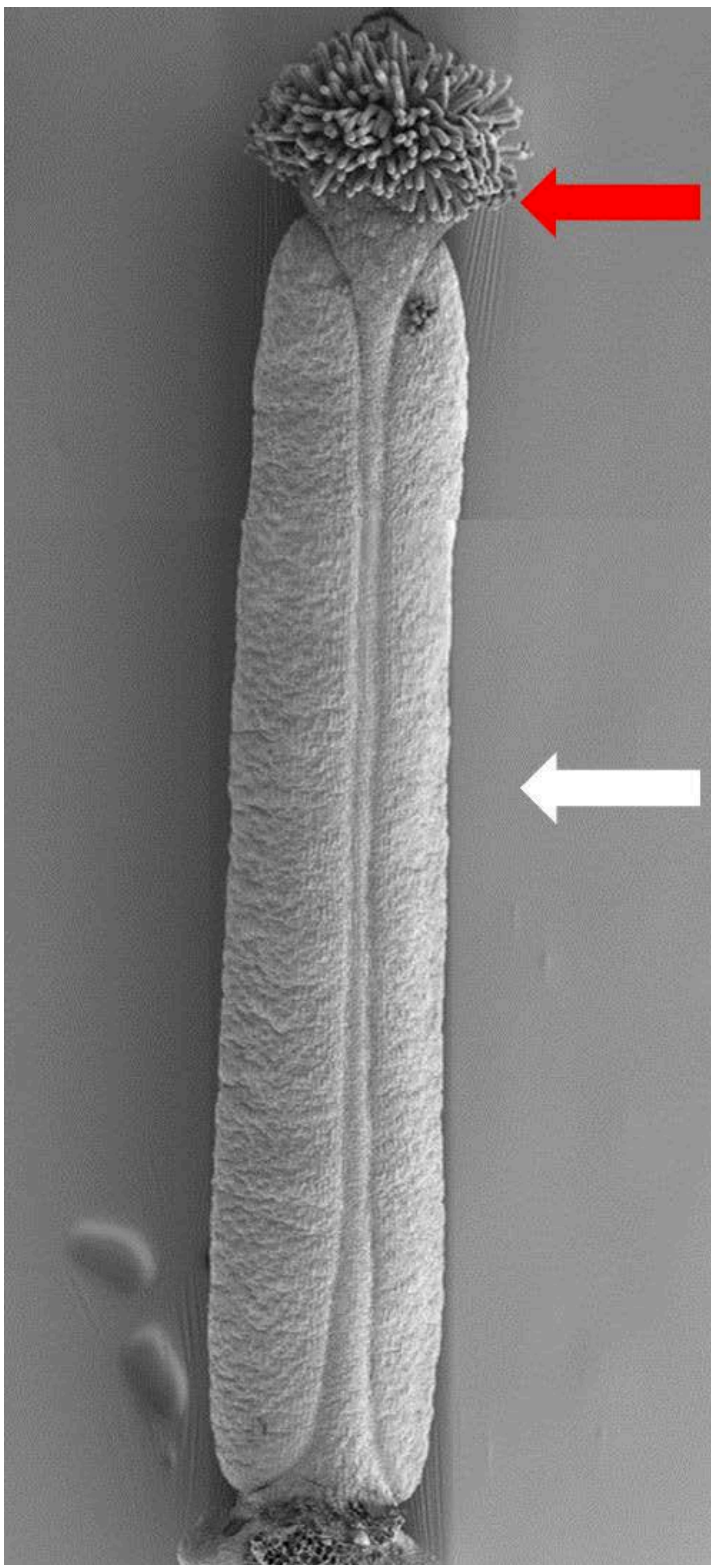


Figure 1: Scanning Electron Microscopy picture of *A.thaliana* WT gynoecium. Red arrow indicates the style, radially symmetric; white arrow indicates the ovary, bilaterally symmetric.

Growing evidence shows that coherent organ growth and symmetry establishment during organogenesis are influenced by post-translational modifications of specific nuclear and cytoplasmatic proteins. My project focused on the role of O-linked *N*-acetylglucosamine modification during gynoecium development. O-GlcNAcylation is a

post-translational modification that consists of a single O-linked *N*-acetylglucosamine attached to either a serine or a threonine residue. It has been extensively studied in animals, where it regulates a wide range of developmental and metabolic processes.

O-GlcNAcylation is dynamically controlled by two enzymes: an O-GlcNAc transferase (OGT) and an O-GlcNAcase (OGA), which add and remove O-GlcNAc, respectively. O-GlcNAcylation occurs in the cytoplasm, nucleus and mitochondria, and it is implicated in cellular processes, including transcription, translation, signal transduction, nuclear pore function, epigenetic regulation and proteosomal degradation. Altered levels of protein O-GlcNAcylation in animals have been associated with neurodegeneration, diabetes, cardiovascular diseases and cancer.

Arabidopsis thaliana has two putative OGTs: SPINDLY (SPY) and SECRET AGENT (SEC) whose role is essential for plant development, since *spy;sec* double mutant is embryonically lethal, similar to the OGT knockout mutant in animals.

Exploring this interesting and at the same time quite complicated topic, gave me the chance of learning and mastering a wide range of molecular biology techniques, such as cloning and Yeast-two-Hybrid. It was amazing to experience practical methods and protocols I had studied during university courses in Rome and to understand how much work, attention to detail and care there is behind even repetitive actions (Figure 2).

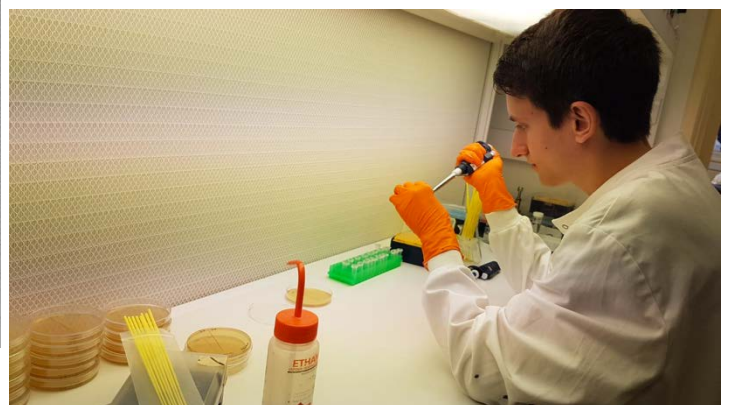


Figure 2: Working with transformed yeast plates in very sterile conditions.

Using the state-of-the-art JIC microscopy facilities, I had the opportunity to look at wild-type and mutant *Arabidopsis* gynoecia at different developmental stages using Scanning Electron Microscopy (SEM). Fixing samples for SEM analysis, dissecting flowers and using machines such as the Critical Point Dryer and the Gold Sputter Coater was a challenging experience, but the final result was

worth the hard work. I was astonished whilst I was conducting SEM analysis as it allows observation of samples at incredible magnifications, providing details of a single cell surface (Figure 3).

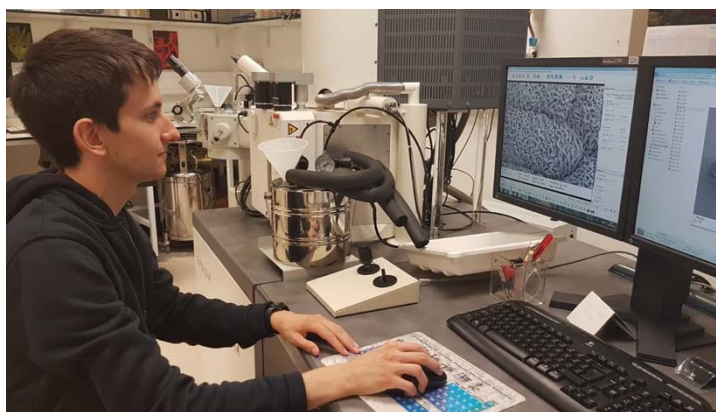


Figure 3: Observation of gynoecia at the Scanning Electron Microscope.

At the end of this experience, I felt extremely grateful for several reasons.

Firstly, I greatly enhanced my knowledge of plant developmental biology. As a “Sapienza School for Advanced Studies” student, in the first year of university, I was keen to work on plants during my Research Project, so I applied to the International Undergraduate Summer School at the JIC. After being selected, I was urged by Dr Moubayidin to apply for a Gurdon/The Company of Biologists Summer Studentship offered by the British Society for Developmental Biology (BSDB). Moreover, working side-by-side an experienced, young principal investigator, such as Dr Moubayidin, has been a rare opportunity and a great inspiration for my future career. Dr Moubayidin has been recently appointed a prestigious Royal Society University Research Fellowship, therefore it has been an exciting time to be part of her lab, experiencing how a research group is built and the importance of teamwork.

Lastly, this summer placement has given me great insight into research career paths and has made me even more aware of how incredibly surprising and stimulating daily lab life can be. Each workshop organized by the JIC Summer School and every seminar held at the JIC has been a great chance for me to learn about new topics, uncovering the research world of an international centre and the beauty of working in a collaborative and stimulating atmosphere.

Altogether, this unexpected chain of events has lead me to immensely broaden my scientific and transferable skills, as well as my perspectives, not only as a scientist, but also as a “world citizen”.

This Summer School experience, set in the incredibly positive environment of the JIC, has reaffirmed my desire of pursuing a career in science, despite all the hard work it actually requires. I wholeheartedly recommend the Gurdon/BSDB Summer Studentship and the possibility to carry on research abroad during university studies, visiting new countries and encountering new cultures. I believe every undergraduate student should be made aware of unique opportunities, like this, available to them.

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Luca Argirò

BSDB Gurdon Summer Studentship Report (36)

Throughout my Biological Sciences degree, I came to realise that I want to pursue a career in medicine that combines clinical practice with research. After having thoroughly enjoyed my final year research project that focused on bacterial genetics, I decided to apply for a studentship in a biomedical research lab. This was with the hope that I'd be able to apply some of the experimental techniques I'd already learnt to understand complex processes in living organisms. Having a good grounding in organismal biology will be useful when applying a research perspective to human systems.

I was very fortunate to complete my Gurdon/The Company of Biologists Summer Studentship under the supervision of Dr. Robert Knight at King's College London. His group uses zebrafish as a model to explore the molecular control of muscle repair and the regulation of muscle stem cells, otherwise known as satellite cells. These cells are characterised by their expression of the pax7b transcription factor (1). The zebrafish is a suitable model organism for their investigation, as it has a

well-defined genome and is transparent in its larval stages. Therefore, genetic manipulations that affect cell and tissue dynamics can be readily visualised. Their work particularly appealed to me, as I am very interested in the use of reverse genetics approaches to investigate genetic diseases and how they arise due to the disruption of development.

Background to project:

The transmembrane Ret tyrosine kinase receptor is activated by the binding of Glial-derived neurotrophic factor family ligands (GFL) to Glial-derived neurotrophic factor receptors (Gfra), as this interaction stimulates Ret dimerisation and subsequently, its activation. Ret signalling has an important role in the development of the enteric nervous system and hepatic tissue, but its role in muscle development is poorly understood. Ret signalling has been implicated in facioscapulohumeral muscular dystrophy, which manifests as the weakening of the facial muscles in its initial stages (2). The binding of artemin2 (artn2), a GFL, to Gfra3 is an interaction required for the activation of Ret related to the development of the cranial muscles in zebrafish (3). My project set out to investigate the role and level of importance of Ret signalling in the development of cranial muscle satellite cells.

Experiments:

1) Is an activating ligand for the Ret receptor able to alter cranial muscle development?

To test this hypothesis, I performed MF20 immunolabelling on zebrafish embryos exhibiting heat-shock inducible artn2 overexpression, as well as controls. Diaminobenzidine (DAB) staining was used to detect the signal from the antibodies, which made myofibres appear orange-brown (Figure 2a). The embryos were fixed and imaged using bright-field microscopy. The sizes of a subgroup of cranial muscles were measured and compared between the experimental and control samples (Figure 1). There did not appear to be a significant difference in muscle size between the two sample groups, suggesting that the activating ligand for the Ret receptor cannot alter cranial muscle development.

2) Is an activating ligand for the Ret receptor able to alter cranial muscle satellite cell formation?

To test this hypothesis, a transgenic line was used, in which pax7b-expressing cells were labelled with EGFP and artn2 was overexpressed. Embryos with this genotype, along with GFP+ embryos with the wild type artn2 genotype, were fixed and imaged

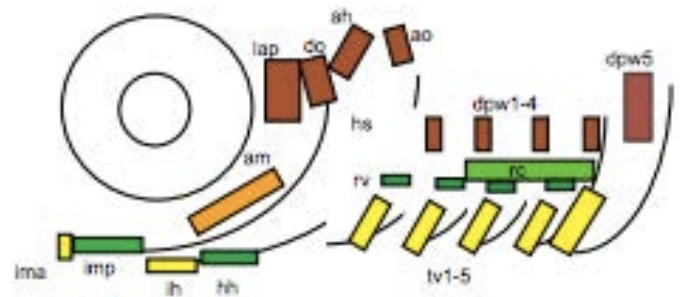


Figure 1: Schematic left-side view of the zebrafish cranial muscles. The muscles of interest in my investigations were the lap (levator arcus palatine), do (dilator opercula), ah (adductor hyoideus) and ao (adductor opercula). These muscles were selected due to their flat shape, making them easy to analyse (4).

using confocal microscopy. The number of GFP+ myofibres and myoblasts within the muscles of interest were quantified and compared between the experimental and control samples. I was unable to discriminate a significant difference, due to the control sample size being too small to be able to perform statistical tests. Therefore, more wild-type embryos need to be imaged and analysed to confirm whether artn2 can alter cranial muscle satellite cell formation.

3) How important are satellite cells for cranial muscle development?

To answer this question, I ablated pax7b-expressing cells during development. A GAL4;UAS system was used, in which the pax7b promoter induced expression of nitroreductase (NTR). Embryos which carried this system were treated with metronidazole, which reacts with NTR to produce a cytotoxic compound. The muscles of these embryos, as well as controls, underwent MF20 immunolabelling and these signals were detected using either DAB or tyramide FITC, to which a green fluorophore is conjugated. Depending on the detection method, the embryos were imaged using bright-field or confocal microscopy, respectively, and the myofibres in each image were quantified (Figure 2). Analysis of the bright-field images suggested a difference in the number of myofibres within the cranial muscles of the experimental and control sample groups. However, quantification analysis of the confocal images did not reveal a significant difference. Therefore, further experiments must be carried out to confirm the importance of satellite cells for cranial muscle development.

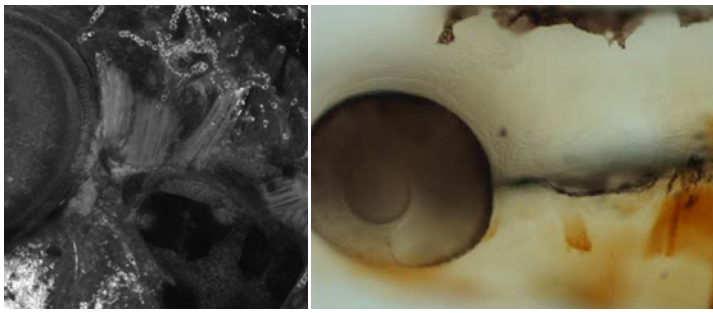


Figure 2: MF20 immunostaining of zebrafish embryos after the ablation of their *pax7b*-expressing cells during development. a) Confocal image of an embryo in which the MF20 signal was detected with tyramide FITC, b) Bright-field image of an embryo in which the MF20 signal was detected with DAB

inhibitor therapy for facioscapulohumeral muscular dystrophy. *eLife*, pp. e11405.

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Isabel Swinburn

Outcomes:

At university, I had only used optical microscopy in practical sessions. However, following my time in the Knight lab, I now feel confident in using a much wider range of more advanced microscopy techniques to gather experimental data. I also appreciate much more the importance of analysing the data - quantifying cells and myofibres within images seemed like a simple task, but it took me weeks! Unlike at university, the data I collected whilst working in the lab was raw and unclear and strict parameters had to be set for its analysis. Although the task was daunting and sometimes difficult, it was very gratifying when the numbers and statistical test results allowed me to test the hypotheses generated and realise that I had made a scientific discovery.

I would like to say thank you to Robert for allowing me to work under his supervision, and to the British Society for Developmental Biology for providing the financial backing to enable me to do so. A special thank you also goes to the rest of the Knight group for all of their support and encouragement throughout. Despite my focus being primarily on a career in medicine, this experience has reinforced my desire to continue to contribute to the type of evidence that will drive medical practice. I would recommend anyone considering a career in biological research to apply for this programme.

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BSDB Gurdon Summer Studentship Report (37)

Developing force inference strategies to analyse tissue-wide stress in the *Drosophila* germband

Morphogenesis is an integral aspect of embryonic development, shaping collections of cells into functional tissues. Developmental mechanics aims to unravel how forces across spatial scales, from cytoskeletal processes, to junctional dynamics and inter-tissue interactions, facilitate emergent transformations in embryonic form. Analysing mechanics across scales requires a systems-level approach, where quantifying tissue-wide stress and material properties is essential. Current methods for directly measuring forces *in vivo* have major short-comings: methods (e.g. laser ablation) are invasive, perturbing the stress field and prohibiting extensive sampling. Non-invasive force inference approaches are useful alternatives, using segmented images of fluorescently-labelled cells to infer relative tension across each cell membrane and pressure in every cell. They do this by fitting tissue-wide tension and pressure nets to these data via the assumption of force-balance.

Focusing on *Drosophila* germ-band extension, a well-studied example of axis extension, I developed computational tools for non-invasive inference of stress distributions from microscopy data. These algorithms consider an epithelial sheet as a 2D curved-polygonal lattice, with edges demarcating cell membranes, and vertices defined where three cells meet (Fig. 1a). Using some simplifying physical assumptions, they use the geometries of edges at each vertex, as well as the curvatures at each edge, to infer relative pressures in every cell and relative tensions at every edge.

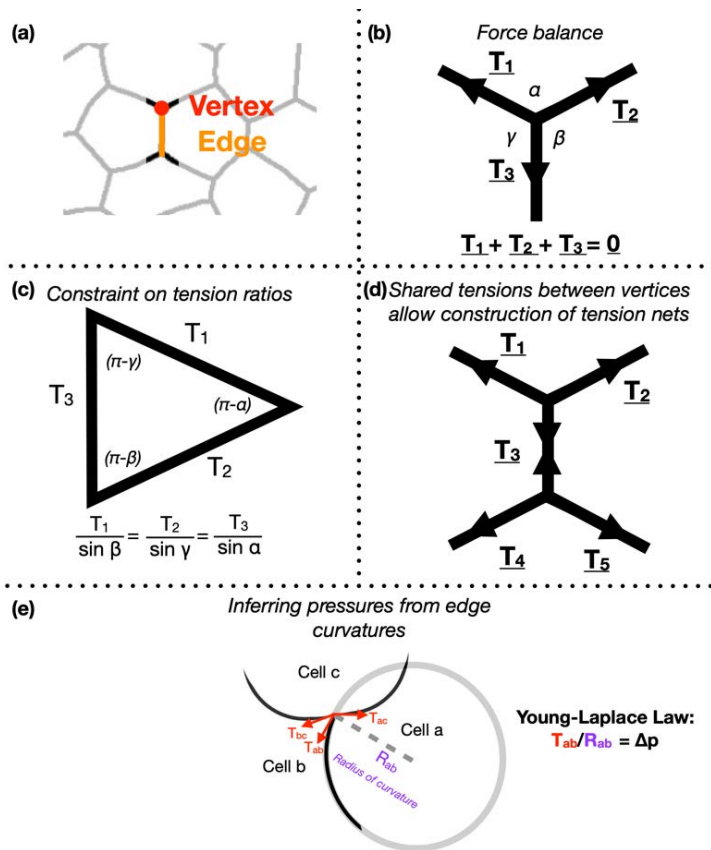


Figure 1

Despite the variation in computational implementation strategy, many existing force inference methods have a common underpinning logic. Specifically, they assume that the tensions at every vertex are balanced; in other words, that the system is in mechanical equilibrium (Fig. 1b). Thus given the angles that edges of a given vertex make with each other, as inferred from microscopy data, one can infer ratios of relative tensions (Fig. 1c). Further, they assume that tension is continuous across an edge, meaning relative tensions can be inferred tissue-wide (Fig. 1d). Cellular pressures can also be inferred. When edges are curved, it is assumed that the cell for which the edge is convex shows higher pressure. In fact, one can infer the pressure differential in terms of the inferred tension and the radius of curvature of that edge using the Young-Laplace law (Fig. 1e).

During my stay with the Sanson lab, I developed a pipeline in Python for force inference. The pipeline takes the many frames of segmented germband movies curated by the lab, uses one of several possible force inference strategies, and outputs the inferred tensions and pressures back to the lab's wider computational workflow (Fig. 2). Given the wealth of data collected by the lab, these strategies now have immediate use in analysing global patterns of stress (indeed without the need for additional experiments), for example in characterising non-intuitive changes to stress

distributions in key morphogenetic mutants (e.g. *sidekick* mutants, see Finegan et al 2019, PloS Biology, <https://doi.org/10.1371/journal.pbio.3000522>). Besides direct analyses of stress distributions, these inferences can now be used to parameterise physical models of the germband, across spatial scales. Beyond this, I have compared the various implementation strategies with regards to their concordance in predictions, and tested their relative capacities of dealing with noise in segmentation. I have also surveyed both the practical and conceptual challenges of these strategies with an intention of refining existing methodologies for faster and more accurate inference.

This project has allowed me to refine skills in programming, especially in visualisation, data processing and algorithm optimisation. I am now putting the algorithms together into a coherent and user-friendly package for use in the lab internally, but also, excitingly, to be released as an open-access resource. Further, working in Dr. Sanson's lab also introduced me to key concepts in mechanics, situated in this biological context.

Given the highly interdisciplinary makeup of this project, supervised by Dr. Alex Nestor Bergmann (mathematician and physicist), Dr. Guy Blanchard (computational biologist), and Dr. Bénédicte Sanson (developmental biologist), I enjoyed how divergent perspectives and methodologies are brought together to solve this multi-scale problem. I endeavour to pursue similar interdisciplinary research in a PhD and beyond, carrying out both dry and wet components.

I would like to thank Dr. Alex Nestor Bergmann and Dr. Guy Blanchard for their fantastic supervision and the Sanson lab as a whole for their support and their fascinating and diverse lab meetings. I finally want to thank the BSDB for providing me the opportunity to carry out this research, and urge other undergraduates to apply to the Gurdon Studentship.

Jake Cornwall Scoones



How to build a spider: investigating the role of Delta in posterior segmentation

Three animal phyla have segmented bodies – the vertebrate chordates, the annelid worms and the arthropods. To understand the evolution and development of these segmented bodies it is necessary to identify what mechanisms regulate segmentation and the similarities and differences of these mechanisms among phyla. Amongst arthropods there are two main different mechanisms for segmentation: long-germ arthropods, such as *Drosophila melanogaster* which develop their segments simultaneously; and short-germ arthropods, constituting the majority of arthropods, which add their posterior segments sequentially from a segment addition zone (SAZ). Under supervision from Dr Anna Schonauer in Professor Alistair McGregor's lab, I aimed to investigate the regulation of posterior segmentation in arthropods by further studying the Delta-Notch signalling pathway in the spider *Parasteatoda tepidariorum*.

Spiders are a useful model for answering questions about the regulation and evolution of segmentation as they develop their prosomal (anterior) segments simultaneously like *Drosophila* but their opisthosomal (posterior) segments sequentially in a manner analogous vertebrate segmentation. It is understood that the addition of posterior segments relies on the formation of the SAZ, which develops at around stage 6 in spider embryos through dynamic Wnt and Delta-Notch signalling. These genes are subsequently also required for segment addition. Specifically, Delta appears to differentially regulate the posterior and anterior regions of the SAZ to maintain *Wnt8* in the posterior SAZ but lower its expression in the anterior SAZ to facilitate the formation of nascent segments. However, little is known about the genes downstream of Delta that are involved in segment addition.

The gene *hairy* is thought to be involved in segment addition and it has been shown to have a similar oscillatory expression pattern to *Delta* leading to the hypothesis that it may be regulated by Delta as part of a gene regulatory network (GRN) that results in segment addition. Previous studies of the role of Delta in segment addition used parental RNA interference to knockdown this gene. However, the consequential loss of the SAZ resulting in a truncated germ band impedes investigation into any specific, localised downstream effects of loss of Delta. To be able to investigate the relationship between Delta and *hairy*

I therefore aimed to use embryonic RNAi to knockdown Delta in subsets of posterior cells. This would allow embryonic development to progress as normal without truncating the germband, but create Delta knockdown clones allowing me to see within an embryo if *hairy* expression is different in cells with and without a knockdown of Delta. Thus I would be able to test whether *hairy* does act downstream of Delta and if so, might be able to infer what potential role it may have in segment addition.

Microinjections of Delta double stranded RNA and biotin into single cells at embryonic stage 1F (when there are only 32 cells) were carried out with the aim of knocking down Delta and at the same time staining the clone of cells derived from the injected cell. The microinjection technique itself was technically demanding, requiring a lot of patience and practice and it took me two weeks before I was able to successfully inject a cell without it bursting. Once I had injected successfully into a single cell (Figure 1) I gained experience in the correct technique needed and I was then able to successfully inject about 15% of embryos in a cocoon (a cocoon containing approximately 200 embryos). The other main technique I used was *in situ* hybridisations (ISH), which used labelled RNA probes to bind to the *hairy* mRNA in all the cells in the embryo to show where *hairy* is being expressed. I carried out the ISH two days after the microinjections as this is when embryos develop their SAZ and begin to add their first segments. As a control, I stained embryos solely for *Delta* or *hairy* as this allowed me to see the wildtype expression of each (Figure 2). I also performed a double ISH for Delta and *hairy* which confirmed their overlapping expression in the posterior of the embryo.

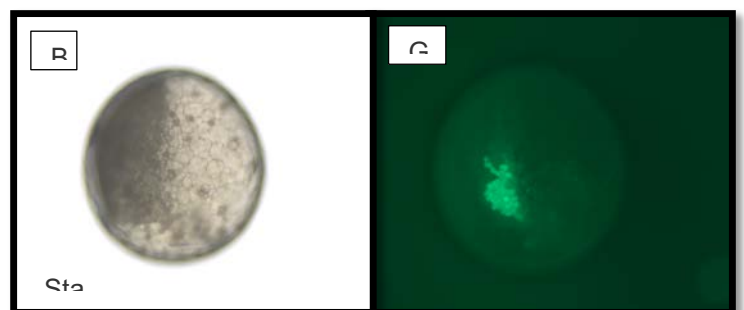


Figure 1: The first embryo I successfully injected with a practice injection mix containing Fluorescein isothiocyanate (FITC). (Left) A brightfield (BF) image of an injected embryo to show morphology and determine that the clone is located in the germ band (darker grey). (Right) The clone of cells derived from the cell indicated with a FITC dye which fluoresces green.

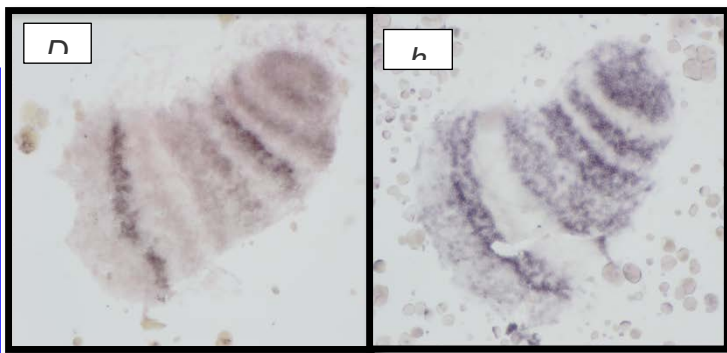


Figure 2: Flatmounts of embryos at late stage 7 of development, the embryos are orientated so that the anterior of the germband is on the left. Wildtype expression of *Delta* (left image). Wildtype expression of *hairy* (right image).

No blastodermal cell fate map exists for *P. tepidariorum* and as such it was never guaranteed that I would get clones in the posterior opisthosomal segments. Unfortunately, all my *Delta* knockdown clones occurred in the anterior prosomal segments so I was unable to draw conclusions about any *Delta-hairy* interaction in the SAZ. My anteriorly located clones however, do suggest an interaction between *Delta* and *hairy* in the prosomal segments. Here, I was able to detect downregulation of *hairy* expression in the subset of *Delta* knockdown cells. Most of our clones occur in a single prosomal segment, however in a stage 8 embryo, the clone spanned four developing prosomal segments, and showed downregulation of *hairy* across all of them. This suggests that *Delta* directs *hairy* in patterning of the anterior segments (data not shown).

Over the course of this project I learned many different things, most importantly that in science, patience and perseverance are key. I was surprised with how involved each technique was and quickly learned to take the advised protocol amendments suggested by my peers. Being part of a team all of whom supported me, helped me and questioned my work ultimately encouraged me to become a better researcher. The experience has confirmed my ambition to pursue a PhD and focused my interest on understanding the fundamental and complex molecular interactions that ultimately regulate and drive development.

Grace Blakely

BSDB Gurdon Summer Studentship Report (39)

Exploring the genetic control of microRNAs in *Drosophila melanogaster*

This summer, thanks to the BSDB Gurdon Studentship, I was able to work closely with a PhD

student in the lab of Sarah Newbury at the Brighton and Sussex Medical School. Under their supervision I was able to get an applied, practical approach to lab work, much different from that experienced during my undergraduate course.

My project involved looking at the genetic control of microRNAs in *Drosophila melanogaster*, otherwise known as the common fruit fly. MicroRNAs are small-noncoding RNAs that participate in RNA silencing and regulation of gene expression. miRNAs are able to base-pair with their complementary target mRNA, and through this they are able to silence them, either by their subsequent degradation or prevention of their translation. Previous studies have shown that exoribonucleases, known as Pacman (XRN1) and Dis3L2 degrade different microRNAs through the mRNA decay pathway, shown in Figure 1.

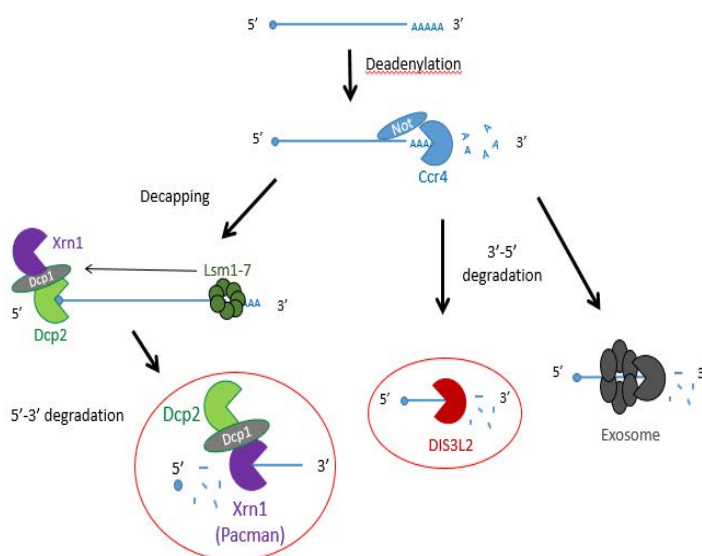


Figure 1: The mechanisms of mRNA decay. Most mRNAs undergo decay through the deadenylation dependent pathway shown above. The poly(A) tail is first removed by a deadenylase (shown here as Ccr4-Not) and then proceeds down 3 possible routes: decapping by enzymes (shown as Dcp1/2), followed by 5' → 3' decay by XRN1 (Pacman in *Drosophila*) or 3' → 5' decay by Dis3L2 or the exosome.

The project made use of wing imaginal discs, which are highly proliferative organs found in *Drosophila* that will eventually develop into the adult fly's wings. Prior work in the lab had found that there were significant differences between the size of these discs in both *pacman* and *dis3L2* mutants, with *dis3L2* mutants having much larger discs (Towler et al. 2016), and *pacman* mutants having smaller ones (Waldron et al. 2015). Both

exoribonucleases are conserved to humans and their defects have shown to be significant in human disease as well. For example, mutations of DIS3L2 in humans have been linked to Perlman syndrome, an overgrowth syndrome which presents as organomegaly and is associated to a high risk of developing Wilm's tumours (Astuti et al. 2012). Together this suggested that there could be an involvement of these exoribonucleases in the control and regulation of cell proliferation and apoptosis within these discs, potentially through their degradation activity. Therefore, the aim of my project was to study the difference between levels of specific miRNAs (which were extracted from these WIDs) in both *pacman* and *dis3L2* mutants, compared to their respective control wildtype.

My results, shown in Figure 2, were obtained through the use of qPCR (quantitative or real-time PCR). Also shown on Figure 2 are two other datasets from previous high-throughput RNA sequencing experiments, known as Cuffdiff and sRNAtoolbox.

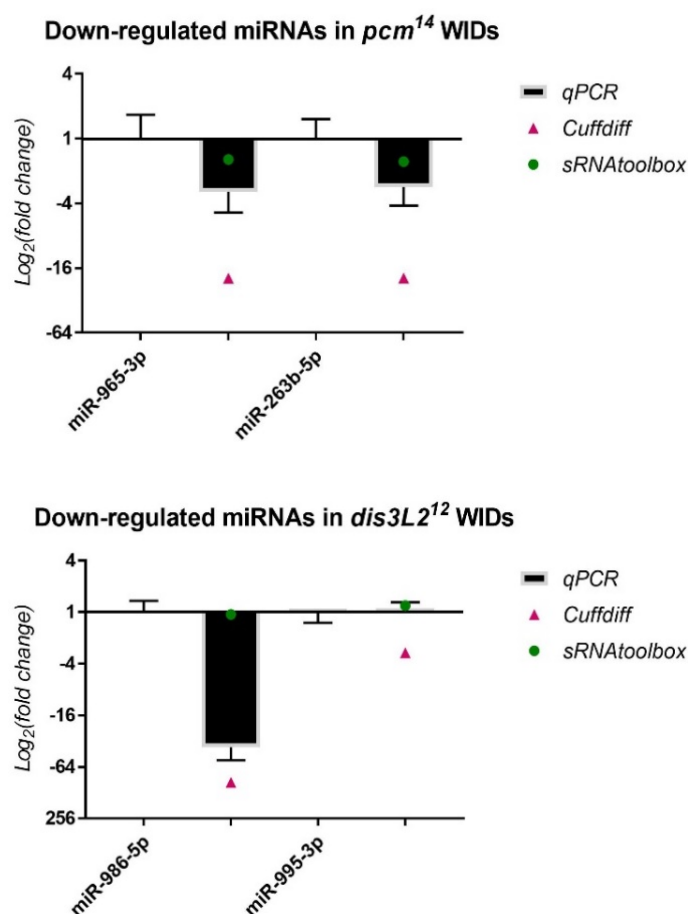


Figure 2: The fold change of miRNAs downregulated in both *dis3L2* and *pacman* (*pcm*) mutants normalized to their controls, obtained through my qPCR and previous RNA-seq methods.

Looking at my data, the *pacman* mutants showed that there was a negative fold change in the levels of two miRNAs, miR-A and miR-B when normalized to their wildtype's levels. This indicated that the two miRNAs are downregulated in the *pacman* mutants. This confirmed the results obtained from the RNA sequencing, as they both showed that the miRNAs were downregulated as well.

Results from the *dis3L2* mutants were less definite. For one of the miRNAs, miR-C, there was a negative fold change when normalized to the wildtype's level. Again, this confirmed results obtained from the RNA-seq, but my data, and data from Cuffdiff, suggested a much stronger downregulation than that from sRNAtoolbox. For the other miRNA, miR-D, qPCR showed that there was no significant fold change in the mutants. This agrees with results from one of the RNA-seq, but not the other. Data from Cuffdiff showed a slight negative fold change of miR-D, suggesting it is downregulated in the mutants. However, my data, and that from sRNAtoolbox, suggested there is no change between the wildtypes and mutants.

Further areas of my project involved looking at the difference in volume of the abdomen and ovaries in flies with a defect in the gene of a TUTase known as Tailor, to see whether it was involved in controlling their size. TUTases, or Terminal Uridyl Transferases, are enzymes that uridylylate miRNAs, potentially serving as a signal for exoribonuclease-mediated degradation such as Dis3L2. This involved me freezing flies in liquid nitrogen, then photographing and dissecting out their ovaries. The limited number of ovaries measured suggested that there were no significant differences in the sizes between the wildtype and mutants.

In addition to this, I also looked at the differences in sizes of wings in Tailor mutant and double mutants of Tailor and Dis3L2 compared to wild types. This included dissecting wings and mounting them on a slide then taking measurements using computer software and a microscope. We hypothesised that the wings from the Tailor mutants would be the same size as the wildtype but the Tailor/Dis3L2 double mutants would have larger wings than the wildtype. My results here were too limited to draw a reliable conclusion but indicated there was no difference in wing sizes between the mutants and wildtype.

Overall, my time in the lab has proved highly valuable and interesting. Learning about the techniques in lectures and actually performing them yourself in a lab are completely different experiences and I am really grateful. I feel it was

really important for me to experience the fly work alongside the molecular work as this has helped me to familiarize myself with numerous practises and therefore determine what is most interesting and suitable for me in the future. But not only did I learn how to perform these techniques, I was also introduced into the world of *Drosophila*, ranging from learning about their genome, recognising their phenotypes, and performing my own genetic crosses to learning their general upkeep and how to do simple things such as egglays or anesthetizing the flies. This experience for me has really increased my interest in developmental biology. Being able to produce my own data and learning to work independently in a lab have also strengthened my desire to do a PhD and I'm very appreciative that I got to experience something not many undergraduate students will. On top of all this, being inside a lab with such a friendly and welcoming group of people has made it all that more enjoyable.

A huge thank you to everyone in the lab for their support and assistance, and to the BSDB for making this opportunity possible through the Gurdon Studentship

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Lauren Mulcahy

BSDB Gurdon Summer Studentship Report (40)

My interest in research and the lack of lab experience I had increased my thirst for a laboratory based summer studentship. Successfully this summer, I was awarded the BSDB Gurdon Studentship to work in Dr David Long's lab at UCL Great Ormond Street Institute of Child Health. As I truly believe that research and medicine go hand-

in-hand, I saw this as a first step towards a career as a clinician-scientist.

As an undergraduate medical student, I had zero lab experience and everything I learnt was new to me. Day to day, I was supervised in the lab by an MB/PhD student and previous Gurdon Studentship awardee, Daniyal Jafree. I was surprised that from the very first day, I started getting my hands on. It took me a good 30 seconds to pipette up 1 ml of liquid; I became quicker as weeks went by. It was even a struggle at the beginning to get my brain thinking of volume in terms of microlitres, rather than millilitres!

I had the privilege to work on a topic that has only received attention in recent years; understanding the role of macrophages during kidney development. For a very long time macrophages were only thought of as part of the immune system and that they all originated from monocytes. But this is not the complete story because the macrophage subpopulation is heterogeneous (they don't just originate from monocytes) and very little is known about the different populations and their functions.

Of all the techniques I learnt in the lab, one of my favourite techniques turned out to be the most challenging. I learnt how to dissect mouse embryonic kidneys under a microscope. I started by trying every tool imaginable, ranging from syringe needles to scalpels to sharp or blunt forceps and scissors. After a few unsuccessful attempts (mistaking the stomach for the kidney!) I learnt how to spot the kidney and eventually became proficient enough to help the research team in other dissections for some big experiments. I also tried my hand at flow cytometry to discriminate different macrophage populations within the developing kidney; another technique which I became independent with.

Perhaps the coolest of the techniques I got to try was imaging. By treating mouse embryonic kidneys with a cocktail of chemicals, adding specific and optically clearing the kidneys (making them transparent!) I could take three-dimensional pictures of entire mouse embryonic kidneys using confocal imaging. Each experiment took up to a week, and it was occasionally frustrating as things didn't always go to plan. For example, after a big experiment that I was really excited to see the images for, I was heartbroken to look under the microscope and see a big bubble in the middle of the kidney, making it almost impossible to get any useful images. This experience taught me that sometimes lab research can be frustrating and

unpredictable. However, sometimes the imaging came out quite well, and I captured some really detailed pictures of the blood vasculature in developing mouse kidneys (**Figure 1**). Using this technique, I found a really unexpected phenotype in one of the lab's mouse models, something that is apparently still puzzling the lab to this day! Apart from learning laboratory techniques and analysis, I also had the opportunity to present at one of Dr Long's bimonthly lab meetings. Scary at first, but looking back, it was an invaluable experience. I got really useful feedback that I look forward to trying out in my future presentations.

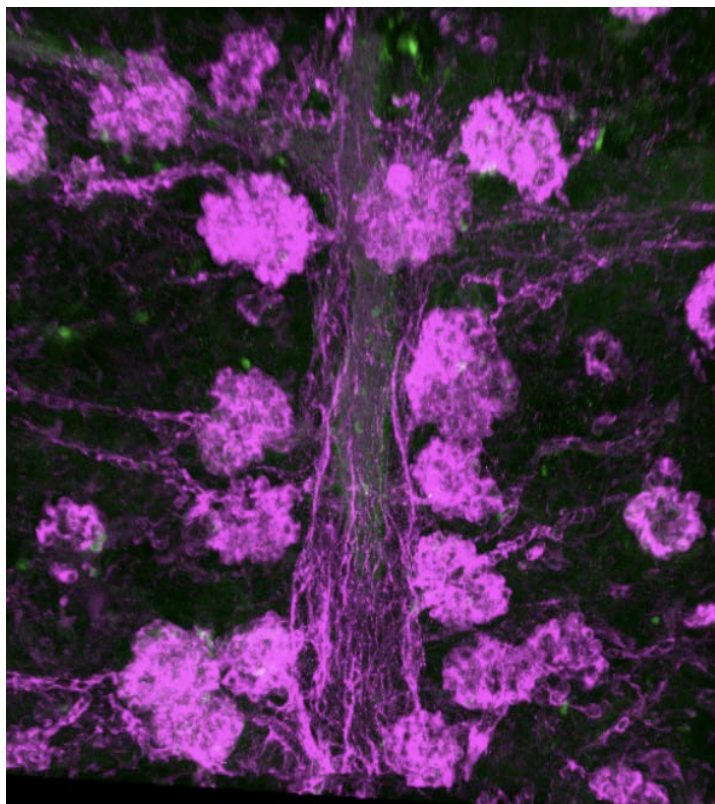


Figure 1: A chain of mouse kidney glomeruli at E18.5. The kidneys were stained for a blood vascular marker, optically cleared and imaged using a confocal microscope.

I was very lucky to have worked in Dr Long's lab. Dr Long always found the time in between his busy schedule to check up on my progress, and to answer any questions that I had. I don't think I have ever experienced eight weeks fly by that fast, and this is largely thanks to Daniyal and everyone in the lab, all who created such friendly and supportive environment. Towards the end of my placement, we even paid a trip to the bowling lanes! (**Picture 2**). Overall, this BSDB studentship has given me an insight into what working in a scientific laboratory is really like, and a taster of what to expect in the career of a research scientist. I highly recommend any undergraduate student, especially those with little or no lab experience, to take up this fantastic opportunity.



Me (last one on the right side of table) along with Dr Long's group having dinner before bowling!

Nivetha Manobharath

BSDB Gurdon Summer Studentship Report (41)

It makes me nervous: identifying inductive signals

Developmental biologists have sought the mechanisms regulating neural induction ever since Spemann and Mangold demonstrated that grafts of the dorsal blastopore lip can induce ectopic neural axes (Spemann & Mangold, 1924). Almost a century later, neural induction still has its mysteries, but perhaps not for long.

The Stern lab now mixes classical embryology with transcriptomics to re-evaluate neural induction in the modern molecular era. Grafts of Hensen's node to a region of competent *area opaca* (Fig. 1A) can induce ectopic neural tubes from ectoderm that does not normally contribute to the nervous system. Combining this assay for ectopic neural induction with RNA-seq at various time points, they have identified all genes that change in response to a node graft up to the time when neural plate formation begins (Trevers et al., 2018). Additionally, many secreted signalling factors have been identified from the transcriptomes of key signalling tissue. These screens have provided a wealth of new tools that have started to shed new light on the complex nature of neural inducing signals and how ectodermal cells respond to them.

My project focused on two secreted molecules that had not yet been explored in the context of neural induction. The aim was to test if either could induce similar transcriptional changes in responding ectodermal tissue as those seen in the neural

induction assay. Excitingly, one of these molecules is novel not only in the context of neural induction but also in terms of its possible role in embryonic development altogether.

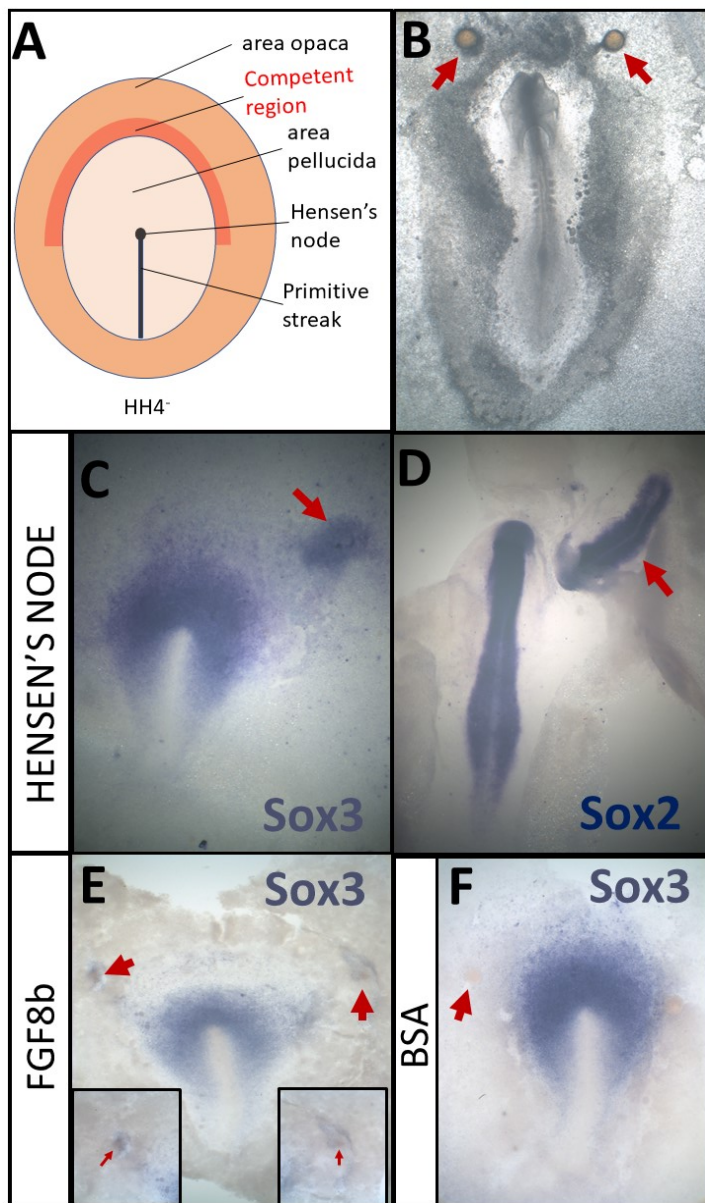


Figure 1: Overview of grafts performed according to the neural induction assay. A: Schematic of a HH4-chick embryo. The organizer, Hensen's node, is the tip of the primitive streak. B: An embryo which was cultured overnight with grafts of heparin-acrylic beads (arrows). C: Sox3 in situ hybridisation of an embryo which had been cultured for 5h with a node graft. D: Sox2 in situ hybridisation of an embryo which had been cultured overnight with a node graft. E: Beads soaked in FGF8b can induce expression of Sox3 after 5h. F: Beads soaked in 0.1% BSA do not induce Sox3 after 5h.

Under the watchful eye of Katherine Trevers (a postdoc in the lab and a great mentor) I learnt how to culture chick embryos (New, 1955; Stern & Ireland, 1981) and mastered the

micromanipulations necessary for my project (Fig. 1B-F).

These consisted of grafting beads soaked overnight in the putative inducer to the competent region of the *area opaca* (Fig1A, B) and incubating them for 5h. Then, I would carefully remove the bead and dissect the (tiny!) region of tissue directly beneath it which had been exposed to the putative inducer. Dissected pieces of tissue were stored at -80°C until I had collected 24 of them – a much bigger challenge than I had anticipated! After considerable perseverance I collected all the necessary samples, which were then analysed by NanoString nCounter technology. This technique uses fluorescently barcoded probes to count the number of mRNA molecules in a sample and the Stern lab has a large probe set that includes all the transcription factors whose expression changes in response to neural induction (more than 200!), as well as many controls.

It was tremendously exciting to quantify the expression of these genes in response to our putative inducers and compare them to a vehicle control. Especially when our analysis revealed that both molecules induced interesting transcriptional responses- one upregulating and the other downregulating different subsets of genes. These results are strong indicators that the molecules I was testing may contribute to neural induction. However, these preliminary results need to be validated by checking the transcriptional responses identified through methods such as in situ hybridisation. Also, loss-of-function experiments would further confirm our observations. All in all, I am happy that in a relatively short time I was able to learn enough embryology as to get to tangible results!

In addition to the experiments described above, I also had the opportunity to repeat some classical experiments myself. By grafting Hensen's node, I confirmed that 5h of signals can induce the neural marker Sox3 (Fig. 1C) while Sox2 can be induced after an overnight culture (Fig. 1D). I also repeated experiments demonstrating that beads soaked in FGF8b (Fig. 1E, F) can induce early markers, such as Sox3 (Streit et al., 2000). Thus, I have not only made a small contribution towards understanding the molecular basis of neural induction, but also repeated some of the key experiments that have been the fundament of research in this field. Although challenging, I found these embryology techniques extremely satisfying and enjoyable. So much so, that I miss being at the bench surrounded by all the amazing members of the Stern lab (part of them in Figure 2). Whenever Nidia (our lovely lab

manager), asked how I was, I would reply that I was having fun. And indeed, I had a wonderful summer in Claudio Stern's lab at UCL as part of the neural induction subgroup.



Thank you!

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