BSDB Newsletter

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British Society for Developmental Biology

www.bsdb.org

My first newsletter – some thoughts on open access publishing and the role of developmental biology in teaching biological sciences.

It's a daunting task to take over the role of BSDB Communications officer from Andreas Prokop. He has done a fantastic job over the years, transforming the society website and general feel of the BSDB communications. He has orchestrated the digitization of the BSDB archive, that is now safely housed within the John Innes Center and spearheaded an advocacy campaign for research and teaching of Developmental Biology that continues from strength to strength. So how exactly does one continue on from a person with such drive and energy? I think the answer is not so daunting after all, and that is to continue to stoke the fires that are already burning.

The look and feel of the website and newsletters will remain the same. For the newsletter itself, the release date has been pushed back slightly to coincide with the BSDB Spring meeting and AGM. The aim is to integrate its contents with what will be discussed at the meeting, so that attendees can know more of what will be discussed. This year, we are planning on opening a discussion around the subject of Open Access publishing. This is a highly pressing issue, as the cOAlitition S group are moving forward with PlanS to be implemented by 2020. Essentially, this will mean that researchers supported by specific funders (including the ERC, major research councils and the Wellcome Trust) will be required to publish only in entirely open access journals. For more on what this will mean for non-for-profit community journals such as those of the Company of Biologists, please see articles 8 and 9. One initiative that the Company of

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Biologists have launched to support the wider commenting of pre-prints is the PreLights platform, read more about this in article 10. If you will be at the Spring meeting this year, come to the AGM to hear more about how the PlanS movement will impact both our membership.

The BSDB archive is continuing to be used a great deal and having all previous newletters published online means that one can easily delve into the history of the society and developmental biology research in the UK. As Andreas pointed out in the last newsletter, our regular communications are principally mediated either by the Node, or directly through our website. This means that the newsletter itself forms a record for all past communications and is important for this function, as well as a complete annual communication of Society activities. Again, we are indebted to Meghana Mortier at the University of Manchester for her time investment in putting the newsletter together. It forms an essential summary of all that has happened over the previous year, at that includes past and upcoming society meetings (articles 4, 5, and 6), treasurer's report (article 7), incoming committee members (article 3) and 2018 award winners (articles 11-14). Our Gurdon summer student program continues to go very well, with another set of exciting research projects that were undertaken last summer. Please take the time to have a look through their reports and see what they got up to this time around (article 16).

Advocacy for developmental biology continues to be a priority for the BSDB. The Company of Biologists have also be a source of great support for the community on this issue, and a series of review articles in Development make for an excellent source of ideas and opinion. At last year's Spring meeting, a few members came to me to say how much they felt developmental biology was of great importance for the teaching of biological sciences. As an initial exploration into this issue, Bethan Clark has nicely summarized the opinions of previous Gurdon summer student awardees (article 15). A key point that was raised is the role tha developmental biology plays in providing a framework for associating multiple aspects of the biological sciences. I would be very happy to hear more of your ideas on this issue and how we might take the discussion forward.

Benjamin Steventon

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

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Chair's welcome note by Ottoline Leyser

"…thanks to the tireless efforts of Andreas Prokop, the BSDB Archive has found a stable home at the John Innes Centre in Norwich. If you can't get there but you really want to know what the Chair wrote in the very first News Letter in 1979, then you can find out, and much much more by visiting the digitised archives via our website. There have already been more than 35000 downloads."

"I would also like to highlight that for our Autumn Meeting this year we are contributing to the European Congress for Developmental Biology in Alicante. We may be leaving the European Union, but we are still definitely in Europe."

This is already my last BSDB News Letter contribution as Chair, giving me the opportunity to quote my favourite science(ish) joke. Time flies like and arrow, fruit flies like a banana.

This year the highlight was without doubt the 70th Birthday Spring Meeting. It was extremely uplifting in these turbulent times to celebrate developmental biology and developmental biologists and to look forward to the next 70 years of discoveries and discoverers. The atmosphere at the meeting was wonderfully positive. Anyone who would like to rekindle that spirit, cheer themselves up when reviewer 3 is particularly energetic with the hatchet, or finally manage to explain to their granny what they do all day can play back the BSDB history rap on our website. For me the meeting really encapsulated what the BSDB is all about- a great community working together to do excellent science.

And if that gets you thinking about BSDB history, this year thanks to the tireless efforts of Andreas Prokop, the BSDB Archive has found a stable home at the John Innes Centre in Norwich. If you can't get there but you really want to know what the Chair wrote in the very first News Letter in 1979, then you can find out, and much much more by visiting the digitised archives via our website. There have already been more than 35000 downloads.

It has been a pleasure and an honour to Chair the Society for the past 5 years. The committee have been wonderful. They truly encapsulate the BSDB collaborative spirit and it's great that so many of you are willing to give their time to run the Society. I would particularly like to thank Kim Dale, Josh Brickman and Andreas Prokop who have provided sterling service as Secretary, Meetings Officer, and Comms Officer respectively. I am deeply grateful to Megan Davy, Sally Lowell and Ben Steventon who have stepped into their shoes, and to Tanya Whitfield, Jens Januscheke and Shankar Srinivas who have joined the committee.

It has also been very inspiring to work with the Michelle Ware and Alexandra Ashcroft, the postdoc and graduate reps. They have worked very hard and with impressive creativity and enthusiasm to ensure that the Society serves the next generation of developmental biologists. It is great that Charlotte Bailey and Jessica Forsyth have taken on these roles with equal verve.

I look forward to seeing as many of you as possible Warwick in April for my last Spring meeting as Chair. I would also like to highlight that for our Autumn Meeting this year we are contributing to the European Congress for Developmental Biology in Alicante. We may be leaving the European Union, but we are still definitely in Europe.

Introducing the new BSDB committee members

"An enduring interest in the lab has been the analysis of signalling events that pattern the anteroposterior axis of the otic placode, precursor of the inner ear."

"Shankar's group takes a multidisciplinary and collaborative approach to address these questions, using techniques such as light-sheet and confocal time-lapse imaging, single cell approaches and embryo explant culture."

Tanya T. Whitfield
Tanya is Professor of Developmental Biology at the University of Sheffield, where she is a member of the Bateson Centre and Department of Biomedical Science [LINK].

Tanya studied early *Xenopus* development for her PhD at the University of Cambridge, under the supervision of Chris Wylie. In 1994, she was an EMBO short-term fellow in the lab of Christiane Nüsslein-Volhard in Tübingen, Germany, where she contributed to analysis of mutations affecting ear development isolated in a large-scale zebrafish mutagenesis screen for embryonic phenotypes. She continued to work on these mutants as a postdoc in the lab of Julian Lewis, first at the Imperial Cancer Research Fund Developmental Biology Unit in Oxford, and later in London.

Tanya established her lab in Sheffield in 1997 to continue work on the developing vertebrate inner ear, using the zebrafish as a model system. The ear is a fascinating system for study, due to its complex three-dimensional arrangement of interlinked ducts and chambers, and multitude of different cell types, including neurons, sensory hair cells, supporting and secretory cells. An enduring interest in the lab has been the analysis of signalling events that pattern the anteroposterior axis of the otic placode, precursor of the inner ear. More recently, a major focus has been on the dynamic epithelial rearrangements that generate the three semicircular canal ducts in the ear, and the use of light-sheet microscopy to image these events in real time in the live embryo. Additional recent highlights from the lab include the identification of glycoproteins required for otolith tethering in the ear, and use of the zebrafish as a screening tool for drug discovery.

Tanya is a committed teacher of Developmental Biology, running courses at both undergraduate and postgraduate levels at the University of Sheffield. Her lab also makes regular contributions to outreach events, introducing the public to the beauty and logic of embryonic development.

Shankar Srinivas
Shankar is Professor of Developmental Biology and a Wellcome Senior Investigator in the Department of Physiology Anatomy and Genetics at the University of Oxford [LINK].

He completed his BSc in Nizam College in Hyderabad, India. He then joined the group of Frank Costantini in Columbia University, New York, where he received a PhD for work on the molecular genetics of kidney development. Following this, he moved to the NIMR in Mill Hill, London, where he worked as a HFSPO fellow in the groups of Rosa Beddington and Jim Smith on how the anterior-posterior axis is established. Here, he developed time-lapse microscopy approaches to study early post-implantation mouse embryos, characterising the active migration of cells of the Anterior Visceral Endoderm that is essential for the correct orientation of the anterior posterior axis of the embryo.

In 2004 Shankar started his independent group at the University of Oxford as a Wellcome Trust Career Development Fellow. His group has shown that the coordinated movement of AVE cells requires Planar Cell Polarity signalling and that a stereotypic multicellular-rosette arrangement of cells in the visceral endoderm is essential for normal AVE migration. Currently, the research in Shankar's group focuses on two main areas. The first is to understand how the coordinated cell movements that shape the mammalian embryo prior to and during gastrulation are controlled. The second, more recent area is to understand how the heart starts to beat. Shankar's group has shown that, during cardiogenesis, the cellular machinery for calcium oscillation matures before the sarcomeric

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"So while it may have been sheep that started me on this journey, I can more confidently attest that it is developmental biology and the sensational role models and colleagues within this community that have led me to where I am today. I am delighted to be the BSDB postdoctoral representative, so that I might give back to the community that has guided me thus far."

machinery for contraction. Shankar's group takes a multidisciplinary and collaborative approach to address these questions, using techniques such as light-sheet and confocal time-lapse imaging, single cell approaches and embryo explant culture.

Shankar is also passionate about science outreach. His group participates regularly in science festivals, for which they have developed 3D printed models of developing embryos and a virtual reality based embryo and microscopy image volume explorer. For more information see Shankar's public engagement page.

Jens Januschke
Jens is a Sir Henry Dale fellow at the School of Life Sciences at the university of Dundee running his lab in the division of Cell and Developmental Biology [LINK].

He did his undergraduate studies at the University of Cologne and moved for his PhD to the University Paris 7 where he got his degree in Genetics in the lab of Antoine Guichet, working on mRNA localization and microtubule-based transport in *Drosophila* oocytes trying to understand how the anterior posterior axis is specified in this system.

After his PhD he moved to the Institute for Biomedical Research (IRB) in Barcelona to start working with neural stem cells, called neuroblasts in the developing fly brain in the group of Cayetano González. During this time, he worked on asymmetric centrosome segregation and discovered that mother and daughter centrioles are differently distributed during asymmetric neuroblast division and shed light on the molecular mechanisms controlling this process. This work identified the first daughter centriole specific protein in *Drosophila*, called Centrobin.

In 2013, Jens started his own group in the cell and developmental biology division of the school of life sciences at the University of Dundee, for which he obtained a Sir Henry Dale Fellowship funded by Wellcome and the Royal Society. Currently, his group focusses on the cell biological mechanisms that control neuroblast asymmetric cell division, which includes studying the establishment of cell polarity, fate determinant localisation and spindle orientation. Jens has been involved in organizing the Scottish Developmental Biology group meeting twice in Dundee and is currently a co-organiser of the UK Workshop on Developmental Cell Biology of *Drosophila*.

Charlotte Bailey
I'll admit it straight away; I don't know how I got here. However, it may have something to do with sheep.

My unwitting journey into the field of developmental biology was almost certainly instigated by the ever so witty and inspired lectures of Dr. Paul Scotting, back when I was an undergraduate at the University of Nottingham. More specifically, I believe it was the images of the single-eyed cycloptic lambs of 1950s Idaho that he presented during his lecture on craniofacial patterning which had me hooked. Unbeknownst to the farmers of Idaho, the phenotype of the lambs was caused by pregnant ewes ingesting the sonic hedgehog signalling (Shh) inhibitor cyclopamine, found in the wild corn lily *Veratrum californicum*. This diet led to the mis-specification of key facial structures in their unborn lambs through disruption of the Shh expression profile required to pattern these tissues in early development. The idea that the localisation of a single morphogen could be so fundamentally essential to a 'macro-scale' process fascinated me. I have had a passion for developmental biology and the molecular regulation of morphogenesis ever since; an admiration for the beauty of cause and effect.

After a brief stint as a research technician, it was this passion that led me to the lab of my personal hero Prof. J. Kim Dale at the University of Dundee. Kim's group works to better understand the molecular mechanisms that come into play to establish the body plan of the vertebrate embryo. Her research focuses on elucidating the molecular basis of both cell fate choices and

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specification within the stem-like cells of the node and primitive streak as well as vertebrate somitogenesis. It was in the latter field that I completed my PhD, building on my love of morphogenetics through visualisation and analysis of the Notch and Wnt signaling crosstalk intrinsic to the molecular oscillator governing periodic somite formation in early development.

Kim's enthusiasm for her subject was palpable and contagious then and remains so today. From the very first days of my time under her mentorship, she encouraged me to join her active involvement with the BSDB and to engage with the developmental biology community within the UK. This network of extraordinary scientists supported my personal and professional development in ways I could never have anticipated, while my regular attendance at BSDB meetings exposed me to a broad range of exciting, cutting edge science and ideas which positively impacted my research.

I have now moved further afield to the Novo Nordisk Center for Stem Cell Biology at the University of Copenhagen in Denmark where I am a Marie Curie postdoctoral fellow in the lab of Dr. Elke Ober. Still pursuing my passion for morphogenesis, I currently mapping the spatiotemporal map of the cell behavioural dynamics underpinning liver regeneration in zebrafish *in vivo*.

So while it may have been sheep that started me on this journey, I can more confidently attest that it is developmental biology and the sensational role models and colleagues within this community that have led me to where I am today. I am delighted to be the BSDB postdoctoral representative, so that might give back to the community that has guided me thus far.

Jessica Forsyth

I thought I would introduce myself as the (not so) new BSDB graduate representative. I am taking over from Alexandra Ashcroft and making sure our needs, as graduate students, are met by the BSDB both at conferences and additional meetings. I also hope to continue Alexandra and Michelle's fantastic work on our website, to help support you throughout your career, whether you decide to stay in academia or not.

A little about me and where I have come from. I am currently in my second year of my PhD (Wellcome Trust Quantitative and Biophysical Biology), and from the title you might suspect that in fact I am not a pure developmental biologist! I completed my Masters of Physics in Physics with Medical Physics, and have chosen to dive into the rapidly expanding field of developmental biology for my PhD.

My first conference was the BSDB Spring 2018 meeting, and I was amazed at how many of the speakers described their need for mathematicians or physicists within their research. I truly felt welcomed by the field and was so excited to start on the BSDB committee to help reflect the need for cross disciplinary work.

I am now working with Berenika Plusa and looking at differentiation within the ICM of pre-implantation embryos. To assist our analyses and join together the spatial and temporal components of developments, I am working with Simon Cotter to develop a programme to allow the 'matching' of cells between different imaging techniques.

I hope that we will continue to develop the career based advice on our website and direct you to this through our Twitter (@BSDBgradstudent), Facebook (BSDB graduate student and postdoc group), and website (https://bsdbpostgrads.wordpress.com/). (We are also hoping to launch an Instagram to display all of your amazing images, so watch this space!) As well as the career focus on our website, we hope these platforms will act as a place for young researchers to communicate and develop their networks through a relatively informal setting.

I'm looking forward to chatting with you over the course of the next three years, if you have any suggestions or concerns please feel free to contact me on students@bsdb.org (or tweet me!). Keep checking back for more blog posts, career stories, interesting science and events.

Meeting Officer's report by Sally Lowell

"Our Autumn meetings are small friendly gatherings either based on a particular theme or run as joint meetings with other Dev Biol Societies around the world."

"The vast majority of you will of course agree that the charms of Warwick University campus easily match the delights of any Mediterranean holiday destination. There are however a few outliers among our membership who occasionally yearn for somewhere more exotic. For those people I have three pieces of happy news…"

The quinquennial BSDB Meetings Secretary Regeneration Process is now complete and I have emerged as the new Josh Brickman. Josh's final triumph was to co-organise our 70th birthday spring meeting along with Alistair McGregor, Berenika Plusa and me. It was HUGE. Thanks to all speakers, attendees and sponsors for helping us to celebrate our anniversary in style.

This was followed in September by a very successful Autumn meeting on Embryonic-Extraembryonic Interactions, held in Oxford. Congratulations to our international grouping of organisers: Tristan Rodriguez (BSDB, UK), Shankar Srinivas (UK), Kat Hadjantonakis (US), Kristen Panfilio (UK/Germany), Susana Chuva de Sousa Lopes.

Our Autumn meetings are small friendly gatherings either based on a particular theme or run as joint meetings with other Dev Biol Societies around the world. They can be organised by any BSDB member and we provide financial support. Please do get in touch with me if you have an idea for a future meeting. Next available slot is not until 2022 but we at the BSDB do like to plan ahead.

Excitement is mounting for the 2019 Spring Meeting. This will be held jointly with our old pals at the British Society for Cell Biology and organised from our end by Tristan Rodriguez (who wins the prize for prolificness in the area of organising-BSDB-meetings) and Rita Sousa-Nunes. One new initiative at this meeting will be a panel discussion with representatives from CRUK to explore the many ways in which developmental biologists can contribute to the research funded by CRUK. Thank you to Anna Philpott for spearheading this initiative and chairing the discussion. Plans are already well underway for our 2020 spring meeting, to be held in Warwick jointly with GenSoc and organised from our side by Clare Baker and Tanya Whitfield.

The vast majority of you will of course agree that the charms of Warwick University campus easily match the delights of any Mediterranean holiday destination. There are however a few outliers among our membership who occasionally yearn for somewhere more exotic. For those people I have three pieces of happy news:

- This October the European Congress for Developmental Biology will hold a meeting in Alicante (that's in Spain, where the sun is). We encourage all BSDB members to attend and we particularly welcome applications for BSDB Conference grants to go to this meeting.
- In Autumn 2020 the BSDB and the International Society for Differentiation will hold a joint meeting in Malta (where the sun also is) organised by Liz Robertson, Josh Brickman and me. Details are still to be confirmed and will appear on our website in due course.
- In Autumn 2021 the International Society for Developmental Biology will come to Europe. The meeting will be held in the Algarve, Portugal (also sunny) on October 17-21, 2021. We realise that many of our members will plan to attend the ISDB meeting and so we have decided not to have our usual large Spring Meeting that year. Instead we will heterochronically graft our Autumn meeting to the Springtime. This will be on the theme of axis elongation, will be organised by Anestis Tsakiridis and Ben Steventon, will be held in Sheffield, and will be excellent.

By 2022 you will all be yearning to return to Warwick and so I'm pleased to tell you that plans are already afoot for a joint meeting with the BSCB in the swish new Warwick Oculus Centre.

Dates and locations of all future meetings can be found on our website: http://bsdb.org/meetings/

Spring Meeting review by Dillan Saunders

"The British Society for Developmental Biology (BSDB) recently held its annual Spring Meeting at the University of Warwick. This was no ordinary meeting, though it is fair to say that BSDB meetings rarely are."

"…finally I got to hear Ottoline Leyser's thoughts on work-life balance; a phrase which misleadingly implies that the two are opposed to one another. It would however be in our best interests, she explained, to see work and life as overlapping and complementary to one another."

This year, is the **BSDB's 70th anniversary**, and this was clearly reflected at our **Spring Meeting**, 15-18 April 2018 in Warwick! Apart from an **outstanding speaker list**, and the award of most **BSDB medals & prizes** of 2018, we saw a very special event with many extras, as is well described here by **Dillan Saunders**. Dillan undertook his BSc Honours with Michael Akam studying centipedes, is currently performing his MSc in the lab of Megan Davey date-mapping the developing limb bud of chick with novel transgenic technologies. and will be returning to Cambridge later this year to begin The Wellcome Trust Developmental Biology PhD program. Dillan's blog post aligns with a **long-standing tradition of the BSDB to engage young members** (see our archive blog), and we strongly encourage PhD students and postdocs to make their voice heard by writing reports or articles for our website and newsletter.

The British Society for Developmental Biology (BSDB) recently held its annual Spring Meeting at the University of Warwick. This was no ordinary meeting, though it is fair to say that BSDB meetings rarely are. This Spring Meeting celebrated the 70th anniversary of the BSDB and did so excellently, birthday cakes and all. With a retrospective look at the past of the society, and fantastic speakers showcasing present and ongoing work, the stage was set for a meeting that not only celebrated a strong history, but also looked forward, critically yet hopefully, to the future of Developmental Biology and of the BSDB itself.

The conference began with a **career workshop** for students and post-docs (*see our blog post*). In keeping with the celebration of the BSDB's birthday, the focus of the workshop was on staying in academia. A variety of speakers and other group leaders fielded questions and shared details of the personal journeys to have brought them to their current positions. I had the opportunity to speak to **Henrik Semb** - whose example shows that not everyone follows a straight, let alone predictable, career trajectory. **Judith Kimble** shared her views on not seeing the lab as a place of work, and finally I got to hear **Ottoline Leyser**'s thoughts on work-life balance; a phrase which misleadingly implies that the two are opposed to one another. It would however be in our best interests, she explained, to see work and life as overlapping and complementary to one another.

The career workshop

After the careers workshop came the first **plenary** talk, in which **Eric Wieschaus** explained his recent work on mesoderm invagination in *Drosophila* and how one transcriptional activation can lead to a sequence of events (*Weng and Wieschaus, 2017*). Thematically paired with this talk was **Maria Leptin**'s plenary lecture, in which she discussed the development of *in silico* models for actin dynamics in order to recapitulate mesoderm invagination (*Belmonte et al., 2017*).

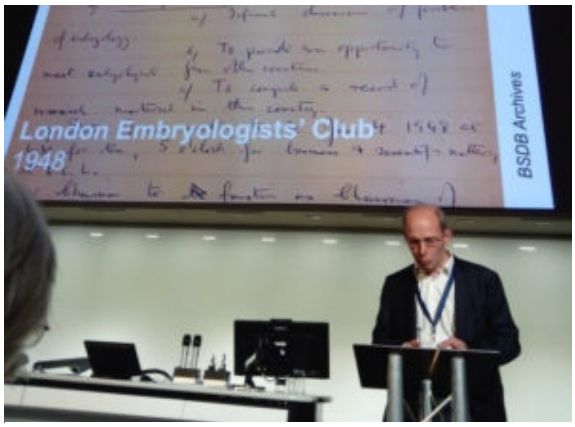
Emilia recieves the Beddington medal from Simon Bullock

"The evening was capped off by three events that celebrated the history, and looked into the future, of the BSDB and Developmental Biology as a whole."

"In the subsequent discussion, Ottoline Leyser pointed out that, what with the advent of new technologies and ideas, we are in fact in the midst of a golden age for Developmental Biology. Indeed, though there are still some who believe that certain areas of Developmental Biology hold no more secrets, recent years have shown new developments…"

Following a short break, the **Beddington Medal** was awarded to **Emily Favuzzi** for the best PhD thesis in Developmental Biology of the year, which she performed on the transcriptional networks at play during interneuron development (*see our blog post*). She then gave a talk that illustrated how meticulous and comprehensive her work was (*Favuzzi et al., 2017*). This was followed up by a plenary talk from **Marianne Bronner** on the transcriptional networks of specific populations of neural crest cells, with attention to how her work with lampreys shows that the neural crest has acquired additional functions in the jawed vertebrates (*Green et al., 2017*). Unfazed by technical difficulties with the final slides of the presentation, Bronner took on the role of the lamprey and humorously indicated on herself the location of the neural crest cells.

The evening was capped off by three events that celebrated the **history**, and looked into the future, of the BSDB and Developmental Biology as a whole. First, came two talks from historians of science, **Nick Hopwood** and **Tim Horder**. Hopwood's talk detailed the story of the crystallization of modern Developmental Biology in the late '40s and '50s. He described how the London Embryologists Club began in 1948 and how it then broadened both its geographical location and the field that it represented to form the BSDB (*see also our archive blog*).



Nick Hopwood's lecture about DB's history

Off the back of the historians' view of the past, came a **panel discussion** of the future of the field. The panel was made up of **Ottoline Leyser**, **James Briscoe**, **Maria Leptin**, **Jonathan Slack**, **Judith Kimble** and **Patrick Lemaire**. They fielded several thought-provoking questions from the audience, which led to a lively discussion. As might be expected from a big anniversary meeting, there was much reminiscing on the early days of molecular Developmental Biology in the 1980s, often referred to as the 'Golden Age.' When asked what made this era such an exciting time for Developmental Biology, Jonathan Slack noted that it was a time when developmental biologists were becoming dissatisfied with the explanations of the previous heyday of embryology in the 1930s.

In the subsequent discussion, Ottoline Leyser pointed out that, what with the advent of new technologies and ideas, we are in fact in the midst of a golden age for Developmental Biology. Indeed, though there are still some who believe that certain areas of Developmental Biology hold no more secrets, recent years have shown new developments in, for example, the study of the anterior-posterior axis in *Drosophila* (*Clark and Akam, 2016*) and the *C. elegans* cell lineage (*Sammut et al., 2015*).

Other points of discussion included the importance of studying development within the context of time and the great potential of computational modelling. Discussed also were the logistics of maintaining an idea of the overall picture without becoming too focused on a single model system. The final event of the day was an informal round table discussion where the points raised previously, and many others, were discussed at length over much wine.

"The highlight of this first evening was the announcement of the Waddington Medal and the Waddington Lecture. The most prestigious prize awarded by the BSDB, the Waddington Medal recognises an individual who has made major contributions to developmental biology in the UK."

"An hour of glitter, glue, and coloured card later, the products of our endeavours included a model of Waddington's epigenetic landscape, an interactive and moving model of chick somite formation, and the winning entry, a performance piece showing the injection of labelled cells into a blastocyst."

Monday began with a **plenary** talk from **Matthew Freeman**, amusingly titled 'Confessions of an ex-developmental biologist', in which he described his current focus on cell signalling and the pertinence of Cell Biology to the understanding of development (*e.g. Christova et al., 2013*). Following this, the two morning sessions covered 'TISSUE AND ORGAN DEVELOPMENT' and 'DEVELOPMENTAL GENE REGULATORY NETWORKS.' I listened to **James Briscoe**'s talk on the Sonic Hedgehog morphogen gradient in the neural tube and the interesting mathematical models that his lab has used to explore the time and precision of its patterning. **Virginia Papaioannou** then spoke about the role of Tbx6 in left-right axis establishment (*Concepcion et al., 2017*).

Also in this session were complementing talks from **Eileen Furlong** (*Mikhaylichenko et al., 2018*) and **Mike Levine** (*Lim et al., 2018*) on the relationships between enhancers and promoters and how chromatin architecture regulates gene expression. After a lunch poster session, the afternoon sessions began with talks on 'MECHANISMS OF GLOBAL GENE REGULATION' and 'CELL BIOLOGY AND DEVELOPMENT'. That afternoon, I caught a talk by **Robb Krumlauf**, in which he showed some fascinating lamprey experiments which supplied further detail on the ancient interactions between retinoic acid and *Hox* genes. Following this, **Caroline Telfer** demonstrated her impressive quantity of PhD work on the upstream regulation of the *GATA* genes, and then **Pavel Tomancak** showed a combination of beautiful live imaging and computational models for serosa closure in *Tribolium castaneum* embryos. The day's closing **plenary** lecture was given by **Janet Rossant**, which included her work on dramatically increasing CRISPR efficiency in early mouse blastocysts.

The highlight of this first evening was the announcement of the **Waddington Medal** and the Waddington Lecture. The most prestigious prize awarded by the BSDB, the Waddington Medal recognises an individual who has made major contributions to developmental biology in the UK. The recipient of the award is, by tradition, kept a secret until the president of the society awards the medal. Ottoline Leyser introduced the awardee of the medal, after a short bit of suspense and the interesting insight that the last three winners of the prize have been accomplished artists. The medal was awarded to **Richard Gardner** for his pioneering work on various aspects of early mouse development from clonal lineage analysis and transplantation to axis determination (*see our blog post*).

In his subsequent lecture, Richard Gardner detailed some of the highlights of his impressive career, punctuated by humorous anecdotes and intriguing details. For instance, he commented on the four passions of Sydney Smith (*who taught Gardner at university*): Darwin, embryology, Ming dynasty porcelain, and wine (*most developmental biologists can relate to at least three*). Gardner also acknowledged his students, his mentor Robert Edwards, and collaborators such as Mary Lyon and Martin Johnson.

After the Waddington lecture, was the **student and post-doc social** in which we were split into teams to create a development-themed piece of art. An hour of glitter, glue, and coloured card later, the products of our endeavours included a model of Waddington's epigenetic landscape, an interactive and moving model of chick somite formation, and the winning entry, a performance piece showing the injection of labelled cells into a blastocyst.



"The final order of business for the day was the BSDB's annual general meeting. This was an interesting insight into the inner workings of the society, which involved the election of new members to the committee and the presentation of committee officers' reports."

"After the wrap up of the AGM was the conference dinner and party. This was a celebration worthy of marking 70 years of the BSDB - complete with balloons, good food, and plenty of wine. The dinner was topped off with cake, cut by four former presidents of the BSDB."

On Tuesday morning, the opening **plenary** lecture was given by **Sean Carroll**. In a similar vein to Matthew Freeman, he described how pursuing his boyhood passion for snakes led him away from developmental biology and to interesting work on the evolution of proteins in snake venom. I then attended the 'EVO-DEVO' session in the morning, which ran parallel to 'STEM CELLS AND REGENERATION'. In this session, I listened to many fascinating talks, which included **Patrick Lemaire**, on his computer models of ascidian cell fate determination, **Karen Sears** on the development of several unique aspects of bat morphology, and **Miltos Tsiantis** on the evolution of leaf form and the identification of a key regulator of leaf shape (*Vuolo et al., 2016*). Finishing off the session, **Peter Holland** covered his group's work on the ParaHox gene, *Pdx*, in a variety of different bilaterian species.

A second lunch poster session followed, and then the afternoon programming kicked into gear. These were talks grouped under the themes of 'POSITIONAL INFORMATION' and 'CELL FATE'. In the former, **Lee Niswander** gave a talk on neural tube closure defects (*Li et al., 2018*), and in the latter, **Olivier Pourquie** spoke about the importance of using cell culture and iPSCs, which his lab used to generate human pre-somitic mesoderm-like cells. In a talk that very much followed the themes of the conference, **James Sharpe** acknowledged the 50th anniversary of Lewis Wolpert's proposal of the French Flag Problem and re-interpreted the potential solutions to the problem through his data indicating that digits are patterned by a Turing mechanism (*Green and Sharpe, 2015*).

The final order of business for the day was the BSDB's annual **general meeting**. This was an interesting insight into the inner workings of the society, which involved the election of new members to the committee and the presentation of committee officers' reports.

After the wrap up of the AGM was the **conference dinner and party**. This was a celebration worthy of marking 70 years of the BSDB - complete with balloons, good food, and plenty of wine. The dinner was topped off with cake, cut by four former presidents of the BSDB.

Also announced were the winners of the post-doc and PhD **poster prizes** (*see our blog* post), as well as the winners of the **advocacy writing competition**, which was initiated specifically for the 70th anniversary of the BSDB and saw submissions from students and post-docs on the history and future of the BSDB (*see our blog post*). Fuelled by the great atmosphere, and likely a bit of wine, the dancing began. It was a great experience to see everyone, at all career stages, let loose and enjoy themselves. Particularly popular were the **Developmental Biology-themed raps**, written and performed by Jerry aka **Gerald H Thomsen PhD**, and produced and mixed by **Philip Larsen**. Overall, it was an excellent and celebratory evening.

Gerald Thomsen, Josh Brickman and Philip Larsen

"Of particular interest to me was how Christiana Ruhrberg neatly combined her early career work in neurogenesis and vasculogenesis to form the focus and direction of her group as a PI, working on the interplay between these two processes. Nicely linking in with the historical theme of the meeting, Ruhrberg noted that she was the first to have ever seen the current BSDB logo (which shows the progression of embryonic development), as the creator of the logo, Jeff Christiansen, was staying at her house when he designed it…"

"This was my first BSDB meeting and it was overall an excellent experience. It showcased cutting-edge science and a great community, the strength of which was demonstrated by the creation of a scientific genealogy, which used pins and thread to plot mentor and mentee relationships as part of a huge interconnected network of developmental biologists."

The final morning of the meeting began with a **plenary** lecture from **Ottoline Leyser**. She spoke about her work with the plant hormone strigolactone, and its role in regulating the plasticity of branching, and the self-organising auxin network in plants (*Ligerot et al., 2017*).The enthralling lecture was enough to make anyone want to become a plant biologist. This was followed by two further plenary lectures from **Connie Eaves**, on the early haematopoietic cell lineage in humans (*Sawai et al., 2016*), and **Edith Heard**, on the role of X-chromosome chromatin architecture and its relationship to *Xist* and X-inactivation (*Galupa and Heard, 2018*). Then the **Cheryll Tickle Medal** was awarded to **Christiana Ruhrberg** (*see our blog post*) by Cheryll Tickle herself. The Cheryll Tickle Medal is given to a mid-career, female scientist for her outstanding achievements in developmental biology. Christiana Ruhrberg then gave a great lecture on her scientific career so far.

Of particular interest to me was how Ruhrberg neatly combined her early career work in neurogenesis and vasculogenesis to form the focus and direction of her group as a PI, working on the interplay between these two processes. Nicely linking in with the historical theme of the meeting, Ruhrberg noted that she was the first to have ever seen the current BSDB logo (*which shows the progression of embryonic development*), as the creator of the logo, Jeff Christiansen, was staying at her house when he designed it (*see our blog post*). The final lecture of the meeting was given by **John Gurdon**, on the stability and reversal of gene expression in development.

This was my first BSDB meeting and it was overall an excellent experience. It showcased cutting-edge science and a great community, the strength of which was demonstrated by the creation of a scientific genealogy, which used pins and thread to plot mentor and mentee relationships as part of a huge interconnected network of developmental biologists.

Weaving pedigree networks: Eric Weischaus, David Ish-Horowicz, Claudio Stern, Austin Smith

I would like to take this opportunity to thank the BSDB for the **conference grant** that enabled me to attend. The meeting gave me a new appreciation for the history of Developmental Biology and strengthened my excitement to be a part of its future. Here's to the next 70 years of the BSDB!

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Autumn Meeting review by Nora Braak and Nestor Saiz

"…it was the first extra-embryonic meeting where team Insect was properly represented and it was such a success we are thinking of getting t-shirts made for the next time #teamInsect."

"The rest of the Monday afternoon discussed how development meets bioinformatics; from Laura Banaszynski telling us about the function of the H3.3 histone variant to Sarah Teichmann, who wants to develop the 'Google Maps Street View' of the human body."

Hello there! This is Nora Braak and Nestor Saiz, we are based in Oxford and New York respectively and we study butterfly and mouse development. Last week we went to the BSDB Autumn meeting, which also happened to be the third workshop on Embryonic Extraembryonic Interactions. We enjoyed it so much that we wanted to share our thoughts with you [disclaimer: these thoughts don't represent those of the BSDB, the organizers, nor, of course, our PIs'...]

NS: Hey Nora, do you know how many developmental biologists does it take to take over an Oxford University College...?

NB: Ha! Tell me... [eye rolls]

NS: Well, about a hundred apparently! Which is as many of us descended onto Corpus Christi College last week to chat about the most *extra* of all tissues: extraembryonic membranes...

NB: [Eye rolls, squared] ehhh... well, actually the Embryonic-Extraembryonic Interfaces ok...?? #bsdb2018EEI The third workshop on this piping hot topic already!

NS: Fine, fine... if you're going to get all serious about it, do you want to tell us about some of the talks that you liked? It was a *very* exclusive meeting, I bet most readers did not get to go.

NB: It was a great meeting; it will be hard to pick highlights but it must be done. To start, it was the first extra-embryonic meeting where team Insect was properly represented and it was such a success we are thinking of getting t-shirts made for the next time #teamInsect. The meeting started off strong with a plenary talk from Liz Robertson. She gave us all a crash-course in early mouse development and all the essential genes in cell-lineage specification and TGFβ signaling. Their paper, still hot off the press shows how loss of both Smad2 and 3 alter the epigenetic landscape and activate extraembryonic gene expression in embryo-derived stem cells.

NS: After Liz's keynote, I think Kristen Panfilio made it very clear to all of us mouse aficionados that #teamInsect was in the house. Turns out insects **do** have extraembryonic membranes, unlike what you might have heard from a certain famous fruit fly… She also showed some absolutely gorgeous movies of *Tribolium*'s amnion and serosa breaking and retracting into the yolk to let the embryo develop further. You can see them and read more about their reporter and how the EE get themselves out of the beetle's way in their paper.

NB: The rest of the Monday afternoon discussed how development meets bioinformatics; from Laura Banaszynski telling us about the function of the H3.3 histone variant to Sarah Teichmann, who wants to develop the 'Google Maps Street View' of the human body. The first day ended with a lovely drinks reception and a three-course sit down dinner in the beautiful hall of Corpus Christi, which made me wish I had dressed up a little. The dinner was followed for many by some more drinks in the Bear Inn, one of the oldest pubs in Oxford.

NS: Ah, the Bear Inn and its low ceilings... Shout out to Miguel Manzanares too (#teamMammal) talking about genome structure in the early mouse embryo and Federica Bertocchini, who is studying chameleon development, which is awesome because… chameleons?? Come on… Did you know chameleons take 200 days from laying to hatching? Did I say chameleon yet?

NB: Sorry, did you say it was about chameleons? I think I missed that…

NS: Tuesday was mouse day

"…it is the first time I see this pitching of the posters at a conference and I thought it was a very neat idea – though it probably only works in small settings like this workshop."

"I also really liked the talks about the placenta by Rosalind John and Myriam Hemberger. Their talks about the importance of the placenta in embryonic development and the influence it can have on the maternal behaviour were both thought provoking and well presented…"

(#mousetastic). In the morning Ayaka Yanagida and I got the honor to present after two of my favorite embryologists, Jenny Nichols and Claire Chazaud! Jenny discussed their latest look at the *Pou5f1* (aka Oct4) mutant, which is very close to her heart, then Claire doubled down on the mutants showing what happens when you knock out both *Nanog* and *Gata6* in early mouse embryos. All of my favorite transcription factors!

NB: Yes it was a great morning, but after this early embryo overdose I was glad to switch to the lightning round of 3 minute presentations from all 24 poster presenters. They really piqued everyone's interest, the poster sessions were so well attended – and not only because of the pastries and beer provided!

NS: I agree, it is the first time I see this pitching of the posters at a conference and I thought it was a very neat idea – though it probably only works in small settings like this workshop. Brief presentations are hard, kudos to the organizers for giving everyone a chance to practice!

NB: In the afternoon we had great talks from Takashi Hiragii and Veronique Azuara. I personally really enjoyed Matthew Stower's talk, who used light sheet microscopy to study visceral endoderm migration, the pictures and the data analysis were amazing! Again the day ended in a 3 course sit down dinner in the beautiful hall of Corpus Christi, this time I was more prepared and knew which bread roll belonged to me and which fork to use for which course.

NS: I still don't know how Matthew managed to take some of us on a pub crawl after lunch **and** then go and deliver his talk. Matthew you're a total star.

NB: What did you think about Wednesday? It was an intense day.

NS: Yeah, Wednesday was packed. It started with all non-mouse mammal models. Berenika Plusa and Ania Piliszek presented their work on preimplantation rabbit development, whereas Stephen Frankenberg and James Turner engaged in their own marsupial cutey contest - for all of you dunnarts, possums and opossums out there: if you are interested in being the next top model organism, being cute will take you far! Jokes aside, theirs were some of my favorite talks. They had really nice data and ideas on the evolution of extraembryonic tissues and X-Chromosome inactivation in mammals

NB: I also really liked the talks about the placenta by Rosalind John and Myriam Hemberger. Their talks about the importance of the placenta in embryonic development and the influence it can have on the maternal behaviour were both thought provoking and well presented – here's one of their papers. The day ended with talks from Diana Laird, on the transgenerational defects of environmental damage, and from Elizabeth Duncan. She looks at bee and aphid reproductive control as a way to understand how animals respond to their environment. Did you know that aphids will change their mode of reproduction and development depending on the season?? Yet the embryos ultimately look the same!

NS: Elizabeth Duncan's talk was so interesting! I think even Queen B would have agreed… (#RoyalJelly)

NB: Right… oh, in the evening we were welcomed in the Natural History Museum of Oxford, with bottomless gin and delicious bowl and finger food. The beautiful surroundings gave everyone a chance to mingle, share their enthusiasm about dinosaurs and admire a live bee colony which were even more of interest after Elizabeth Duncan's great talk.

"All in all, a wonderful little meeting – science, weather and setting all came together to make for a truly great week. Thanks so much to the organizers, Susana Chuva de Sousa Lopes, Kat Hadjantonakis, Kristen Panfilio, Tristan Rodriguez and Shankar Srinivas for putting it together and we're looking forward to 2022!"

NS: Finally Thursday came around. It started with two great talks by #teamInsect, from both Maurijn van der Zee and yourself, Nora. You both seem to enjoy poking insects with infected needles… I guess it's an effective way to trigger immune responses by the serosa – one of the many critical roles of the extraembryonic tissues in insects, as we had learned from Siegfried Roth's talk on the evolution of Toll signaling! I personally loved Di Hu's talk, from Shankar Srinivas' lab, she had done some beautiful imaging of the early post-implantation mouse embryo and delivered like a pro. We also saw Zofia Madeja, Vasso Episkopou and Jaime Rivera, who is doing "dunkin' transgenics!". Delivering Cas9 to do CRISPR into mouse zygotes by bathing them in media with virus is definitely a slam dunk.

NB: Yes. The day was finished by two phenomenal speakers, Mariya Dobreva, who won the Dennis Summerball Award and presented her workon the role of Smad5 in the amniotic ectoderm, and Ali Brivanlou who wrapped up the meeting with some absolute eye candy on their work in *in vitro* models of human development.

NS: After that, awards were given to the three best poster presenters, Peter Baillie-Johnson, Matthias Teuscher and Berna Sozen. Well done them!

All in all, a wonderful little meeting – science, weather and setting all came together to make for a truly great week. Thanks so much to the organizers, Susana Chuva de Sousa Lopes, Kat Hadjantonakis, Kristen Panfilio, Tristan Rodriguez and Shankar Srinivas for putting it together and we're looking forward to 2022!

Treasurer's report by Christopher Thompson

"The success of these Spring and Autumn meetings means that plans are being made to use these as a basis for a new pan European Developmental Biology Meeting to be held every 2 years. This will undoubted provide an opportunity to further strengthen UK-European ties."

The Society remains vibrant with a verified paying membership of 1325 (a rise of 45 members) at the end of July 2018. Membership numbers are therefore buoyant, 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 875 full and 450 student members. The financial situation of the Society remains in good financial shape and this has allowed us to continue our new activities to promote developmental biology, described below.

Report on the financial year 2017-18

As shown in the accompanying provisional accounts for the Society for the period August 2017 - July 2018, the last year has seen us invest heavily in activities to support the community. This is because a decision was taken to invest a portion of our reserves which have been building and has seen our expenditure exceed our income by almost £41,500. Despite this, the Society remains in good financial health, due to the continued good performance of our investments. Furthermore, our reserves have been boosted by the receipt of a one off sum of £25,000 to support the award of a new prize. This prize (Dennis Summerbell Award) recognises the achievement of a talented postdoctoral scientist in Developmental Biology and provides support for travel to and registration at the Autumn BSDB meeting (last year held in Sweden, and this year held in Oxford).

This year saw the Society mark its 70th Anniversary at the Spring meeting. Unusually, the meeting was solely hosted by the BSDB, rather than in partnership with another society. We awarded an unprecedented number of 120 travel grants to allow student and postdoc members to attend the BSDB Spring Meeting 2018 in Warwick. In addition, due the support of the Company of Biologists PI Grants, we were able to open up funding to PIs, allowing us to award 21 grants to PIs. This allowed PIs with little funding to attend our flagship meeting, thus generating a community supportive atmosphere. As their students and postdocs were also encouraged to attend by these PIs, we believe that this will sow the seeds for future generations.

We also funded 18 grants to attend the Autumn Meetings in Sweden, held jointly with the Scandinavian Developmental Biology Societies. This was almost double the number of awards usually provided. The success of these Spring and Autumn meetings means that plans are being made to use these as a basis for a new pan European Developmental Biology Meeting to be held every 2 years. This will undoubted provide an opportunity to further strengthen UK-European ties.

Our own expenditure on travel grants (£65,790) was higher than the income the Society received from its membership (£36,203), and reflects the fact 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 (£15,800 total). We also receive an amount (£37,500) to spend on CoB/BSDB travel awards to help towards the costs of our members' attendance/travel to overseas meetings. In total, 70 CoB/BSDB travel awards were made in 2017-18 (£31,612), reflecting the high demand for the awards, with awards being made to all eligible applicants. Although our spending was slightly less than the

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

"…the Society continues to have a very healthy reserve to cope with unforeseen events (e.g., cancellation of a meeting) and, indeed, to invest in new activities to promote Developmental Biology."

amount awarded, we spent more on the PI travel grants (£23,460) than awarded by the CoB. Finally, we were also grateful to receive a dedicated award (£5,000) to support travel to practical courses and training courses. 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 cost of these courses. So far, we have spent slightly more than the allocated amount in this area (£5,075). We expect the small amount of remaining travel money will be spent before the end of the calendar year.

Future Plans

Although from the accounts it appears that our expenditure was greater than our income, this was planned for and approved by the committee.
Furthermore the Society reserves have actually risen slightly, due to the continued good performance of our reserves, as well as the investment in the Dennis Summerbell fund. 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 Spring meeting in 2017 and expect to receive some return from the Spring 2018 meeting as well. As a result, the Society continues to have a very healthy reserve to cope with unforeseen events (e.g., meeting cancellations) and, indeed, to invest in new activities to promote developmental biology. Our overall solid financial health means that we can do this without any significant threat to the core business of the Society. The other expenditure items (e.g., prizes, administration, ISDB membership) were in line with previous years.

In light of the financial buoyancy of the Society we are continuing to promote developmental biology in the UK. We will continue to award of 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 have been 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 £30K over the next 5 years. This allows 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 (£35K) from CoB to run the Society's activities, to subsidise our Spring and Autumn Meetings and to award graduate student prizes. This allows the Society to use its own funds to fund travel grants to mainly 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 hold 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 the CoB and our projected costs for next year include £25K for meetings and £16K 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 (£37.5K). Demand for these awards remains high and in the last financial year we awarded travel grants totalling £31,612 to 70 members. At present, we award grants which cover around 40% of the costs requested per applicant,

"…we have seen an increase in the number of applications for expensive residential practical courses, which is a sign of the integration of new methodologies and interdisciplinary nature of Developmental Biology Research."

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 we have been given the chance to administer the new CoB PI Support Grants (£25K) and Practical Course Grants (£5K) that allow us to dedicate greater levels of funding for PI travel and training. The trial of the PI grants was successful, and although initial uptake of the PI awards was slow, they have risen in popularity. Indeed, we spent more than the allocated allowance on these awards (£23,460), allowing us to channel applications for travel grants from PIs to this route. 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, which is a sign of the integration of new methodologies and interdisciplinary nature of Developmental Biology Research. We are therefore happy to administer these awards in 2018-19, as we see them as fundamental for continuing the success of Developmental Biology research in the UK.

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

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BRITISH SOCIETY FOR DEVELOPMENTAL BIOLOGY

Accruals Basis

Balance Sheet

2016/17 £		2017/18 £
	Investments	
91,514	L&G Global 100 Index Trust ®	103,528
360,479	Baillie Gifford Managed Fund	399,547
	Current Assets	
49,037	Barclays Bank High Interest Account	49,095
35,313	Barclays Bank Current Account	17,430
3,056	Barclays Bank: Louie Hamilton Account (1,2)	3,056
3,167	PayPal	4,497
90,573	**Total Current Assets**	74,077
0	Less: Unpresented cheques	
0	Debtors – Creditors	
90,573	Net Current Assets	74,077
542,566	**Total Funds**	**577,151**

Income & Expenditure Account

Income	£	Expenditure	£
Membership (Standing Order & PayPal)	36,204	CoB Grants (BSBD Meetings)	65,790
Block Grant (CoB)	35,000	CoB Travel Grants (Overseas & Courses)	31,612
Travel Grant Fund (CoB)	37,500	CoB PI Travel Grants	23460
PI Travel Grant (CoB)	20,000	CoB Practical Courses Grants	5075
Practical Course Grant (CoB)	5,000.00	Gurdon Summer Studentships	14,400
Spring Meeting 2017	7,127.08	Autumn Meeting 2017	2,126
Spring Meeting 2018	3600	Spring Meeting 2018	14,587
Autumn Meeting 2017	0	Autumn Meeting 2018	13,000
Refunds in	0	Prizes	5,032
		Committee & administration	10,101
		ISDB membership	0
Inte Barclays High Interest a/c	58	RSB membership	695
Barclays Louie Hamilton a/c	0	Bank Charges	71
		Refunds out	35
Amata Hombruch/Summerbell Donation	25,000.00		
Total Income	**169,489**	Total Expenditure	**185,984**
		Net Surplus for the Year	**-16,496**
		Unrealised Gains on L&G	12,014
		Unrealised Gains on Baillie Gifford 1	39,068
		Unrealised Gains on Baillie Gifford 2	0
		Fund balance at 31st July 2017	542,566
		Fund balance at 31st July 2018	**577,152**

Notes

These accounts were prepared under the accrual basis convention, in accordance with the applicable accounting standards and Recommended Practice of Accounting by Charities. There have been no major changes to our financial arrangements this year.

1. The Louie Hamilton account valuation is at xxx

2. This is the only restricted account and no call was made on it in the financial year 2017/18

Hopes and concerns for PlanS by Benjamin Steventon

"…we are keen on opening a debate among the BSDB membership to raise awareness of the positive and negative impacts that PlanS might have on the community."

"At Development, the cost of publishing OA is subsidised so that the APC can be maintained as low as possible while still allowing for the community support contributions run by the Company of Biologists. These contributions are greatly valued and utilised by the community, not least the direct contributions that the Company of Biologists makes to the BSDB!"

In September 2018, a new initiative called "Plan S" was launched by the "cOAlition S" consortium to dramatically speed up the transition towards completely open access publishing. The coalition is driven by Science Europe, major national research agencies of 13 countries and other research bodies such as the Wellcome Trust[1]. For researchers receiving funding from these sources, the initiative will mean a major change as it stipulates that they must publish their work in fully Open Access (OA) journals by 2020. This is a significant plan, but one that at the moment has a very short deadline with little concrete understanding of how this will affect researchers and research communities such as the BSDB. Of major concern is how non-for-profit publishers such as The Company of Biologists will be affected, who use profits from field-specific journals to feedback into the scientific community. Therefore, we are keen on opening a debate among the BSDB membership to raise awareness of the positive and negative impacts that PlanS might have on the community.

The move towards OA publishing has been a steady progression, with approximately 3-10% of the life science literature now being published in entirely OA access journals such those of the PLOS group, BMC, and eLife[2]. Alongside this, many pay-to-view journals have taken on hybrid model, offering authors the option of either publishing behind a paywall, or paying an up-front publication fee (or "author processing charge" (APC)) to publish open access. Funders such as the Wellcome Trust have further supported OA publishing by taking on the cost of these charges. The hope of OA proponents was that by giving publishers the middle option of being Hybrid, it can help mediate the transition towards becoming completely OA. However, this transition has not been fast enough for many, and PlanS seeks to force the hand of many journals to become fully OA in the immediate future. One potential concern is double-dipping: taking in money from subscription charges while also taking additional fees from authors and their funding bodies to publish OA where requested. Many journals, especially from not-for-profit publishers have put in measures to avoid double-dipping but is not universal.

In the digital age, the perceived cost for publishing academic research might be expected to have dropped considerably due to massive reductions in print costs. However, the bulk of the costs for publishing still remain, due to editorial and peer review selection and management and other forms of quality control. Journals offer more than a medium for peer review and publishing, they see themselves as taking on the role of science curation; "With over a million biomedical science papers being published each year, it's increasingly important that readers have help in finding those papers most relevant to them. We believe that community, field-specific journals like Development are essential for this." – Katherine Brown, Company of Biologists. Therefore, if we want to continue to gain from well curated and presented research communications, then the price has to be paid from somewhere. Under the current model, accepted papers must cover the cost of reviewing all rejected papers for a given journal, meaning that highly selective journals have a higher cost commitment per article published. At Development, the cost of publishing OA is subsidized, meaning that the community is probably not aware of the true cost of quality publishing. The community support contributions from by The Company of Biologists comes from its subscription revenue; these contributions are greatly valued and utilised by the community, not least the direct contributions that the Company of Biologists makes to the BSDB!

Many not-for-profit learned societies, membership charities and community publishers have concerns about exactly

"OA is a worthy aim, and few people would argue against it. It is intimately related with Open Research initiatives aimed at finding new ways for researchers to make their data and analysis feely open to the community."

how PlanS will impact them. However, against major for-profit publishing coalitions such as Elsevier, they often find it difficult to get a seat at the table for discussions with those driving PlanS forward, and time is running out. Thankfully, a Society Publisher's Coalition has now formed that can make their voices heard. They have released a statement (re-printed in full at the end of this article) detailing their position and are now in consultation with cOAlition S to gain a better perspective on how the negative impacts of PlanS can be mitigated, while still supporting the principles of open scholarship.

Currently, the exact form that PlanS will take, and how the move will be managed by society publishers is not clear. However, the Company of Biologists told us: "Over the years we have always provided authors with options that should allow them to comply with funder / institute mandates and we want this to continue. Final Plan S policy hasn't yet been announced, but – subject to any surprises - we expect to provide compliant options". As further details on who PlanS will actually look emerge, we believe that it is important to open a discussion of how our research community could be affected. Some issues already arising for researchers could be a fear that PlanS will result in a considerable restriction in where researchers with a particular funding source might be able to publish. Is it fair that funders should dictate where and how their researchers publish their work? Could it affect collaborations with research groups who do not have the same restrictions, or even make certain collaborations less attractive due to these restrictions? Above all, does the desire to restrict the unfair profit making of large publishing conglomerates lead to the running over of smaller non-for-profit community institutions. After all, which of these groups have the resources to weather the storm?

OA is a worthy aim, and few people would argue against it. It is intimately related with Open Research initiatives aimed at finding new ways for researchers to make their data and analysis feely open to the community. BioRxiv has become increasingly popular in the Developmental Biology community, something that can be seen easily from following the monthly preprint summary on the Node[3], or the success of the recent Company of Biologists "PreLighters" scheme (see article in this newsletter). It's important for the research community to discuss how it is that they want the future to look in terms of both Open Research and OA. We hope to continue this discussion at this year's AGM at our Spring meeting, and feel free to contact us directly with your thoughts and opinions on the matter.

PlanS consultation response from the Society Publishers Coalition

"We support the principles of open scholarship and believe that open access to research outputs will benefit researchers across our shared communities."

The not-for-profit learned societies, membership charities and community publishers represented by this letter all publish journals as part of our charitable missions, collectively publishing over 17,000 articles in 2018. Our author base is truly global and we share a belief that authors must be able to publish in our journals regardless of their funding status or ability to pay.

Our position

We support the principles of open scholarship and believe that open access to research outputs will benefit researchers across our shared communities. We also believe that authors should retain copyright in their works with no restrictions, and that open access publication fees should be paid by funders or institutions, not by individual researchers. Ability to pay should not be linked to ability to publish. We support the San Francisco Declaration on Research Assessment (DORA) as a driver to improve research assessment by evaluating the work itself, rather than using the venue of publication as a proxy for quality. We recognise the importance of open archives and repositories, such as preprint servers, for hosting research

"As a group of societies that publish journals, we share a common aim of transitioning to open access in a sustainable way, and we seek to engage with funders, institutions and consortia to find a way forward within the spirit of the Plan's principles; to this end, we have also included some suggestions of how cOAlition S can help to ensure that a transition is potentially achievable."

"At the present time negotiating read and publish deals is only realistic for the very largest commercial publishers. Experience has shown us that the small size (and large number) of learned society publishers means we do not get a seat at the table in such negotiations."

outputs, which we see as a fee-free complement to open access in journals.

Despite having these principles and ambitions in common with Plan S, we have concerns about the Plan, as it is currently written, and have detailed these below. As a group of societies that publish journals, we share a common aim of transitioning to open access in a sustainable way, and we seek to engage with funders, institutions and consortia to find a way forward within the spirit of the Plan's principles; to this end, we have also included some suggestions of how cOAlition S can help to ensure that a transition is potentially achievable.

Our concerns

Plan S explicitly refuses to fund APCs in 'hybrid' journals. While we acknowledge the frustration funders and universities have expressed regarding the perceived slow progress towards universal open access, an outright ban on the hybrid model is a source of concern for this group. Many of our journals operate on the hybrid model, and removing funding from hybrid will reduce our ability to flip these journals to open access. It will also cause real damage to us as society publishers and thereby to our communities, while creating new commercial advantages for very large publishers who can capitalise on their scale.

Hybrid publishing is a transitional model from subscription to open access publishing, predicated on funder, community and institutional support. As more funders mandate immediate open access of the version of record, and as more scholars and institutions select and support open access for published outputs, hybrid journals publish fewer subscription articles and eventually reach a tipping point where a flip to pure open access becomes viable. The pace of this transition differs by subject area, with many in the arts, humanities and social sciences lacking funding to pay for open access. The fact that so few journals have flipped is not because society publishers have stood in the way of open access, but because only a minority of the world's funders mandate (and fund) immediate open access.

Our collective understanding of scholarly communications and our experience with open access over the past twenty years suggests that withdrawing support for hybrids will actually retard the movement towards immediate open access of the version of record:

- By withdrawing support for open access fees in hybrid journals, many authors will revert to publishing their articles behind paywalls in their preferred journals, backed by immediate deposition of the accepted manuscript in a repository ('green' OA).
- Green OA articles are generally less discoverable than the version of record, with discoverability and accessibility highly dependent on the variable technical standards of each repository instead of relying on international standards for linking and markup. Very few repositories currently meet these standards.
- Disciplinary coverage of OA journals is patchy. In many disciplines, predatory or otherwise dubious commercial publishers are the primary alternatives to high-quality society journals.

In addition, while we are willing to explore alternative models, we remain unclear about what, specifically, qualifies as being a transformative agreement. We are also unable to negotiate terms around these experimental and yet-to-be defined offerings, within the constraints of the prescribed Plan S deadlines, without taking large risks that jeopardize our revenues and, by extension, our ability to continue to re-invest in and support the research communities we serve. Creating a universal, successful and sustainable alternative publishing environment that aligns with our strong belief in high-quality publications cannot be achieved in as short a timeframe as Plan S currently allows.

At the present time negotiating read and publish deals is only realistic for the very largest commercial publishers. Experience has shown us that the small size (and large number) of learned society publishers means we do not get

"We wish to work with cOAlition S to reframe the blanket prohibition on hybrid journals and, instead, develop a set of clear rules to eliminate double dipping and allow those hybrids which follow them to be funded by cOAlition S."

a seat at the table in such negotiations. This means that Plan S (with its emphasis on transformative agreements) actually risks advantaging the large, commercial players at the expense of the learned society sector.

How cOAlition S can help

Stability
We urge the members of cOAlition S to be consistent in their application of the principles of Plan S and encourage other funders to do the same. We are more likely to be successful in transitioning to full open access under a uniform, stable set of rules than under a patchwork of mandates.

Clarity
We request that all cOAlition S members clarify which types of scholarly outputs are in scope (confirming specifically whether the mandates apply to primary research only, or if they extend, or are likely to extend in the future, to review articles, commentaries, editorials and other such outputs). We also ask that the cOAlition be specific about what criteria will be used to determine whether an agreement qualifies as being 'transformative'.

New guidelines and 'flipping thresholds' for hybrids
We appreciate that one of the main objections to hybrid is concern over some publishers 'double dipping' by maintaining or increasing subscription prices even as they generate revenue from open access article processing charges. We wish to work with cOAlition S to reframe the blanket prohibition on hybrid journals and, instead, develop a set of clear rules to eliminate double dipping and allow those hybrids which follow them to be funded by cOAlition S. We suggest that these guidelines should be paired with recommendations on when journals should flip from hybrid to pure open access based on percentage of open access content rather than an arbitrary time deadline. This will provide society publishers with a clear, sustainable route to open access that also meets the needs of funders, institutions and researchers.

Preparation and groundwork
We appeal to cOAlition S to ensure that institutions, consortia and funders are able to reorganize purchasing channels and realign budgets so that new offerings, developed in support of a transition to open access, are relevant and applicable to institutions. We are ready to support and collaborate in order to achieve this; our best intentions to transition to open access will fail unless funding commitments and payment workflows are compatible with (or capable of supporting) new, transformative deals. This need extends to ensuring that workflows cater to unfunded and self-funded researchers.

Opening doors
As described above, the smaller self-publishing society publishers within the group - those of us who do not partner with large commercial entities - have experienced real difficulty in initiating negotiations for potential transformative agreements. We would therefore ask that cOAlition S consider this when developing implementation policies. In order not to rule out (exclude) an important set of publishing relationships cOAlition S could: (i) provide support in the construction of a framework licence for a transformative agreement that would not violate competition law and (ii) actively encourage consortia to come to the negotiating table with us and with other societies.

Signed: The Society Publishers' Coalition

Biochemical Society and Portland Press
British Ecological Society
British Pharmacological Society
British Society for Immunology
International Water Association Publishing
Microbiology Society
Royal College of Psychiatrists
Royal Society Publishing
Society for Applied Microbiology
Society for Endocrinology
The Company of Biologists
The Physiological Society

preLights – a community platform for preprint highlights

"One of the many advantages of preprints is that they can open up the discussion of non-peer-reviewed research. Despite this, public commenting on preprints has been very limited so far. A further challenge of preprint posting is volume: over time, it will become increasingly difficult to navigate and keep up with the preprint literature."

"Not only does preLights raise awareness of preprints and the associated research, but it also aims to promote and support the early-career researchers who write the posts."

The posting of preprints (non-peer-reviewed manuscripts) has rapidly taken off in the biological sciences in the past 5 years - since the launch of bioRxiv in late 2013, both preprint submissions and readership numbers have grown exponentially.

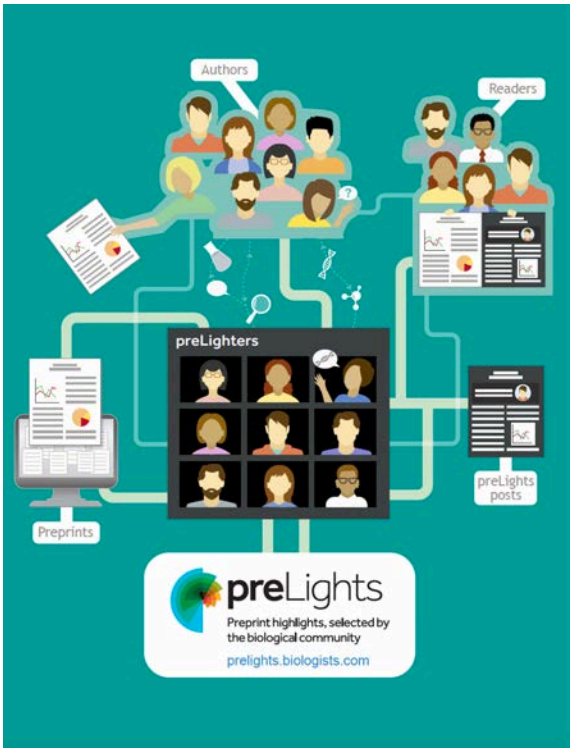
One of the many advantages of preprints is that they can open up the discussion of non-peer-reviewed research. Despite this, public commenting on preprints has been very limited so far. A further challenge of preprint posting is volume: over time, it will become increasingly difficult to navigate and keep up with the preprint literature. To address these challenges, The Company of Biologists launched preLights (https://prelights.biologists.com/) - a community platform for selecting, highlighting and commenting on preprints across the biological sciences - in February 2018.

At the heart of preLights is the team of early-career researchers (called 'preLighters') who select which preprints to feature and then summarize the key findings of the preprint, highlighting why they think the study is interesting/important. Uniquely, the preLighters often directly question preprint authors about their work, and the resulting discussions are published at the end of the article.

Not only does preLights raise awareness of preprints and the associated research, but it also aims to promote and support the early-career researchers who write the posts. Each preLighter also has the opportunity to create their own 'Community' profile, and several have been featured in the 'Meet the preLighters' interview series on the site (for example, see https://prelights.biologists.com/news/meet-prelighters-interview-erik-clark/ for an interview with Eric Clark, who was also an earlier winner of the BSDB Beddington medal).

preLights just celebrated its first anniversary; to find out more about the first year and some of preLights' future plans, take a look at this Development editorial by James Briscoe and Katherine Brown http://dev.biologists.org/content/146/4/dev176651.

If you are an early-career researcher who would like to gain experience in science communication, keep up-to-date with the latest research in the field and build a scientific network through exciting interactions with fellow ECRs, you can find information and details on how to apply at https://prelights.biologists.com/about-us/



A growing number of biology preprints are deposited by authors on servers e.g. bioRxiv. Early-career researchers ('preLighters') select interesting biology preprints and write highlights on them ('preLights posts'). They interact with preprint authors who reply to questions raised in the post. Readers can find the author's responses together with the digests of selected preprints on prelights.biologists.com and are welcome to join the discussion.

The Waddington Medal

"Scientifically, Richard is well known as a pioneer in the study of early mammalian development, having made many hugely important discoveries relating to the fate of cells in early mammalian development and the properties of stem cells derived from early embryos. These were made possible by his strong knack for identifying important questions and addressing them in innovative and at the same time definitive ways, always with extremely elegant experimental design."

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 2018 winner Richard Gardner who won the 2018 Waddington medal for his outstanding work in the field of early embryogenesis and stem cells, as well as continued contributions to the development of our field and the shaping of science policy in the UK.

Born in 1943, Richard Lavenham Gardner studied at St. Catharine's College and the University of Cambridge from 1963-1966, graduating with a First Class Honours B.A. in Physiology. For his PhD, he remained in Cambridge in the Physiological Laboratory of Robert Edwards (Nobel prize winner, pioneer in reproductive medicine and *in vitro* fertilisation/IVF), where he worked alongside Martin Johnson and was awarded his title in 1971 for his thesis entitled *"Investigation of the mammalian blastocyst by microsurgery*". He stayed on in Edward's lab as a research assistant for another three years, from where he moved to a University Lecturer position at the Department of Zoology, University of Oxford (1973-77). During that time (and beyond) he was a Visiting World Health Organization Fellow in Warsaw and Zagreb and Student of Christ Church (Oxford). In 1978 he became Henry Dale Research Professor of the Royal Society at the University of Oxford, where he remained until 2003. Thereafter he held positions as Edward Penley Abraham Research Professor of the Royal Society (2003-8), Honorary Visiting Professor at the University of York (2007-16), and is now an Associate at the University of Oxford and Emeritus Student of Christ Church, Oxford.

Scientifically, Richard is well known as a pioneer in the study of early mammalian development, having made many hugely important discoveries relating to the fate of cells in early mammalian development and the properties of stem cells derived from early embryos (see selected papers below). These were made possible by his strong knack for identifying important questions and addressing them in innovative and at the same time definitive ways, always with extremely elegant experimental design. His numerous important scientific contributions include: being the first to use clonal analysis to fate map the early mouse embryo (originally using terato-carcinoma chimaeras), along with experimental manipulations to assess the potency of individual cells, establishing how the germ line is segregated in the early embryo, and pioneering blastocyst injection for studying stem cell potency. His work laid essential foundations for preimplantation genetic diagnosis, now widely used in human fertility clinics, and for the embryonic stem cell (ESC) field. He was one of the pioneers developing and using micromanipulation techniques in mammalian embryos, the kind of technique now commonly used, for example for human IVF and cloning (such as the cloning of the sheep Dolly). He is also known for his work on embryonic stem cell derivation (together with Frances Brook), demonstrating that ESCs originate from the epiblast and that the most efficient method to derive them in mouse is to use delayed-implanting blastocysts (diapause blastocyst).

Throughout his education and scientific career, Richard has excelled in outstanding performance, as is clearly demonstrated by the long list of awards and honours (see Box); and he has always been a committed member of the

"But it should also be pointed out that aside all this prolific work in science as well as science administration and policy, Richard still has been finding time for an impressive number of hobbies, of which he lists ornithology, music, sailing (unfortunately no longer!), gardening, clay shooting and painting landscapes in watercolour."

Developmental Biology community who made notable contributions also in policy making relating to ethical issues connected with access and use of human embryos in research, ethical aspects of cloning, and ethical use of animals in research. His dedication is clearly reflected in the many important positions he served in throughout his career:

- Editor of the journal Development (formerly J. Embryol. Exp. Morph, 1977-91) and editorial board member of the journals Gamete Research, Placenta and Cancer Surveys
- President of the Institute of Animal Technology (1986-2006)
- Independent Member of the Advisory Board for the Research Council (1989-93)
- together with Walter Bodmer (head of ICRF) he co-founded the Cancer Research UK Developmental Biology Unit at Oxford's Zoology Department (attracting the likes of Andy Copp, David Ish Horowitz, Jonathan Slack, Julian Lewis and Phil Ingham), of which he was Honorary Director (1986-96)
- Vice President of the Zoological Society of London (1991-92)
- Vice-President and Member of the Laboratory Animal Science Association Council (1996-99)
- Trustee and then chair of the Edward Penley Abraham Research Fund (1999, 2003)
- President of the Institute of Biology (now Royal Society of Biology; 2007- 08)
- Chair of the Royal Society Working Group on Stem Cells and Therapeutic Cloning (1998-08)
- Chair of the Animals in Science Education Trust (AS-ET; current)
- Author of numerous reports to commissions, committees and inquiries of significant political impact
- Organiser of various scientific conferences, meetings or discussion forums.

Richard's enormous influence is also reflected in the fact that he was an influential mentor to many illustrious embryologists, including Janet Rossant (PhD, 1976), Andrew Copp (DPhil, 1978), John Heath (DPhil, 1979), Paul Tesar (DPhil, 2007), Virginia E. Papaioannou (postdoc, early 70s), Jenny Nichols (PhD, 1990), Karen Downs (1989-93) and the recipient of the 1999 Waddington medal Rosa Beddington (D. Phil., 1983) - to name but a few.

But it should also be pointed out that aside all this prolific work in science as well as science administration and policy, Richard still has been finding time for an impressive number of hobbies, of which he lists ornithology, music, sailing (unfortunately no longer!), gardening, clay shooting and painting landscapes in watercolour. To illustrate Richard's continued dedication, he donated his latest three watercolour paintings to the AS-ET and they were sold for a gratifying £1150 to provide bursaries and other awards to enable laboratory animal technicians to advance their education and training.

The BSDB would like to congratulate Richard Gardner for the Waddington award, of which he certainly is a most worthy recipient.

Awards and Honours

- Waddington Medal of the British Society of Developmental Biology (2018)
- Patrick Steptoe Memorial Lecturer and medallist (2015)
- Honorary Doctorate of Science from the University of Cambridge (2012)
- Annual Lecturer Cumberland Lodge (2010)
- Honorary Fellow, St. Catharine's College, University of Cambridge, UK (2007)
- Knight Batchelor in the Queens' Birthday Honours (2005)
- Albert Brachet Prize of the Belgian Royal Academy (2004)
- Karl Beyer Visiting Professor, University of Wisconsin, Madison, WI, USA (2001)
- Royal (Queen's) Medal of the Royal Society (2001)
- March of Dimes International Prize in Developmental Biology (1999)

- Elected Fellow of the Royal Society of London (1979)
- Scientific Medal of the Zoological Society of London (1977)
- Belfield-Clarke Prize for the Biological Sciences (1966)
- Elected Scholar of St. Catharine's College (1966)
- Kitchener Scholar (1963-66)
- Prizes for Physics and Biology (1963)
- First Prize in Natural History Essay (1959)
- First Prize in Natural History Essay (1958)

An eclectic selection of some of Richard Gardner's major landmarks publications:

1. Gardner, RL (1968) Mouse chimeras obtained by the injection of cells into the blastocyst. Nature 220: 596-7 -- *This paper describes the method of blastocyst injection in which small groups of donor cells derived from a genetically-distinct blastocyst are injected into the blastocoel cavity of a host blastocyst; chimeric blastocysts are then transferred to a foster mother and gestated to term. The paper also demonstrates that blastocyst cells contribute to the adult animal and germ line. The technique of blastocyst injection is still used routinely both to generate transgenic mouse models using genetically-modified embryonic stem cells.*

2. Gardner RL, Lyon MF (1971) X chromosome inactivation studied by injection of a single cell into the mouse blastocyst. Nature 231: 385-6. -- *Using blastocyst injection of single inner cell mass (ICM) cells combined with genetic markers, this paper shows that the adult animal is derived from the ICM. It is also a landmark paper in the history of the discovery of X-inactivation.*

3. Gardner RL, Papaioannou VE, Barton SC. (1973) Origin of the ectoplacental cone and secondary giant cells in mouse blastocysts reconstituted from isolated trophoblast and inner cell mass. J Embryol Exp Morphol. 30: 561-72. -- *In contrast to "blastocyst injection" (above) to determine the fate/potency of ICM cells via injection into the blastocoel cavity, the technique of "blastocyst reconstitution" was created to discover the fate and potency of the trophectoderm. The paper demonstrates that the trophectoderm gives rise to major components of the chorionic component of the placenta but not to the embryo proper. This allowed him to create the first fate maps of the mouse conceptus.*

4. Gardner, RL (1982) Investigation of cell lineage and differentiation in the extraembryonic endoderm of the mouse embryo. J Embryol Exp Morphol. 68: 175-98. -- *At implantation, the ICM segregates into epiblast and primitive endoderm (PE). Using blastocyst injection, this paper shows that PE generates visceral and parietal endoderm, which are supporting tissues for the ICM-derived epiblast. This study expanded the mouse fate map to show that ICM gives rise to epiblast and primitive endoderm.*

5. Gardner RL, Meredith MR, Altman DG. (1992) Is the anterior-posterior axis of the fetus specified before implantation in the mouse? J Exp Zool. 264: 437-43. -- *This paper provides the first evidence that head-tail orientation of the early embryo is established prior to the overt appearance of the primitive streak.*

A. Prokop would like to thank Berenika Plusa for helpful information, Richard Gardner for sending information, images and approving the draft of this article, and Claudio Stern and Jonathan Slack for helpful information and thoughts taken from their nomination text.

Who else to name under mentorship?
Edward Ilgren, D. Phil. (1980)
Sohaila Rastan, D. Phil. (1983)
Gillian Rands, D. Phil. (1984)
Anuja Dokras, M.D./D. Phil. (1992).
Suresh Jesuthasen, D. Phil. (1995)
Gary Uy, D. Phil. 2001)
Amatul Mateen, D. Phil. (2003)
Claire Labrousse, PhD (2006)

Postdoctoral trainees
Dante Picciano, Scientist, Biogenics
Katherine Bechtol
H. Alexandre, Dean of Biology, Mons University, Belgium
John West, Lecturer, Dept. of Obstetrics and Gynecology, Edinburgh
David Cockroft , Chief Scientific Officer, Imperial Cancer Research Fund; deceased
Patrick Tam, Senior Scientist, Melbourne, Australia
Karen Downs, Professor, University of Wisconsin - Madison, USA
Jonny Pearce, TTP Ventures, Cambridge, England
Luis Palazon, Post-Doctoral researcher, Centre for Genomic Regulation, Barcelona
Yo Ninomiya, Current

Richard is a prominent figure in the UK's Developmental Biology landscape who essentially shaped mammalian embryology in Britain. His early work on human embryos was heavily influenced by the work of XXX Richard on other mammalian species.

Richard has received many honours including the Royal Medal of the Royal Society (2001), the Albert Brachet Prize of the Belgian Royal Academy of Sciences and a knighthood "for services to the biological sciences" in 2005, and we feel that his recognition by the British developmental biology community is very overdue.

The Cheryll Tickle Medal

"Christiana has been a mentor to 11 PhD students and 6 postdocs, 3 of whom have now established themselves as independent investigators."

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 2018 awardee **Christiana Ruhrberg**. The medal will be presented at next year's **Spring Meeting** where Christiana will give the Cheryll Tickle Award Lecture.

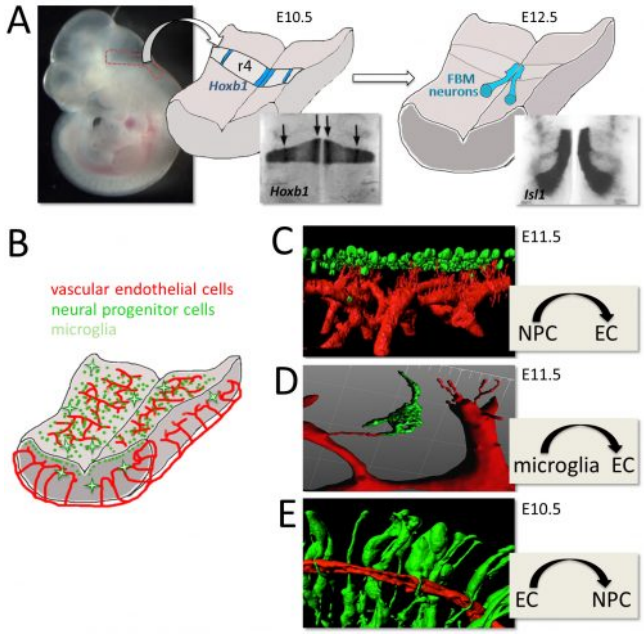
Christiana Ruhrberg, winner of the BSDB Cheryll Tickle Medal 2018

The BSDB congratulates the 2018 awardee **Christiana Ruhrberg**. The medal will be presented at the 2018 **Spring Meeting** where Christiana will give the Cheryll Tickle Award Lecture.

Christiana Ruhrberg studied Biology at the Justus Liebig University (Giessen, Germany), and obtained her first class Diploma/MSc degree in 1992. After taking on an MSc/research assistant position at the University of Sussex for two years to elucidate genetic changes in ovarian cancer, she moved to Imperial College London to work for another two years to study the genomic organisation of the gene-rich human 'surfeit' locus. She then carried out her PhD project in the laboratory of Fiona Watt at the Imperial Cancer Research Fund (1994-97) where she identified and described the function of the envoplakin and periplakin genes. Her postdoctoral research in the laboratories of Robb Krumlauf at the National Institute for Medical Research in London (1997-1999) was funded by a MRC postdoctoral training fellowship and dedicated to studying the role of *Hoxa1*, *Hoxb1* and *Hoxb2* during hindbrain development. During her second postdoc with David Shima at the Imperial Cancer Research Fund in London (2000-2002), she was funded by a ICRF fellowship and worked on VEGF-A-mediated blood vessel branching. Having received an MRC Career Development Award in 2003, she became an independent investigator at University College London's Institute of Ophthalmology studying links between vascular and neuronal development, with particular focus on the roles of VEGF and SEMA3A signalling during facial nerve and blood vessel formation. Staying at that same institute, she was appointed Lecturer in 2007, promoted to Reader in 2008 and then full Professor in 2011. Christiana has an excellent record in obtaining research funding, as illustrated by a Wellcome Trust Junior Investigator Award in 2011 and a Wellcome Trust Investigator Award in 2016 for her research on vascular biology and neurovascular interactions.

Christiana has been a mentor to 11 PhD students and 6 postdocs, 3 of whom have now established themselves as independent investigators. She has published many influential papers in the fields of vascular, neuronal and neural crest cell development, including primary research articles and reviews,

"I was initially attracted to working in the field of developmental biology when the first mouse knockouts became available. Many of them had lethal phenotypes, making embryological studies imperative to determine the physiological functions of the ablated genes."



Using the mouse embryo hindbrain to elucidate neuronal and vascular development. (**A**) The hindbrain from an embryonic day (E) 10.5 mouse was dissected to perform visualise the expression of *Hoxb1* in rhombomere 4 (**A**), the origin of the *Isl1*-positive facial branchiomotor (FBM) neurons, which can be observed during their caudal migration by *Isl1* at E12.5 (**B**). (**B-F**) Main cell types (**B**) and cell interactions (**C-F**) in the developing mouse hindbrain. In (**C-F**), dissected hindbrains were stained with the vascular endothelial marker IB4 (red) and markers for mitotic neural progenitors, microglia or neural progenitor processes, shown in green in **C-E**, respectively)**.** Note that neural progenitors attract sprouting blood vessels (**C**), the physical contact between microglial and endothelial processes (**D**) and that neural progenitor processes contact vasculature (**E**).

methods papers and book chapters. Twelve of her research papers have been listed as recommended reads by the Faculty of 1000, five have been featured with cover images and six have been featured in editorials in influential journals such as JCB, PNAS, Nature, Science, Neuron and JCI.

Christiana received an impressive amount of honours, including the title 'Young Cell Biologist of the Year' (BSCB, 1996), the 'Werner-Risau-Prize' (German Society for Cell Biology, 2003), the MRC's 'Science Heirloom' (Suffrage Science, 2011). She was also named an 'Academic Role Model' (UCL, 2013) and is listed in EMBO's 'Expert Women in Life Sciences' (2013) and 'AcademiaNet' (Robert Bosch Stiftung, Germany, 2014). Besides all these achievements, Christiana takes on regular institutional responsibilities, is a member of various grant committees and a contributing member of the Faculty 1000, editor for PLoS One, and serves on programme committees of a number of scientific meetings.

The BSDB makes it a tradition to ask the Cheryll Tickle Medal awardees a number of questions concerning our field and its future. Please, read Christiana's answers below.

What were the questions that inspired you to work in the field of Developmental Biology?

I was initially attracted to working in the field of developmental biology when the first mouse knockouts became available. Many of them had lethal phenotypes, making embryological studies imperative to determine the physiological functions of the ablated genes. I initially examined mouse knockout models to identify molecules that regulate the migration of facial branchiomotor neurons and subsequently to determine how the growth factor VEGF orchestrates blood vessel morphogenesis. By answering two different biological questions with the mouse embryo hindbrain as a model system, I serendipitously identified VEGF as the elusive migratory cue for facial branchiomotor neurons. This

"Personally, I have always been fascinated by how the vertebrate body develops to enable postnatal life. Developmental studies also yield striking images of a multitude of diverse cellular processes that coordinate organ morphogenesis, making this type of research not only exciting, but also aesthetically pleasing."

"…knowing how functional tissues are built normally might one day soon provide a gold standard for designing therapeutic strategies to recreate or repair dysfunctional tissues."

finding inspired me to continue investigating VEGF functions in neuronal and vascular development, with a more recent strive to apply knowledge gained through developmental studies also to further our understanding of disease processes in the adult.

Why should young researchers continue to engage in Developmental Biology?

Personally, I have always been fascinated by how the vertebrate body develops to enable postnatal life. Developmental studies also yield striking images of a multitude of diverse cellular processes that coordinate organ morphogenesis, making this type of research not only exciting, but also aesthetically pleasing. The PhD students, postdocs and technicians who train in my laboratory share these sentiments and have gained much deserved appreciation for their developmental biology research work through journal cover images and when winning presentation prizes at conferences. Developmental biology research also impacts on public health, because understanding how embryonic processes yield functional organs informs regenerative medicine. In particular, knowing how functional tissues are built normally might one day soon provide a gold standard for designing therapeutic strategies to recreate or repair dysfunctional tissues. That said, the developmental biology community is increasingly faced with the challenge of having to convince funding agencies that developmental biology research can underpin research into tissue repair and regeneration!

Which were the key events or experiences in your life that influenced your career decisions and paved your path to success?

My career path has not been straightforward, but encompassed a series of obstacles and opportunities. For example, the failure to appoint a successor for our retiring genetics professor at my home university in Germany could have persuaded me to switch subjects from molecular biology and genetics to a different one to avoid a significant delay to graduation, but I took this challenge as an opportunity to study for a year in the UK, being the first student on my course to embark on such an overseas placement. I ended up staying at the University of Sussex for almost 2 years to complete a research project all the way to publication, returning to Germany only to submit my thesis. Incredibly, after all the long hard work, I almost did not graduate, because those in charge at my German University deemed an English-written thesis unacceptable! This experience encouraged me to return to the UK to continue academic research in an English-speaking environment. Unfortunately, I initially chose a PhD supervisor at the Imperial Cancer Research Fund who turned out to be rather unsupportive of my endeavours; yet, I was able to make a 'lateral' move within the same organisation to re-start my PhD with Fiona Watt. She was a most inspirational PhD supervisor and mentor, and later matched me with an ideal postdoc supervisor in Robb Krumlauf at the National Institute of Medical Research. In Robb's lab, I discovered both my love for developmental biology and the inspirational community of scientists working in this area. In a nutshell, it was not careful planning that allowed me to get to my current career stage, but my unwavering enthusiasm for research combined with resilience when faced with adversity and the will to take advice and encouragement from my fabulous mentors Fiona and Robb.

What advice do you give young researchers towards a successful career?

Whether you choose to continue on an academic career or embark on an alternative career, I recommend everyone to take advantage of transferable skills training to complement the technical training gained in the research environment. Strengthening your verbal and written communication skills, learning about project and team management and developing effective networking skills will provide a strong foundation to equip you for success in a diverse range of career options.

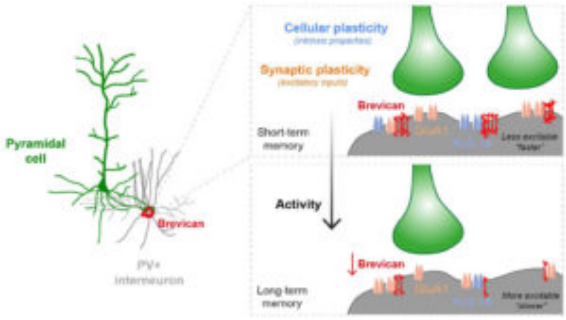
The Beddington Medal

"She discovered that the perineuronal net component Brevican is involved in the gating of parvalbumin interneurons by controlling their intrinsic properties as well as extrinsic input through excitatory synapses…"

"Emilia also took ownership within a parallel project, where she collaborated with another lab member to set up protocols to isolate different populations of interneurons and screen for genes involved in the specific synaptic targeting of cortical interneurons to the different compartments of pyramidal cells."

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 2018 winner of the Beddington Medal, **Emilia Favuzzi**, and would like to take this opportunity to give a brief overview of her career and her PhD project that was awarded the Beddington medal.

Emilia started her studies in 2007 at the Sapienza University of Rome and was awarded a B.Sc. in Biological Sciences with highest marks in 2010. She stayed at the same university for her Master's project which she performed in the laboratory of Sergio Nasi at the Institute of Molecular Biology and Pathology (CNR, Rome). She completed her M.Sc. in Neurobiology in 2011, again with highest marks. In 2011 she joined the group of Beatriz Rico at the Institute of Neuroscience in Alicante (Spain) and moved with that group to the Centre for Developmental Neurobiology at King's College London in 2014 where she terminated her project work. Her PhD in Neuroscience was awarded in 2017 by the University Miguel Hernandez of Elche (Spain) also with *summa cum laude*. Since 2017 she is a postdoctoral associate in Gordon Fishell's laboratory at the Broad Institute and Harvard Medical School.



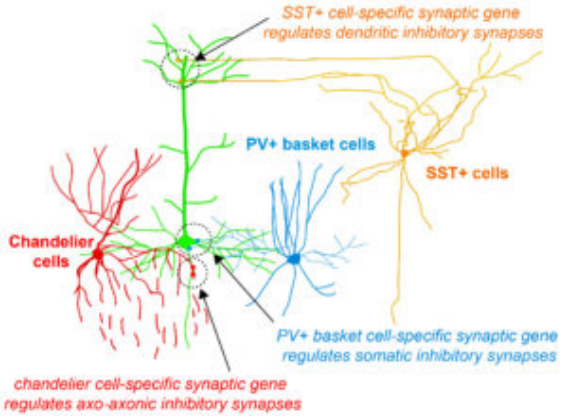
Activity-dependent gating of parvalbumin interneuron function by the perineuronal net protein Brevican

During her PhD, Emilia worked on two projects which were both based on candidate and genome-wide screen approaches aiming to identify genes that were involved in GABAergic synapse formation. In one project, she investigated the role of perineuronal nets during the synaptic development of GABAergic interneurons. She discovered that the perineuronal net component Brevican is involved in the gating of parvalbumin interneurons by controlling their intrinsic properties as well as extrinsic input through excitatory synapses (Fig.1). This paper was published as a featured article in *Neuron* (2017). Emilia also took ownership within a parallel project, where she collaborated with another lab member to set up protocols to isolate different populations of interneurons and screen for genes involved in the specific synaptic targeting of cortical interneurons to the different compartments of pyramidal cells. This work led to the discovery of validated candidate genes involved in specific interneuron synapse formation, as shown via loss and gain of function approaches (Fig.2). The respective manuscript is in preparation and Emilia will be shared first author.

Her PhD supervisor Beatriz Rico said about her: "*Emilia is a gift for a supervisor: she goes ahead of you, technically and conceptually and pushes*

"Emilia is a gift for a supervisor: she goes ahead of you, technically and conceptually and pushes you forward. She is brilliant, extremely motivated and creative person and resistant to any difficulties she has found during the development of her project."

you forward. She is brilliant, extremely motivated and creative person and resistant to any difficulties she has found during the development of her project. She never gave up and pursues her aims with an impressive efficiency. She is extremely independent and hard worker. She is fully committed to science, a dream for a supervisor."



Highly selective cell-type specific programs regulate inhibitory synapse specification

Emilia receives the Beddington medal from Simon Bullock

Thesis abstract: Cell-type specific programs regulate the assembly and dynamics of cortical circuits

Understanding how neuronal connections are established and organized in functional networks during development is critical to understand brain function. In the mammalian cortex, GABAergic interneurons are characterized by a remarkable diversity of types and connectivity patterns. As such, they are uniquely suited to orchestrate functionally relevant circuit-specific roles and critically shape cortical function. Yet, how inhibitory circuit specificity is achieved during development is largely unknown. We revealed the transcriptional dynamics of different cortical interneurons during brain wiring and identified subtype-enriched synaptic molecules. Moreover, we showed that the functional connectivity of different interneurons relies on the cell-specific expression of such synaptic genes. Altogether, our results demonstrate that highly selective molecular programs emerging during development in cortical interneurons support their early wiring and underlie inhibitory circuit specificity. After their integration into canonical circuits, activity-dependent plasticity endows neurons with the flexibility required for adapting to sensory experience. Parvalbumin (PV+) interneurons have been shown to play a critical role in this process but the molecular mechanisms by which experience influences PV+ interneuron plasticity were poorly understood. We revealed how perineuronal net (PNN) proteins drive PV+ cell wiring as well as network adaptation to experience. We showed that the PNN protein Brevican simultaneously regulates the excitatory inputs and firing properties of PV+ interneurons by controlling the localization of AMPA receptors and potassium channels, respectively. We also showed that, by modulating Brevican levels, experience influences cellular and synaptic forms of plasticity in PV+ cells and this is required for normal cognitive function. These findings uncover a cell-specific molecular program through which a PNN protein dynamically gates PV+ interneuron function both during development and upon experience-dependent plasticity.

Papers by Emilia so far *(* co-first authors)*

Favuzzi E*, *Deogracias R*, Marques-Smith A, Maeso P, Exposito-Alonso D, Balia M, Jezequel J, Kroon T, Hinojosa AJ, Rico B. Highly selective cell-type specific programs regulate structural synapse target specificity (manuscript in preparation)*

***Favuzzi E**, Marques-Smith A, Deogracias R, Winterflood CM, Sánchez-Aguilera A, Mantoan L, Maeso P, Fernandes C, Ewers H, Rico B. Activity-dependent gating of parvalbumin interneuron function by perineuronal net proteins. **Neuron** (2017)*

Marques-Smith A, **Favuzzi E*** & Rico B. Shaping Early Networks To Rule Mature Circuits: Little MiRs Go A Long Way. **Neuron** (preview), (2016)*

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Dennis Summerbell Lecture Awards

"This work impressed the judges of the Denis Summberbell Lecture award as a thorough study that sheds light upon both the origin of amnion and the molecular dynamics of its development combining cutting-edge, classical, and original techniques."

"…she currently studies the developmental mechanisms underlying the rapid evolution and adaptive radiation of Darwin's finches from Galapagos islands."

Following a generous donation, the BSDB has instituted the **Dennis Summerbell Lecture**, to be delivered at its annual Autumn Meeting by a junior researcher at either PhD or Post-doctoral level. The 2018 lecture awardee was Mariya Dobreva (VIB-KU Leuven Center for Brain & Disease Research and Department of Human Genetics, KU Leuven, Belgium) with her submitted abstract "**Amniotic ectoderm expansion in mouse occurs via distinct modes and depends on Smad5-mediated signalling**". Her award lecture was presented at the Autumn Meeting 2018: Embryonic-Extraembryonic Interactions – from genetics to environment, 10-13 September 2018 in Oxford, UK.

Mariya's work so far

Upon receiving a 4-year VIB International PhD Program grant, Mariya joined the lab of An Zwijsen in Leuven, Belgium to study the origins of amniotic stem cells and to dissect the unique extraembryonic defects of the *Smad5* knock-out mouse embryos. SMAD5 is a downstream effector of BMP signaling, a major pathway involved in many processes in development and cancer. Mariya was fascinated by how entangled the development of embryonic and extraembryonic tissues during early development is, and appreciated the importance of understanding better these neglected parts of the conceptus. She contributed to the finding that *Smad5* mutant embryos develop an ectopic primitive streak-like/tumor-like structure in their amnion due to defective signaling (*Periera et al., 2012, Development 139(18)*), and identified amnion-specific set of marker genes for mouse and human (*Dobreva et al., 2012, Stem Cells Int. 987185*). The culmination of Mariya's PhD and postdoc work at Zwijsen's lab was her most recent paper entitled "Amniotic ectoderm expansion in mouse occurs via distinct modes and requires SMAD5-mediated signalling" (*Dobreva et al., 2018, Development 145(15)*). This work impressed the judges of the Denis Summberbell Lecture award as a thorough study that sheds light upon both the origin of amnion and the molecular dynamics of its development combining cutting-edge, classical, and original techniques.

After a career brake, Mariya received a 2-year Marie Skłodowska-Curie fellowship and in 2016 moved to the UK to join the lab of Arkhat Abzhanov at Imperial College London. Expanding her research interests towards evolutionary developmental biology, she currently studies the developmental mechanisms underlying the rapid evolution and adaptive radiation of Darwin's finches from Galapagos islands.

"We attribute the two Smad5 mutant defect types to impairment of progenitors of the two main cell populations in amniotic ectoderm, and to compromised cuboidal-to-squamous transition of the anterior amniotic ectoderm."

Lecture abstract:

Upon gastrulation, the mammalian conceptus transforms rapidly from a simple bilayer into a multi-layered embryo enveloped by its extraembryonic membranes. The embryonic-extraembryonic junction is a hot spot for dynamic cell rearrangements that drive early morphogenesis. The innermost extraembryonic membrane, the amnion, develops at the embryonic-extraembryonic interphase and gradually encases the developing conceptus. Impaired amnion development causes major embryonic malformations, yet its origin remains ill-defined. Mouse embryos, deficient in the BMP signalling effector SMAD5, show aberrant amnion and ventral folding morphogenesis and delayed closure of the proamniotic canal. I developed a microdissection technique and sequenced the transcriptomes of individual *Smad5* mutant amnions isolated before the first visible malformations appear (E7.0-E7.5). I revealed two sets of defective amnions: one with a primitive-streak mesoderm signature and another one with unexpected chorionic ectoderm signature. Tetraploid chimera and immunostaining assays indicated that, in both cases, a deficit in the expansion of amniotic ectoderm results in inclusion of non-amniotic, non-squamous tissues in the amniotic microenvironment. Interestingly, the inclusions can be either of embryonic or of extraembryonic origin. To explain the different types of *Smad5* mutant defects and to clarify the origin of mouse amnion, we related our findings to existing clonal analysis of early mouse embryos performed by Kirstie A. Lawson (University of Edinburgh). She traced the fate of single cells labeled before amnion formation. Four clone types contribute to the amniotic ectoderm with distinct growth patterns. Two main clone types were identified, with progenitors in the extreme proximal-anterior epiblast. Their early descendants initiate and expand amniotic ectoderm posteriorly, following the progression of the developing amniochorionic fold. Surprisingly, descendants of cells remaining anteriorly, later expand the amniotic ectoderm from its anterior side. The progenitor regions of all types are close to BMP sources in extraembryonic ectoderm and visceral endoderm. We attribute the two *Smad5* mutant defect types to impairment of progenitors of the two main cell populations in amniotic ectoderm, and to compromised cuboidal-to-squamous transition of the anterior amniotic ectoderm. In both cases, SMAD5 is critical for expanding the amniotic ectoderm rapidly into a stretchable squamous sheet to accommodate exocoelom expansion, axial growth and folding morphogenesis.

See article: Dobreva et al., 2018, Development 145(15).

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

www.biologists.com

Developmental Biology in Bioscience teaching by Bethan Clark

As part of an ongoing effort to explore ways in which the field of developmental biology impacts science and society, we have begun to explore its role in teaching the biological sciences at undergraduate level. To investigate students' attitudes to the teaching they recieve, we asked previous recipients of The Gurdon/The Company of Biologists Summer Studentship about their experience of developmental biology in their university courses. It should come as no surprise that these particular students had enjoyed learning about development. What is more interesting is the shape this enjoyment took. Overwhelmingly, these students found that being taught developmental biology provided a framework that set other subjects in context. Drawing together concepts from cell biology, genetics, evolution, and more, this developmental framework acts as both a focal point and launchpad for learning.

"I think it really makes you understand the building blocks of life and from this you can then understand other areas of medical science". Iona Imrie

The close connection of development with other biological fields has not gone unnoticed in the literature. Intriguingly, our investigation suggests these connections are reflected in the ways students engage with developmental biology in their undergraduate education, affording a window into the potential for furthering teaching of the field.

Developmental biology introduced students to other research fields and motivated learning for subjects they had struggled to engage with in isolation. Interdisciplinary in nature, developmental biology may be uniquely positioned to do so. From evo-devo to cancer biology, cell signalling to regenerative medicine, students felt that developmental biology underpinned much of the rest of their degree courses.

"It was so different and so abstract that anything I had been taught before. Rather than soaking up tonnes of information as medical students become accustomed to, I had to stop, think and picture in my head the developmental processes being described in lectures." Daniyal Jafree

These advantages do not come easily. It was noted that the experimental techniques do not lend well to timetabled practical classes, hindering a practical appreciation of the field. Several students initially found it difficult to conceptualise developmental processes, hampering their early grasp of core concepts. This was often the case for medical students in particular, as developmental biology encourages a different approach to learning than the usual content of medical degrees. Despite the difficulties, medics appreciated the shift in perspective and realised the importance of the framing effect for their understanding of other areas.

"Although I found developmental biology a difficult subject, I realized from the beginning that this was a really important subject. It helped to frame a lot of what I was learning on human anatomy and pathology into context for me". Ji Hye Moon

The potential of the developmental biology framework to motivate learning for other topics raises the question of timing. Would an earlier introduction to the field be beneficial – not only for development, but also more widely? Students had mixed opinions, but on the whole preferred an early introduction in the first or early second year of university: an A-level understanding of cell biology was felt sufficient to engage with developmental biology.

"Early exposure to the topic, and thus more time to tailor our understanding and to choose specific areas of developmental biology that were of interest to us later in the degree was, I feel, the best way to approach the subject." George Choa

There is even scope to introduce developmental biology in A-level courses. It is worth noting that concepts such as stem cells, pluripotency, and differentiation are commonly included in GCSE and A level biology syllabuses. In terms of content, introducing developmental biology would be a relatively straightforward extension, and in fact would help put stem cell topics into context.

"I think that developmental biology should also be taught in high school, A-level or IB level Biology Standard and High levels. I think students would benefit from learning about developmental biology earlier, as they could pursue courses at universities dedicated to developmental biology straight from start rather than choosing Cell biology pathway from Year 2 or Year 3 at university". Agata Czap

Tellingly absent among all this feedback is plant developmental biology. This may well stem from a

marginalisation of plants within development courses. Of course, our observations could simply be down to chance, hinging on which individuals from the studentship scheme gave feedback. It may even reflect the trend of projects funded by this scheme. Yet this is by no means the first time that the matter of teaching plant developmental biology has been raised; it warrants further attention.

Overall, these students' attitudes suggest that the framework effect of developmental biology could be a valuable tool for improving learning experiences. Highlighting links with other fields when teaching development, and encouraging reciprocation from other courses, could be a simple starting point for harnessing this unique, potentially powerful, effect.

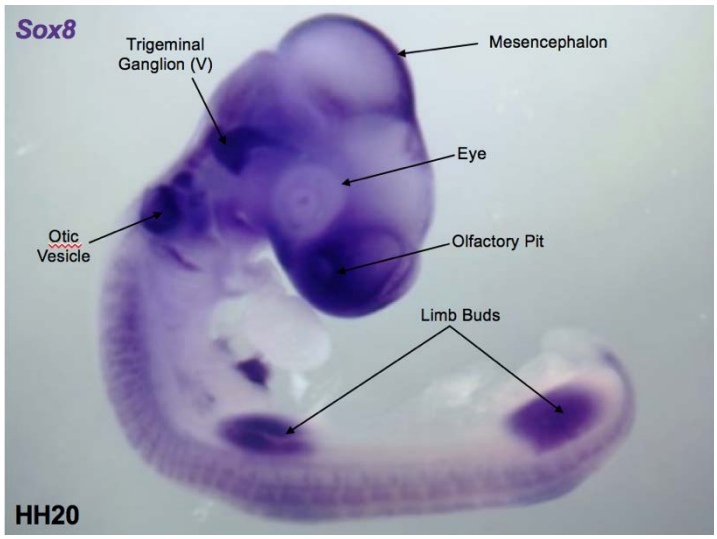
Gurdon Reports

BSDB Gurdon Summer Studentship Report (22)

As a second-year neuroscience undergraduate, I wanted specialist involvement in a working lab to progress my knowledge beyond the practical classes offered on my course. The Gurdon Studentship provided the support which allowed me to translate my interest in research into tangible experience. I was therefore very grateful to be able to join Andrea Streit's lab at King's College London for eight weeks. During my studies, my embryology module caught most of my attention. In particular, part of my coursework focused on a paper that used the chick model to observe the development of craniofacial features. When reading around the subject I encountered various techniques used in chick and wanted to see their implementation first hand. Therefore, the Streit lab was ideal because not only do they use some of these methods, but they were also able to take me on as an intern.

One of the objectives of the Streit lab is to investigate the mechanisms behind how progenitor cells become committed to a certain lineage, specifically focusing on sense organs like the ear. They have previously characterised a circuit of eight transcription factors at the top of the gene network that governs the way in which cells progressively commit to ear identity. (Chen et al., 2017)

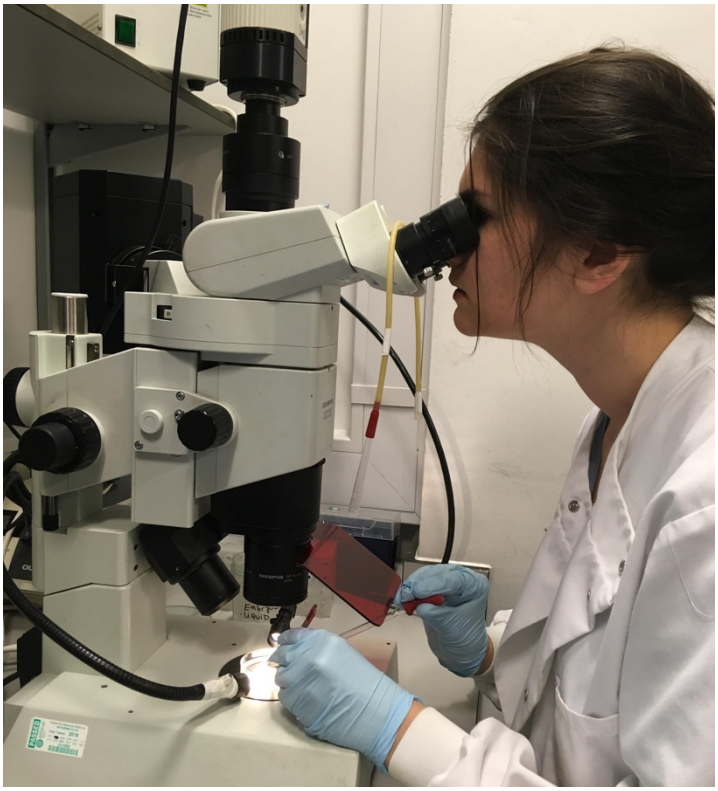
To build upon this discovery, the question my project aimed to address is whether or not this transcription factor module is active elsewhere in the chick during development, and if so how its architecture changes. In humans mutations in some of these factors not only result in deafness, but also in kidney and limb abnormalities. This suggests these regions could share common features with the ear module. To begin to establish if this is the case, I first performed in situ hybridisation (ISH) on a range of chick stages in order to analyse the expression patterns of these factors. I used antisense probes complimentary to the mRNA of each of six transcription factors present in the ear module: *Lmx1a, Prdm1, Sox8, Sox13, Pax2* and *Zbtb16*. The probes were labelled with DIG (digoxigenin) allowing the use of anti-DIG antibodies followed by a colorimetric reaction to detect where each gene is expressed.



An image of one of my in situs, depicting the expression of Sox8 in a HH20 stage chick embryo. Structures that stain a deep purple indicate gene expression in that area.

The procedure itself is relatively straight forward. However, the process is quite slow since several steps require a long time to complete. Therefore, planning and managing time pressure is one of the main challenges I came across. This was apparent when juggling several experiments at once. At first, it was a difficult to balance the fragility of the samples with furiously pipetting washes to get them in the incubator before the day's end. The ability to multitask was a skill I had not previously considered to be important as a scientist. However, my experience has helped me see how I need to improve my organisation in order to get the most out of lab hours. Learning this lesson early stands me in good stead for my research project in third year. Eventually, I became more efficient at managing my time which lead to me feeling able to attempt a more complicated procedure. Having

established expression patterns, the next challenge was to assess whether some of the regulatory relationships in the ear circuit are maintained in other organs. For example, the *Pax 2* enhancer that is active in the ear, but does it also show activity in the kidney or limb? This was accomplished through the electroporation of a reporter plasmid, where the enhancer drives GFP, followed by fluorescence imaging. This involved successful embryo culture, plasmid injection and transfer of the plasmid using a current – many steps involving numerous opportunities for things to go wrong. The samples were a challenge to handle owing to their small size. Therefore, it took several attempts to build up enough dexterity and confidence to execute each step properly. Initially, it was frustrating when most of the cultures didn't survive or the plasmid injections missed their target. Yet, this was outweighed by the satisfaction of when it all came together and I saw the fluorescence through microscope signifying my first successful electroporation.



A picture of me preparing tissues for fluorescent imaging

Overall, an internship was a big time commitment but one that was invaluable in helping me validate my desire to pursue a career in research myself. My time in a supportive working lab has taught me not only how to obtain results but also how to interpret them. Each day I was becoming more accustomed to techniques and equipment simply through practice. However, through engaging with the lab and their work as a whole, both in formal meetings and in conversation, I became more familiar with what a scientist looks for in their experiments, and crucially, assessing how what they found could apply to a wider context. I have learnt the importance of being aware of the work outside one's own. As a student, going beyond a surface level understanding of what you are doing begins with immersing yourself in the field. An internship in a lab working on a project you have interest in is a great way to start.

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Annabel Adams

BSDB Gurdon Summer Studentship Report (23)

Do embryonic mouse tails regenerate?

This summer, with the incredible help of the Gurdon/The Company of Biologists Summer Studentship, I was lucky enough to work under the supervision of Prof. Colin Jahoda in his lab at Durham University. The project I worked on aimed to determine whether epimorphic regeneration occurs in the tips of embryonic mouse tails.

Epimorphic regeneration has scarcely many examples within mammalian systems. The most famous cases among animals are found in the limbs of salamanders, which can regrow fully functional limbs at any stage of their life cycle (Godwin & Rosenthal, 2014). Mammals are far more restricted, with cases found in nail buds, and ear pinnae (Seifert & Muneoka, 2018), but none in hugely complex developmental organs, such as limbs.

The process of epimorphic regeneration begins as the wound site re-epithelializes, and the surrounding tissue dedifferentiates to form a proliferative regeneration blastema. This is then followed by the re-initiation of developmental growth and patterning (morphogenesis). Late last year, the Jahoda lap reported both rapid wound sealing and growth in E13.5 embryonic mouse tails (being studied for other purposes). These highly novel observations therefore correspond with the definition of epimorphic regeneration. Curious, we decided to take a closer look.

The main bulk of my project worked towards elucidating whether the growth which had been observed previously could be classified as actually proliferative, regenerative growth, or simply growth by cellular expansion (not regeneration). I examined this using EdU proliferation markers – a thymidine analogue incorporated into DNA molecules during replication – along with immunohistochemical methods.

The experiments took place with mouse tails removed from E13.5 embryos. Most of the culturing took place on collagen filters, with an EdU pulse three hours before they were frozen down for sectioning. An issue we faced with the collagen filters is the tendency for the wounded end of the ablated tails to adhere to their surface. This would mean of each litter, most tails fail to close fully, blocking us from observing any regeneration in these tails. We tried overcoming this design limitation through the use of 3D hanging drops. While this generally got good results for shorter cultures, long term tail cultures appeared unhealthy. By the end, we tried merging the two methods of short and long-term culture, which seemed to work (unfortunately my time ended before we could generate a refined organ culture method).

Most tails which survived from culture to sectioning contained an EdU profile and an immunohistochemical stain of either fibronectin, or collagen IV, allowing us to identify the position of the EdU stain relative to the basement membrane. We were looking for staining behind the basement membrane, with pronounced upregulation at the tip, which would correspond to the forward growth just beneath the wound site (i.e. within the regeneration blastema). There were several good examples of this taking place when the sections were cut in the middle of the tail (fig. 1 – note that this tail did not have an additional stain). Something notice in this figure is the horizontal orientation of cells right beneath the tip - this is synonymous with patterns seen within regeneration blastema's, giving support to our hypothesis that epimorphic regeneration was taking place at the tip.

Unfortunately, my finite time in the lab, combined with the harrowing challenge of producing perfect sections at the very centre of the tail, meant our dataset was limited. Consequently, we were unable to confidently state whether the proliferation was congruous with regeneration. This became something of a theme throughout my project; but something I have since come to respect about the nature of research.

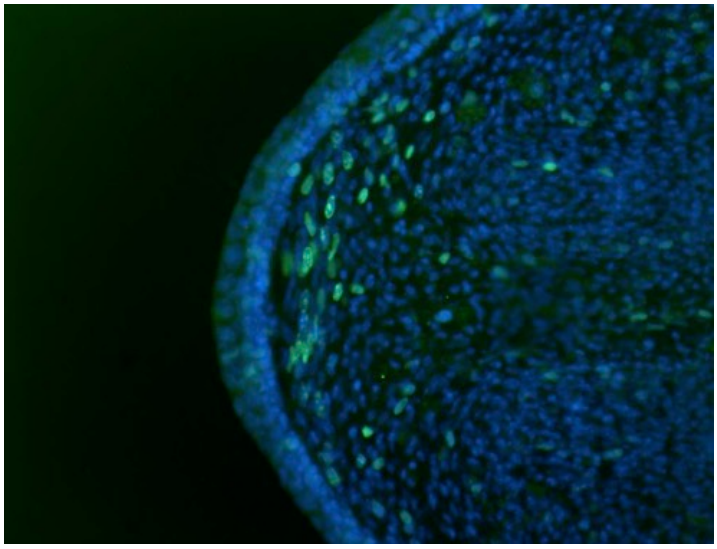

Figure 1: *Fluorescent image from the tip of an amputated tail following 24 hours in organ culture. Green stain - EdU; blue stain – DAPI.*

We briefly attempted to find whether dedifferentiation occurred on any large scale towards the tip. Our methods again applied immunohistochemistry to observe this epigenetic phenomenon. We used three separate, global histone methylation markers, alongside our EdU analysis. Unfortunately, our markers were too general to notice any significant patterns of dedifferentiation within our samples. It seems the restricted extent to which tissues de-differentiate was matched in their extent of epigenetic repatterning.

Although we are still a way away from positively characterising these phenomena as regenerative processes, it has opened many exciting questions to be explored and debated before a firm statement can be made. Personally, this experience has been exceptionally beneficial for my understanding of research, and has taught me to appreciate new ways to carefully interpret results from a critical perspective. It was also a lot of fun! I would like to send the warmest thanks to Colin and Adam for being endlessly helpful, patient and welcoming, and look forward to hearing about what more results come through in the future.

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Oliver Beaven

BSDB Gurdon Summer Studentship Report (24)

The cerebellum provides a good model for the study of the cell cycle and differentiation of neurons in the brain as a whole due to the great number of neural progenitors it produces. Tom's lab focuses on the bone morphogenetic protein (BMP) signalling pathway and how the manipulation of proteins within this pathway affects the timing of a neural progenitor cell's exit from the cell cycle, leading to terminal differentiation. When BMPs bind with their corresponding receptor on the cell surface, SMAD proteins are activated and these can initiate transcriptional changes through downstream signalling within the cell. By introducing an altered SMAD protein via vector into chick embryos through microinjection, the team was able to follow the effect of permanently "turned on" SMAD proteins in the embryo's cerebellar development. To begin with in my project, we injected plasmids containing GFP or Tomato to perfect our aim and competence with electroporation.

Chicks are great model organisms for developmental research due to the ease of access to their embryos and their significant genome homology with humans. The cerebellum; the focus of the lab's research, is an area of the brain where birds and mammals share a similar physiology. Chicks and humans share a highly proliferative external granule layer; the origin of a great number of cerebellar neural progenitor cells, which form our densely packed cerebellum, buckling into the highly folded structure seen in both mammals and birds.

As an undergraduate student at The University of Liverpool I was lucky enough to be awarded the Gurdon/BSDB Summer Studentship this year. This allowed me to spend two months in Dr Tom Butts' lab within the Department of Cellular and Molecular Physiology at the University of Liverpool, researching neuronal development within the cerebellum. In my first few days in the lab, I was mostly shadowing Graham and Hal, both Masters students nearing the end of their projects and helping Wen; another undergraduate on her summer placement. Whilst watching Graham injecting E4 embryos I was a little stunned when he finished an embryo and asked me if I'd like to try a few. Suddenly feeling very much in the deep end, I took him up on the offer and spent an exceptionally long time tentatively breaking through membranes (in constant fear I would damage the embryo) and shakily making my first injection and electroporation of the rhombic lip within the hindbrain, from which the cerebellum develops. Although a delicate procedure, I was quite surprised I was able to accomplish it, then even more surprised to see the following day that one of my embryos had taken up some DNA in the brain (surely beginner's luck!). With the continual support and enthusiasm of everyone in the lab, the "deep end" I had felt I was in quickly became much shallower.

As time went on and I became more practiced (and more importantly, more confident) working on the chicks, I was finishing electroporation of half a dozen eggs in less than half the time it took me to do two in the first week. I spend a lot of time early on practising dissection of the chick embryos to establish the skill required to create histological brain sections for imaging under confocal microscope. This was a far trickier procedure than the injections primarily due to the size of the embryo (weighing a tiny ~0.05g at E4) and it required a knowledge of chick physiology as to isolate the correct section of the brain. After the first month we also began targeting our injections to the floor plate of the mid-brain, of which some of my results can be seen below. With every good result I found myself more eager to get in each morning and analyse the previous day's electroporations. I also had my first attempt at presenting a journal club, more good experience for someone who wants to pursue a career in research.

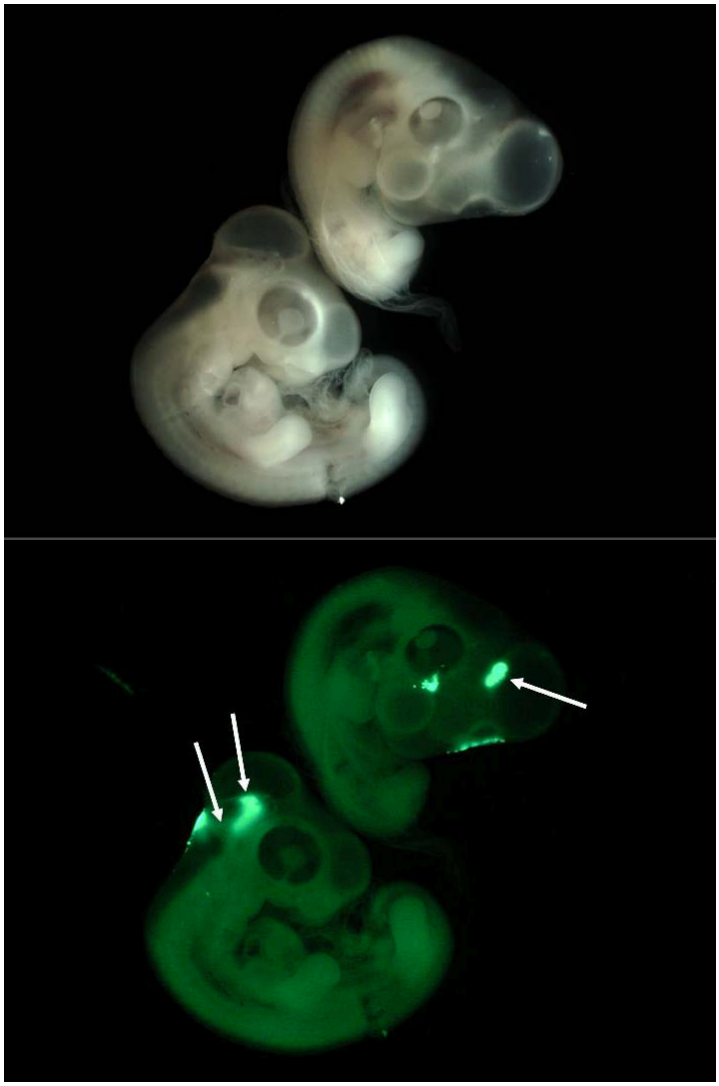

Figure 1: *Two E5 chick embryos 24hrs after injection and electroporation of a GFP-containing plasmid injected into the midbrain. Arrows indicate successful injections into the area of interest.*

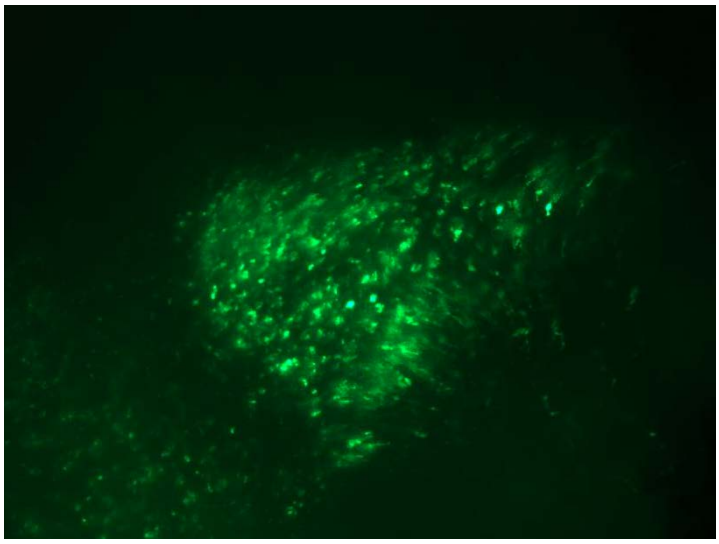

Figure 2: *Midbrain floorplate section dissected from a chick in Fig. 1, viewed under confocal microscope. Neural progenitor cells are visible, labelled with GFP.*

Wen, Lydia (another undergraduate on summer studentship) and I also worked on mapping a vector. We did not have the exact sequence and wanted to confirm the presence and order of the inserts such as the promoter, GFP label and the MCS. This was a project I felt more confident starting on with my background in genetics and we were mostly free to design the primers and run our PCRs and gels ourselves, with a little guidance from Tom. Throughout the plasmid analysis, I had to produce a comprehensive report of the primers used and results gained to allow future students to continue our work. This gave us a chance to work as an independent group, rather than following a rigid step-by-step guide with a demonstrator watching over us, as is easy to become accustomed to in lab sessions at university.

Having spent many hours peering down a dissecting microscope performing injections, electroporations and dissections, I have had a real confidence boost in my capabilities in the lab which I'm sure will go a long way as I move into my final year of university and begin my dissertation project. I have finished my summer studentship with a newfound eagerness to continue from university into a career in research in developmental biology. I am greatly appreciative to Dr Butts and everyone I worked in the lab for giving me a fascinating and fully immersive working lab experience, and very thankful to have been awarded the Gurdon/BSDB Summer Studentship, allowing me to take up this position over summer.

Natalie Dugdale

BSDB Gurdon Summer Studentship Report (25)

The Development of microphthalmia in Pax6 mutant mice

Every 4 ó minutes, a neonate in the USA is born with a birth defect, this totals up to 120,000 babies per year from the USA alone [(1)]. As an embryology student, the underling mechanisms which cause birth defects are of prime interest to me, in hope that understanding the cause of the defect can potentially lead to prevention. This summer I was able to conduct my own research on a birth defect called microphthalmia.

Microphthalmia is a disorder in which one or both eyes are abnormally small. This birth defect is closely associated with a gene called *Pax6*, the so-called 'master regulator gene' of the eye. *Pax6*$^{-/-}$ in both mouse and human causes anophthalmia (absence of the eye) due to

failure of lens placode induction [2]. *Pax6*$^{+/-}$ causes microphthalmia (Figure 1), as well as aniridia (absence of the iris), cataract and corneal opacity [2]. In mice, all *Pax6*$^{+/-}$ have microphthalmia, but in humans, *Pax6*$^{+/-}$ individuals usually have aniridia, cataract and corneal problems but tend to have normal size eyes. However, it has been shown that point mutations in *Pax6* are strong risk factors in the development of microphthalmia [6][7]. The mechanism for this is not clear, but it can be studied in mice because all Pax6$^{+/-}$ develop microphthalmia. Microphthalmia seems to arise due to the lens being sensitive to *Pax6* dosage, for instance it has been found *Pax6*$^{+/-}$ mice have a 50% reduction in the number of cells in the lens during early embryogenesis [2]. The lens is crucial in eye development as it secretes growth factors, thus a reduction in lens cells leads to a decrement in growth factors [3]. In addition to this, *Pax6*$^{+/-}$ lens cells tend to undergo one less round of division when compared to *Pax6*$^{+/+}$ mice [2]. Why this occurs in *Pax6*$^{+/-}$ lens remains a mystery, however it can be hypothesised that cell cycle time is increased leading to fewer cell divisions. Thanks to the BSDB Gurdon's Studentship I was able to further investigate this hypothesis alongside Professor Martin Collinson at the University of Aberdeen.

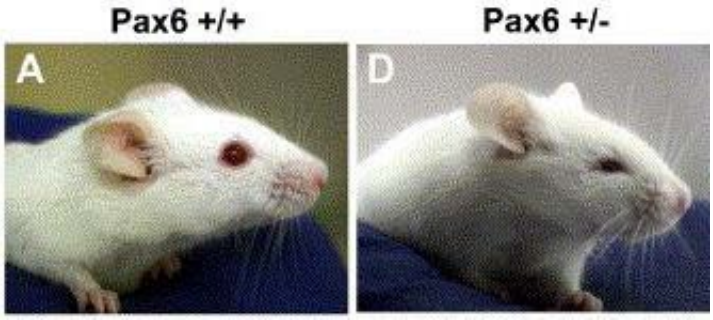

Figure 1: *Wild type mouse (**A**) in comparison to* Pax6$^{+/-}$ *mouse (**B**) displaying microthalmia*

My projected started with timed matings of *Pax6*$^{+/-}$ x *Pax6*$^{+/-}$ mice. At E14.5, the pregnant mice received an injection of iododeoxyuridine (IdU), a thymidine analogue that is incorporated into the replicating DNA of cells in S-phase of the cell cycle. 60 minutes later a second injection of ethynyl-deoxyuridine (EdU), another thymidine analogue, was given. 30 minutes after, mice were killed, and embryos were harvested and fixed in paraformaldehye. The genotypes were confirmed by PCR and electrophoresis using a small piece of tissue from each mouse embryo, *Pax6-/-* embryos were not used in this experiment because they do not have eyes. After the genotype of each embryo was confirmed, I dehydrated the embryos in ascending concentrations of ethanol (75%, 80%, 95%, 100%) and placed them in xylene. Next, my favourite part of the experiment: paraffin wax embedding. Once the embryos were embedded, a cryotome was used to cut sections which were placed onto poly-L-lysine slides. Immunohistochemistry was conducted on these slides, Anti- EdU conjugated with a green flurophore (Alexa 488) and Anti-IdU conjugated with a red fluorophore (Alexa 594) were used to detect EdU and IdU labelled cells respectively (Figure 2). DAPI staining was used to visualise all nuclei present in the mouse embryo (Figure 2). The images produced where magnificent, as shown below:

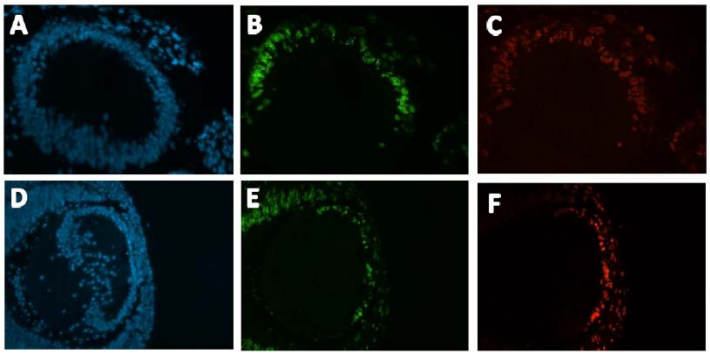

Figure 1: *Florescent Immunohistochemistry Images of E14.5 mouse embryo lens. Blue corresponds with DAPI. Green corresponds with EdU positive cells. Red corresponds with IdU positive cells.* (**A-C**) from a Pax6$^{+/+}$ developing mouse lens. (**D-F**) from a Pax6$^{+/-}$ developing mouse lens.

By counting the proportion of single labelled IdU or EdU cells in the lens epithelium, and the proportion of double labelled cells, the cell cycle time and length of S phase could be calculated using the following equations:

Length of S phase (Ts):
Ts= Ti / (L cells / S cells

Cell Cycle time (Tc):
Tc = Ts / (S cells / P cells)
(Ti = Length of IdU exposure, L cells = IdU only positive cells, S cells = EdU only positive cells, P cells = total number of cells) [5]

On average T_s and T_c lasted longer in *Pax6*$^{+/+}$ than *Pax6*$^{+/-}$ lenses (Figure 3 and 4), however, when a t-test was conducted there was no significant difference shown between *Pax6*$^{+/+}$ and *Pax6*$^{+/-}$ (t- test values; Ts = 0.11947 and Tc = 0.19446). The *Pax6*$^{+/-}$ lenses were very variable, which perhaps reflects the clinical variability of Pax6 mutation symptoms. If I had

extra time, I would repeat the experiment with more embryos to allow for an increased statistical power for T_s and T_c between *Pax6*$^{+/+}$ and *Pax6*$^{+/-}$ mouse embryos.

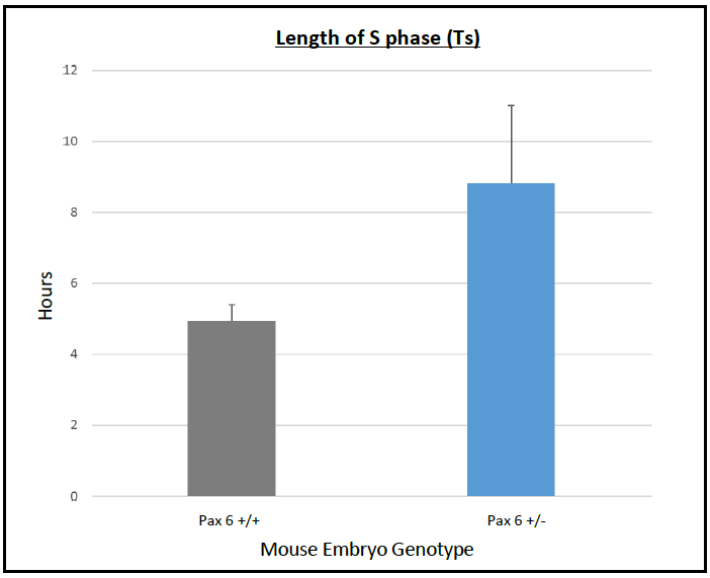

Figure 3: *Histogram showing the length of S phase in hours, with error bars representing the standard error of the mean (SEM)s. There was a trend for S phase to last longer in* Pax6$^{+/-}$ *compared to* Pax6$^{+/+}$.

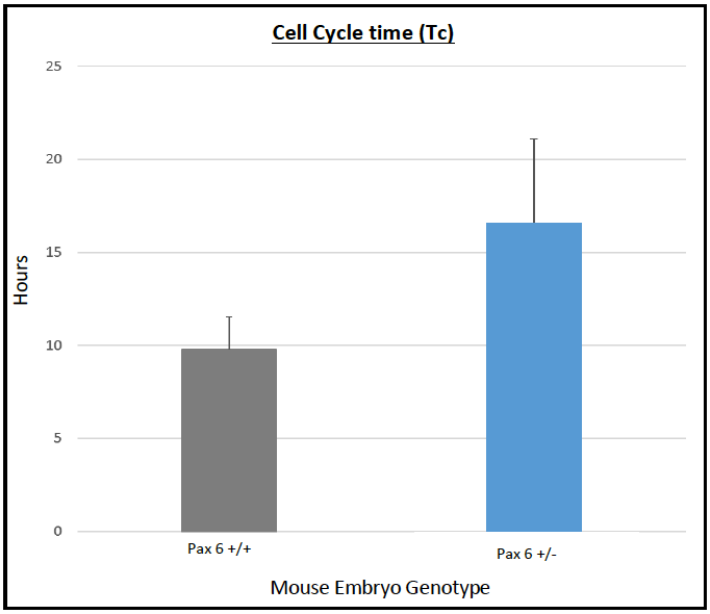

Figure 4: *Histogram showing the length of Cell Cycle Time in hours, with error bars representing SEM. Cell cycle time lasted longer in* Pax6$^{+/-}$ *compared to* Pax6$^{+/+}$

Looking back at my time in the lab, I can't believe how much I have learned. I could have never imagined myself conducting research independently as an undergrad, however, from week 2 I felt confident enough to proceed with protocols on my own accord. My 8-week project has sadly come to an end, but I feel more excited than ever for a future in developmental research. I would like to thank Professor Martin Collinson and the Gurdon Summer Studentship for giving me this opportunity and making my summer in Aberdeen a lot less grey.

Melissa Gomez

A tiring but amazing 10-hour hike to Lochnager with the girls from my lab!

BSDB Gurdon Summer Studentship Report (26)

Deciphering the dynamics of neuromesodermal progenitors at the end of axis elongation in the zebrafish embryo: A *tail* of a summer research project

I was introduced to developmental biology in the second year of my undergraduate degree at Durham University. From the first lecture, I was amazed and I left the lectures with more questions than answers on many occasions. This curiosity stemmed my quest to find a lab where I could begin to answer some of my questions. Of particular interest to me, is the elongation of the vertebrate body axis with a key question: How does the body axis stop elongating?

I was lucky enough to come across the Steventon lab who focus their research on a population of bipotent stem cells called neuromesodermal progenitors (NMps). NMps co-express Sox2 and Brachyury (neural and mesoderm markers respectively) and they provide progenitor cells for the spinal cord and mesoderm during vertebrate axis elongation (Steventon and Martinez-Arias., 2017). Furthermore, NMps are a conserved source of spinal cord amongst vertebrate species making comparative studies to be of great interest (Steventon et al., 2016).

In mouse and chick embryos, NMps are a population of bipotent, self-renewing progenitor cells whose derivatives undergo a great deal of cell proliferation that is one of the main drivers of axis elongation. On the other hand, zebrafish body axis extension is more a product of cell movements rather than of volumetric growth (Steventon et al., 2016). Therefore, a key question is: To what degree do NMps self-renew in the zebrafish embryo to give rise to both neural and mesodermal

cell fates? To begin answering this question, I carried out lineage tracing at single-cell resolution from a light-sheet movie of the zebrafish tail. This analysis meant that I got to grips with embryo mounting and I worked closely with computer scientists and engineers from the Cambridge Advanced Imaging Centre (CAIC). I was lucky to have access to a light-sheet microscope in which the stage position continually corrected to follow the tail. This allowed the tail to stay in view whilst the embryo was undergoing development, which is essential for long-term imaging of an elongating structure.

From the light-sheet dataset, all nuclei were segmented and automatically tracked using TGMM tracking software (Amat et al., 2014). To select my area of interest, the tailbud cells, computer scientists at CAIC wrote a Matlab script allowing me to select the area I wanted to track. I was then able to manually correct the tracks of interest using a Fiji plug in called MaMuT (Figure 1B) and assign fates according to gene expression data (figure 1A). The cells were tracked from 21 somite stage to the completion of somitogenesis, the stages where NMps contribute to the final stages of the body axis (Steventon and Martinez-Arias., 2017). From this data we concluded that little cell division occurs in the NMp population and that NMps are mono-fated progenitor cells, either giving rise to the neural or mesodermal lineages, but not both (Figure 1B, C, D). Therefore, in zebrafish, NMps do not undergo vast amounts of cell division to continually contribute to the elongating body axis.

Apoptosis takes place at the end of axis elongation in chick embryos. This occurs following a rise in retinoic acid signaling and the loss of FGF dependent mesoderm identity (Olivera-Martinez., 2012). Considering the different cell behaviors and contribution of NMps to the body axis in zebrafish, I next asked the question: Does apoptosis have a role in terminating the body axis in zebrafish embryos? To gain insight into this, cells at the end of the presomitic mesoderm (PSM) were photo-labelled by injecting embryos, at one cell stage, with a photoconvertible fluorescent protein mRNA called Kikume. A confocal microscope was then used to shine UV light onto the posterior PSM to convert the cells from green to red (figure 2A) and these cells could then be followed over time (figure 2B, C). It was found that the labelled cells did not noticeably undergo apoptosis and they did not segment (figure 2). It will be essential to confirm this finding with antibody immuno-labelling of apoptosis associated proteins such as caspase 3 or with a TUNEL assay. Nonetheless, morphological analysis suggests that apoptosis does not precede the termination of axis elongation in zebrafish embryos.

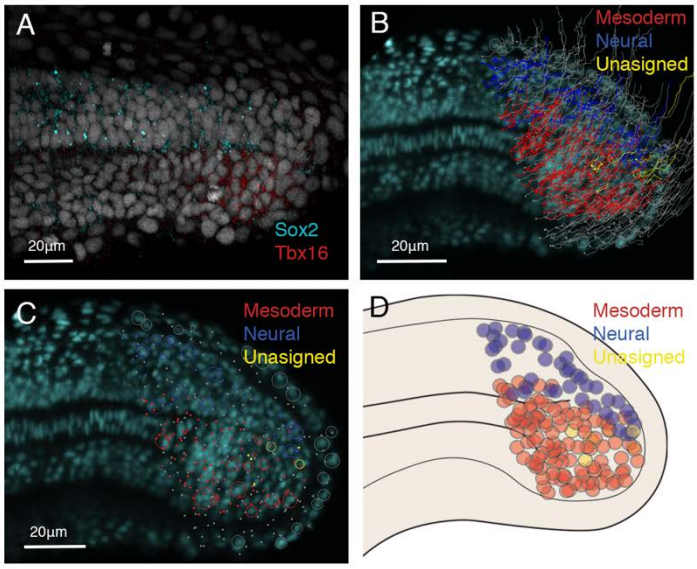

Figure 1: *Single-cell tracking of cells in the tailbud during the end of somitogenesis.* (**A**) HCR of a zebrafish tailbud showing a mesodermal marker (Tbx16), a neural marker (Sox2), and DAPI in grey. (**B**) Individual tracks of cells in the tailbud with fates assigned: Red-Mesoderm, Blue-Neural, Yellow-unassigned, overlying a still image of the light-sheet tailbud movie. (**C**) Cell fates (red-mesodermal, blue-neural) shown overlaying a still image of a light-sheet tailbud movie. (**D**) Schematic representation of tailbud progenitor fates, red-mesoderm, blue-neural.

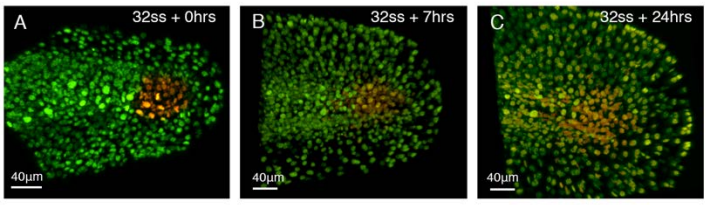

Figure 2*: Zebrafish embryo tailbuds with photo-labelled cells of the posterior presomtitic mesoderm (PSM). Embryos were injected with a photoconvertible protein mRNA, Kikume, at one cell stage. Using a confocal microscope, the protein was converted from green to red in the selected area of the PSM and successive photos were taken.* (**A**) Image taken immediately after photo-labeling at the 32 somite stage (ss). (**B**) Image taken 7 hours after initial photolabeling. (**C**) Image taken 24 hours after initial photolabeling. Note, the cells at 32ss plus 24 hours are undergoing division presumably as the fin begins to develop after these stages.

As well as the two main projects above, I also began to analyse the light-sheet data to understand which cell movements are responsible for elongating the body axis. This was carried out on Imaris software, which allowed me to view the tailbud in 3D and to select different tissues (e.g.

PSM) for analysis. Further to this, I used photolabelling (method previously described) to look at the contribution of different tailbud progenitor populations to the PSM and somites.

This experience has been invaluable to me and I have thoroughly enjoyed mixing lab experiments with computational analysis, which are both important in science.
My interaction with academics from CAIC made me realize the importance of interdisciplinary science in order to make scientific research more productive. It allows biologists to gain better insights as well as improving computational techniques for the field as a whole. I have also attended lab meetings and had the opportunity to present my work. Further to this, I attended a fantastic conference "Engineering Multicellular Self-Organisation III". When I thought that my summer could not get any better, my light-sheet data and analysis presented here has been accepted as part of a research article in the Development journal. Together, the skills gained here have taught me to be more critical and have begun to equip me for an exciting career in research.

I would like to thank Ben Steventon for making this incredible experience possible and for the great advice and discussions throughout the project. Thank you to the Steventon group: Lewis, Tim, Kane, Susie, Berta, Carolina, and John for creating a welcoming and enthusiastic working environment, not forgetting the tea breaks and pub nights! Last but not least, thank you to the BSDB Gurdon Studentship for financial support.

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Courtney Lancaster

BSDB Gurdon Summer Studentship Report (27)

Like many other lucky students, I had the chance to participate in a real cutting-edge research this summer thanks to the Gurdon Studentship award. Until then I spent my time learning the essential theory and mastering various lab techniques. What I was missing, however, was doing actual research that leads to brand new findings, rather than predictable results I'd get in a practical, which had been tried many times before. To me, the summer project represents a transition from only learning a theory and lab techniques to joining a team of scientists in a real-life lab and producing new data, that can advance the field. That is really important to me because contributing to the general pool of knowledge has always been my greatest motivation to study science.

I was hosted by the lab of Prof Pauline Schaap in the University of Dundee. The lab concentrates on several species of slime moulds that are members of the Dictyostelia clade, in particular the model organism *Dictyostelium discoideum*. These social amoebas are unicellular under normal conditions but environmental stress – especially lack of nutrients or draught – can trigger formation of multicellular fruiting bodies that consist of many hundreds differentiated cells that are derived from the individual amoebas. Some individuals within the structure encapsulate and survive the harsh conditions in form of spores that germinate when environmental conditions improve. The formation of fruiting body is a complex process, which involves intricate cell signalling that ensures a coordinated movement and differentiation of cells.

The long-term mission of the Schaap lab is to understand how this and similar processes evolved from ancestral pathway controlling encystation in more primitive, solitary amoebas and thus partially uncover how multicellularity evolved.

Fruiting body formation in *Dictyostelium discoideum*

D.discoideum is a species of social amoeba that is unicellular under normal conditions. However, low concentration of food source in a combination with a high density of amoebas in the surrounding environment t leads to an exit from the unicellular life cycle. The signals they produce activate PKA (cAMP-dependent kinase), which results in cAMP production. As cAMP diffuses to the environment it acts as a chemoattractant. Individual cells not only respond to this attractant, migrating closer to the source, but they also produce more cAMP, causing pulses of this chemical, which drive more amoebas towards the source. This results in aggregation of individuals that form a mound, which elongates and eventually topples over to create a migrating slug-like structure. Populations of cells start to differentiate into different cell types like pre-spore and pre-stalk cells. (1)

The slug follows environmental cues such as light or warmth to move towards the soil surface. Once it reaches the destination, the cells differentiate further into terminal cell types as the fruiting body develops. Some cells differentiate to form the stalk that serves as a scaffold to hold a mass of differentiated spore cells. A basal disc structure is formed at the base to support the stalk and cells also form upper and lower cups to support the spore head attachment to the stalk. (1)

My project

I worked under a day-to-day supervision of an amazing, patient PhD student Gillian. She's been studying potential marker genes for distinct parts of the fruiting body (stalk, basal disc, lower cup, upper cup and spores) and the signalling pathways linked to formation of these structures.

Previous work done in the lab identified a number of genes that could play an important role in formation of one of the fruiting body structures due to their enrichment in a specific cell type. Out of these, I studied two genes that looked most promising and went on to establish whether they are expressed in the same parts of fruiting body as hypothesised. For simplicity, I will call them gene A and B.

I used the PCR to multiply the promoter sequence of each studied gene then inserted it into a plasmid, which I then used for transformation of *E. coli*. As the bacteria proliferated, I was able to obtain enough DNA to sequence it and confirm I had the correct sequence. The confirmed promoter sequence could then be inserted into a plasmid I used for transforming *D.discoideum*. For this purpose, I used a plasmid containing the LacZ reporter gene directly after the promoter-insertion site. This LacZ gene encodes the enzyme β-galactosidase; therefore, since the expression of LacZ was controlled by promoter of the studied gene, the B-gal production mirrored expression of the studied gene.

Next, the gene expression could be visualised using the β-galactosidase substrate, X-gal. After addition of X-gal, a blue precipitate forms at the areas of the fruiting body where the promoter was activated. Hence, allowing us to locate where our gene of interest is expressed and determine whether they are cell-type specific. (2)
The genes that I worked on - A and B were hypothesised to be expressed in the stalk and cup, respectively. After I'd spend a great deal of time on optimisation of PCR conditions and several attempts to transform *D.discoideum*, I acquired transformed amoebas on which I could perform the X-gal staining.

You can see the result of this experiment in Figure 1. In the case of gene A, the stalk was clearly stained, while fruiting bodies of amoebas transformed with gene B promoter showed staining of cup cells (both upper and lower cup). Therefore, the hypothesis was confirmed for both genes.
If I had more time, it would be interesting to find out if these genes are essential for formation of the respective structures by knockout experiments. Furthermore, it could be tested what signalling molecules trigger expression of these genes to further investigate their role in fruiting body formation.

I would like to thank the lab of Prof Pauline Schaap for hosting me and offering a great amount support within a friendly environment. I am also very grateful to my day-to-day supervisor Gillian, who has taught me so much during my placement. Finally I would like to thank and appreciate the British Society for Developmental Biology for making this experience possible by selecting me for the Gurdon Studentship award. The summer project made me realise that I would really like to pursue a PhD and I would strongly recommend this scheme for any student who is considering a career in science.

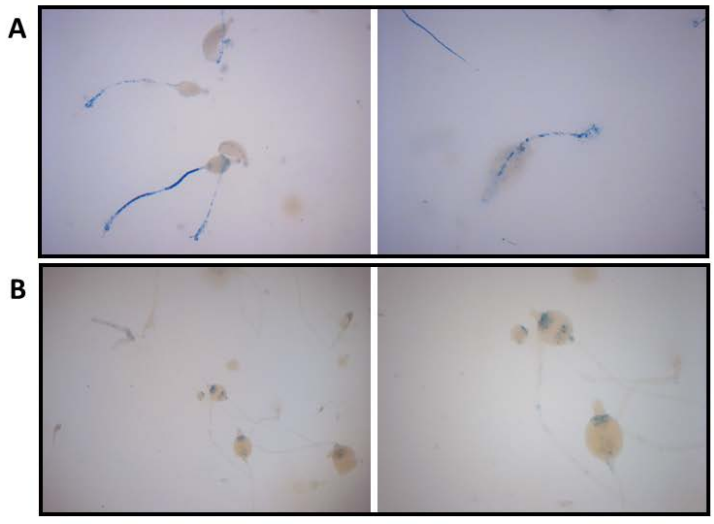

Figure 1: *β-Galactosidase assay in D. discodeum.* (**A**) Gene A, hypothesised to be expressed by stalk cells. Results of the assay confirm this hypothesis. Left: 5x magnification, Right: 10x magnification. (**B**) Gene B, hypothesised to be expressed in the (lower and upper) cup cells. Even though it was not expressed as strongly as gene A, it was found in cup cells, as predicted.

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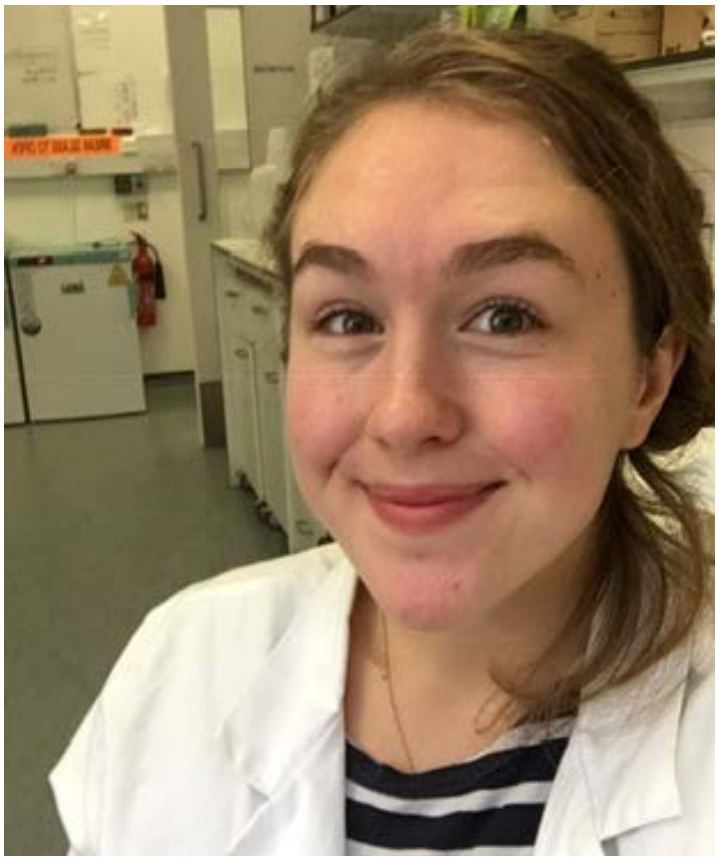
Marketa Novotna

BSDB Gurdon Summer Studentship Report (28)

Do environmental teratogens influence craniofacial development? Exploring embryopathies and birth defects in the context of maternal diabetes

My name is Lucienne Pullen and I am a third year undergraduate studying Medicine at Merton College, at the University of Oxford. This summer, I had the immense privilege of working for a Gurdon/Company of Biologists Summer Studentship, working in the Sherrington building in the Sparrow lab. My supervisors, Dr Duncan Sparrow, BHF Senior Basic Science Research Fellow, and Dr Nikita Ved, Novo Nordisk Post-Doctoral Research Fellow, undertake research in the Department of Physiology, Anatomy, and Genetics, and are focussed on embryonic cardiac development and its perturbation by genetic and environmental factors. Dr Ved in particular specialises in how pre-existing maternal diabetes induces embryonic heart defects.

I have been interested in the pathophysiology of Diabetes Mellitus since our first year lectures on metabolism and the problems that arise when it is dysregulated, and further study in the second year allowed me to explore the autoimmune and mal-resolving inflammatory aspects of the disease in more detail. Entering the Final Honours School of my course, I was highly motivated to continue this exploration in a different area: the effects of maternal diabetes on the developing embryo. The BSDB Gurdon/Company of Biologists Studentship project was designed to complement Dr Ved's research and my FHS project into the effects of diabetes on the placenta.



It may not be widely appreciated, but maternal diabetes carries a highly increased risk of having a child with birth defects (the incidence of birth defects among women with Type 1 and Type 2 diabetes is around 3-5 times higher than among non-diabetic mothers); yet exactly how and when these defects arise during embryonic development has been relatively sparsely studied. The aforementioned statistic is particularly alarming given that routine diabetes testing does not occur until around the 24-28 week stage of pregnancy, despite organogenesis usually occurring within the

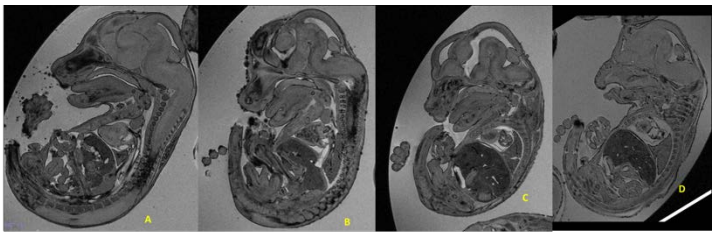
first three to eight weeks of gestation. Therefore, integral to the project was adding to the existing body of evidence that diabetes is associated with embryopathy, and limb and craniofacial defects more specifically. Any support for a causative link between diabetes and embryopathies can help build a body of evidence to show that early intervention and potentially pre-emptive treatment (or at the minimum earlier screening) would be beneficial to maternal and foetal health, minimising the risks to the developing embryo.

I was personally motivated to undertake this project as I am hugely interested in a career in reproductive medicine, both clinically and in a research capacity. Entering a specialisation in this field in the future would allow me to engage with a research career into areas of developmental biology integral to improving women's health. The ultimate goal of this project, Dr Ved's research, and that of scientists in different groups around the world is to produce data that can change guidelines, therapies, or procedures for the benefit of women everywhere.

My project involved using an inducible mouse model system of diabetic embryopathy (the ßV59M mouse model), in which a variety of developmental defects can be seen, including heart, craniofacial, and skeletal defects. The accuracy of this model's replication of clinical occurrences is supported by the incidence of these defects in human patients. Clinical evidence also indicates that other anomalies occur, including caudal regression syndrome, hypoplastic femur, clubfoot, and improper formation of the cranial bones.

I explored the relatively under-researched area of craniofacial defects; the embryos were investigated using MRI imaging, which provided detailed images which were measured and analysed using FIJI/ImageJ. 82 diabetic and 21 non-diabetic control embryos were analysed with four parameters: snout length, snout angle, tongue length, and lower jaw length of the diabetic mice.

Once the embryos have been collected by around E14.5, they are arranged in cylinders to be scanned using magnetic resonance imaging (MRI). The MRI scans can then be analysed, with four embryos per MRI 'slice' measured at a time. At first I found it a little unsettling and difficult to orientate myself with the mouse embryo image, however it was highly interesting and satisfying to learn to recognise key features, and begin to note down when and where I spotted additional abnormalities, such as hydrocephaly, anencephaly, and widespread oedema, which were present in several of the embryos. Furthermore, the analysis process helped me to develop key scientific research skills, such as having specific reference points and scrupulous attention to detail when making measurements; the integrity of the data was dependent on having comparable and standardised measurement techniques.



Example embryo MRIs, showing the severity of deformities. (**A**) is from a control non-diabetic pregnancy. (**B**) and (**C**) are both pre-pregnancy induced diabetic embryos, and show the developmental delay in their reduced size and also exhibit craniofacial deformities; (**D**) is from a post-pregnancy induced diabetic model, exhibiting severe craniofacial defects including failure to develop a tongue.

Difficulties sometimes arose when the craniofacial areas were so heavily deformed it was difficult to find these standardised reference points, however through speaking to my supervisors it was always possible to find a suitable compromise or alternative way of measuring the embryo. On some occasions it was not possible to make measurements due to extreme deformities of particular embryos, which was important in teaching me that research can sometimes be frustrating, and that experimental hurdles can arise that require patients and creativity to overcome.

Preliminary data obtained suggests that in this particular set of embryos, there are no significant differences in the four craniofacial measurements obtained, however further analysis is possible, including looking at alternative parameters and undertaking alternative measurements, including area analysis and transformation to 3D imaging to provide further angles to explore. It would also be interesting to look at this data in conjunction with a companion research project into the effects of placental insufficiency on embryo development in diabetic pregnancies.

I would like to wholeheartedly thank Dr Sparrow, Dr Ved, and the BDSB for this invaluable experience, which has helped me hone my research skills and broaden my horizons in terms of possible future clinical research careers. I would encourage those thinking of applying to do so without hesitation!

Lucienne Pullen

Analysis of Rapgerf5 and canonical Wnt signalling in embryonic mouse development

During the summer of 2018, I worked with Dr John Griffin in Dr Karen Liu's lab at King's College London. My focus was on the gene *RAPGEF5*, which was previously identified as a candidate gene for heterotaxy, a congenital disease affecting heart development and the spatial arrangement of organs. It is estimated that 1 in 10,000 people are diagnosed with heterotaxy, and is the cause of 3% of all congenital heart cases[1]. However, the genetics of heterotaxy are still unclear. Thus research is necessary to understand the disease mechanism in more detail.

Not much is known about RAPGEF5 protein, but we know it is involved in the canonical Wnt pathway, in the transportation of beta-catenin into the nucleus[1]. When Wnt is active, a cascade of chemical reactions prevent the degradation of beta-catenin in the cytoplasm, allowing it to bind to a transporter protein to enter the nucleus. Our current model suggests that in response to Rap-GDP conversion to Rap-GTP by RAPGEF5, beta-catenin can dissociate from the transporter protein.[2] This frees beta-catenin, allowing it to interact with DNA-binding proteins to alter gene expression. Therefore, my project aimed to answer three key questions:

1. Where is canonical Wnt signalling active during embryonic development?
2. Where is RAPGEF5 expressed during embryonic development?
3. Does loss of RAPGEF5 lead to any developmental abnormalities such as heterotaxy?

To answer my first question, I used genetically modified mouse embryos carrying a TCF/Lef-dependent reporter to visualize the areas with active Wnt signalling. When Wnt is active, the transcription factors TCF/Lef are active and bind to specific binding sites on DNA. This activates a promoter that causes the GFP reporter gene to be expressed and produce proteins that fluoresce under a specific wavelength.

I dissected embryos from their sacs at weeks E11.5, E12.5, E13.5 and E14.5. They were then photographed using a fluorescence microscope. In general, fluorescence can be seen in the ears, edges of limbs, spine, branchial arches, whiskers and brain. The heart was only visible in the E11.5, as the skin over the heart was too thick at later stages (Figure 1.a). At week E14.5, fluorescence was only faintly visible at the ear, due to the thicker skin.

In response to question 2, I fixed and dehydrated the E11.5 embryos for whole mount mRNA in situ hybridization. A *Rapgef5*-specific probe was used to stain the embryo, and the result was shown in figure 1.b. RAPGEF5 mRNA was expressed in the heart, brain, spine and the tip of the hind limb.

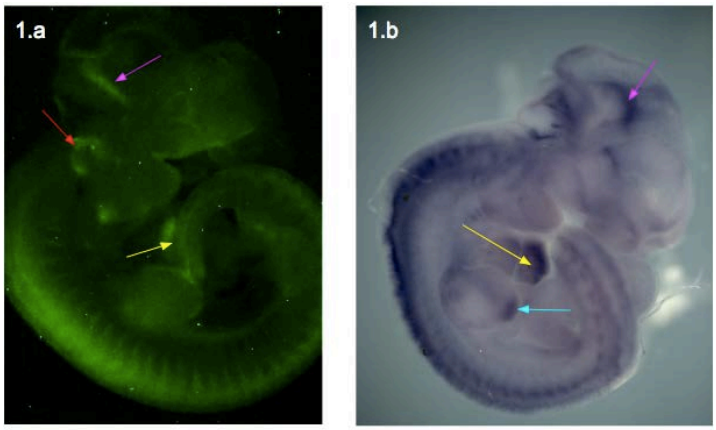


Figure 1: *Both photographs are of a TCF/Lef E11.5 mouse embryo. The left shows GFP signal reporting active Wnt., and the right shows the whole mount in situ hybridization with Rapgef5 probe Structures highlighted are the heart (yellow arrows), mid brain (pink), ear (red), tip of hind limb (blue).*

Figure 1 presents two photographs of an E11.5 embryo, one showing the distribution of RAPGEF5 specifically, and the other for active Wnt signalling. When compared, the distribution appears similar, however there are discrepancies such as the ear, and tip of the hind limb.

Finally, for my third question, we bred RAPGEF5 mutant mice and inspected them at stages E9.5, E10.5, E14.5 and 6 weeks after birth. Tail clippings were taken from the embryos and ear clippings from the pups for DNA extraction and PCR to confirm their genotype, as they could either be wild-type, heterozygous or homozygous. Unfortunately the genotyping was still in the stages of trial-and-error, as the bands in the gel electrophoresis did not match the reference DNA ladder, and further tweaking with the PCR temperature and primers is necessary.

However, there were some phenotypic changes found. Out of the total of 9 E9.5 amniotic sacs, 4 were had healthy embryos, 4 were empty and 1 was malformed and underdeveloped. It is possible that this embryo was in the process of being reabsorbed to match the 4 other empty sacs. For the E10.5, there were 8 embryos in total, and 2 had

underdeveloped heads and lacked proper surface morphology. All 8 of the E14.5 embryos were phenotypically normal.

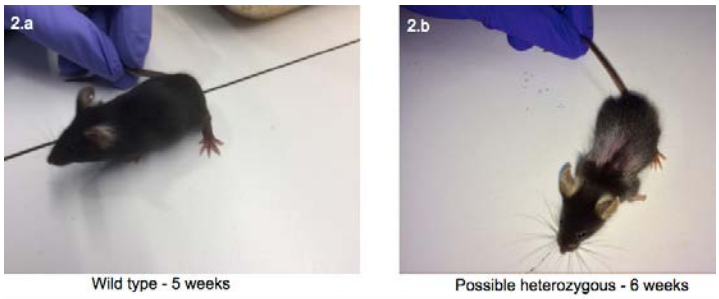


Figure 2

Interestingly, as seen in figure 2, when compared with the wild-type, the 6 week old pup had bald patches in a 'Christmas tree' pattern and a possible front limb deformity. Both were similar in size and behaviour.

I thoroughly enjoyed my summer studentship at King's, and learnt many new techniques such as wax sectioning and mounting, in situ hybridisation and using fluorescence microscopy. I would like to thank Mr John Griffin, Dr Karen Liu and the Liu lab for taking time out of their schedule for their help and guidance.

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Rachel Wong

BSDB Gurdon Summer Studentship Report

Characterising myelination in zebrafish with IPO13 mutations

This summer I was privileged to receive a Gurdon Summer Studentship to work for 8 weeks in Professor David Lyon's Laboratory at the Centre for Discovery Brain Sciences (part of the University of Edinburgh). I have just finished the first year of my undergraduate degree in Mathematics and Biology at the University of Edinburgh and have enjoyed the different challenges posed by both subjects. I wanted to spend my summer break developing my practical skills, and also to be able to gain insight into how quantitative methods are useful in neuroscience.

Why study myelination in zebrafish?

Myelin is a lipid-rich substance that coats the axons of neurons, forming an electrically insulating layer. Myelin sheaths are produced by oligodendrocytes that are wrapped around axons in our central nervous system (CNS). Many neurological diseases result from damage to myelin, such as multiple sclerosis (MS). Myelination speeds conduction of nerve impulses, and also provides trophic support to the underlying axon (Klingseisen, A. and Lyons, D. A., 2018).

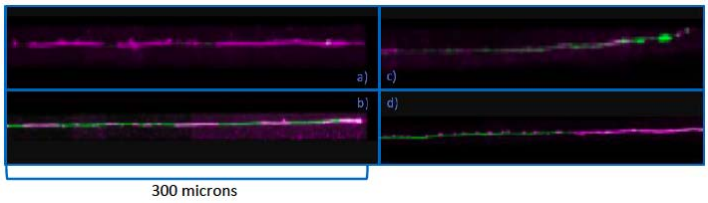

Figure 1: *Myelination is reduced in mutant axons. a) 3dpf image of a mutant axon b) 5dpf image of a mutant axon c) 3dpf image of a wildtype axon d) 5dpf image of a wildtype axon. Unmyelinxated regions are shown in magenta (tagged using contactin 1a reporter).*

The process of myelination begins around birth in mammals, when the CNS is already complex and difficult to image. As zebrafish embryos develop outside the mother they are accessible for imaging from a single cell stage. Zebrafish larvae are only a few millimetres long and are optically transparent, which allows for non-invasive live imaging. The fish can be returned to growth medium after imaging sessions and the same fish can be reimaged days later (Bin, J. M. and Lyons, D.A., 2016).

The Lyons Lab has a zebrafish line that is heterozygous for an IPO13 mutation.
IPO13 encodes the protein importin 13, which is a member of the importin- ß superfamily that transports cargoes bidirectionally across the nuclear membrane (You et al., 2012). Homozygote fish with IPO13 mutation exhibit reduced axon calibre which is most obvious for the Mauthner axons, which are the largest axons in fish. Dr. Jenea Bin (my supervisor) has observed that in some instances the Mauthner axon remains partially unmyelinated (Figure 1), therefore, my project aim was to analyse this hypomyelination phenotype

What techniques have I learnt?

During this project I gained skills in the breeding of adult fish, the mounting and screening of fish, super-resolution imaging, microinjection into zebrafish eggs at a single cell stage and also the analysis of images using Image J software.

Every week, I mated heterozygote IPO13; Mauthner:Gal4; UAS:GFP fish and microinjected the embryos with a UAS:tdtomato-contactin1a reporter. TdTomato-Contactin 1a is a fluorescently tagged transmembrane protein that gets excluded from the axonal membrane upon myelination, thus unmyelinated regions of the axon are labelled in fluorescent red. In addition, with this transgenic line, the Gal4 UAS system is used to label the Mauthner axon with GFP, allowing for visualization of the entire axons, whether myelinated or unmyelinated. Figure 1 shows the labelling of the axon with GFP and tdTomato.

I screened the larvae at 3dpf (days post fertilisation) to see if they had green (GFP) and red (tdTomato) fluorescence present along the Mauthner axon. Those that were positive for GFP and tdTomato were imaged using the Zeiss LSM 880 Laser Scanning Microscope with Airyscan. These Z-stack images were processed and analysed using Image J. Creating the full axon images involved using and editing macros to remove background and stitch images, and the analysis allowed me to explore many of the tools that Image J has to offer. I calculated the percentage of each full axon image that was unmyelinated, along with the number of boutons along the axon labelled in both tdTomato and GFP (shown in Figure 2) and the number of filopodia-like boutons (shown in Figures 3 and 4). The fish were genotyped and split into wildtype (WT), heterozygous (HET) and mutant (MUT) groups.

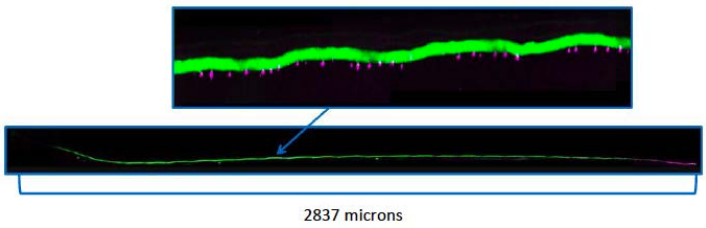

Figure 2: *Representative image of normal morphology of synaptic boutons along a Mauthner axon of a wildtype phenotype fish 5dpf (days post fertilisation).*

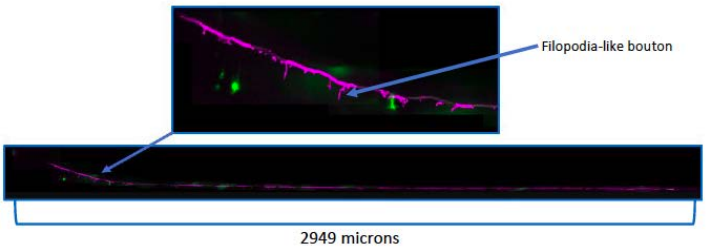

Figure 3: *Extreme mutant phenotype in a 5dpf fish, showing extensive unmyelinated regions and pronounced filopodia-like boutons.*

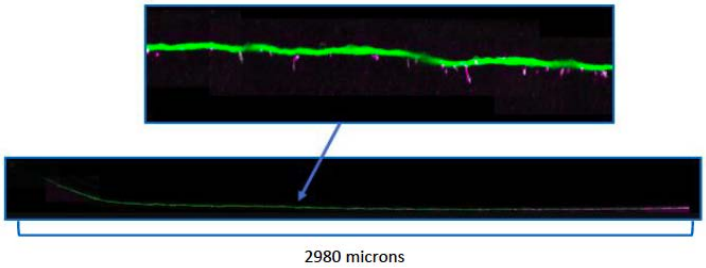

Figure 4: *Representative phenotype of a 5dpf mutant fish, displaying a few filopodia-like boutons, but much less extensive unmyelinated regions than the extreme mutant phenotype fish.*

Results

Significance tests were carried out using a one-way ANOVA. The difference between the length of the axons of wildtype, mutant and heterozygous fish was found to be insignificant at 5dpf. The percentage of unmyelinated regions along the axon were significantly different between the wildtype/heterozygote and mutant fish (Figure 5). The number of boutons (Figure 6) was significantly higher in the wildtype/heterozygote fish than in mutant fish. The number of filopodia-like boutons (Figure 7) was significantly higher in the mutant fish than in wildtype/heterozygote fish.

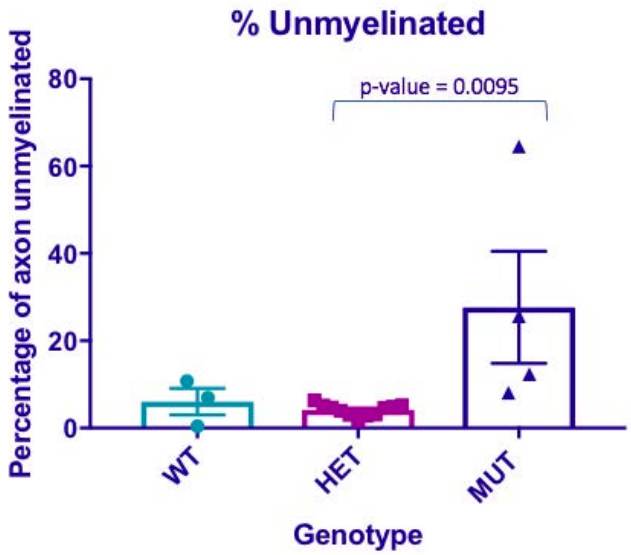

Figure 5: *Bar graph with standard error of the mean (SEM) showing the percentage of unmyelinated regions along each axon of wildtype (WT), heterozygote (HET) and mutant (MUT) IPO13 fish at 5dpf.*

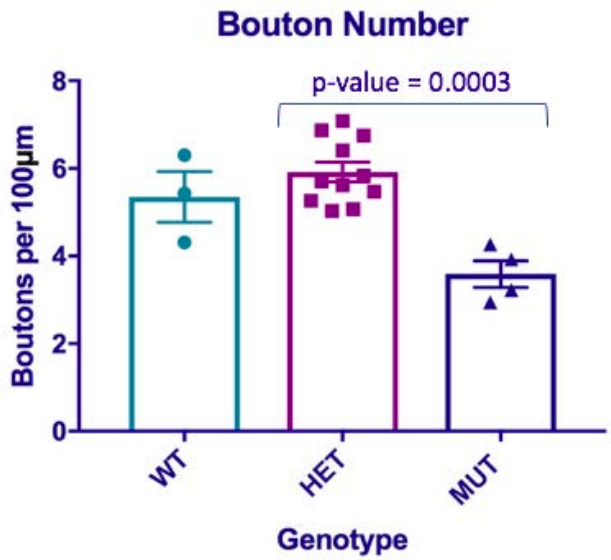

Figure 6: *Bar graph with SEM error bars showing the number of synaptic boutons along each axon of wildtype (WT), heterozygote (HET) and mutant (MUT) IPO13 fish.*

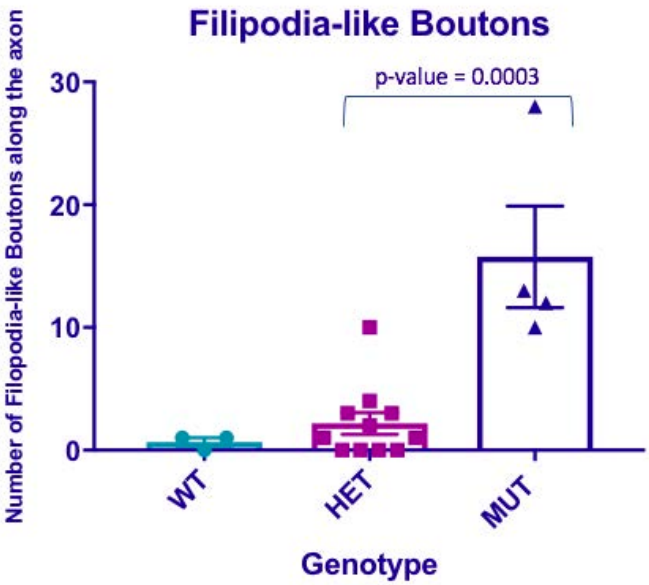

Figure 7: *Bar graph with SEM error bars showing the number of filopodia-like boutons along each axon of wildtype (WT), heterozygote (HET) and mutant (MUT) IPO13 fish.*

Conclusions

During my project I was struck by the huge amount of work involved in this type of research – over the 8 weeks we injected and screened over 3000 embryos and only imaged 25 fish. As this research is so labour intensive to obtain data, it is vital that analysis methods gain as much information as possible from each image. In future, as the volume of data continues to increase, I am sure mathematics will become ever more useful in modelling axons.

Overall, I have had a fantastic time working in the Lyons Lab this summer. Thank you to Dave and Jenea for supervising me, and to the whole lab for being so welcoming. I have developed a lot of skills, which I will utilise in my future scientific career. Finally, thank you to BSDB for their support.

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Rachel Jackson

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