SANTANDER
INTERNATIONAL SUMMER SCHOOLS
FOR DOCTORAL STUDENTS



GETTING IN SHAPEVISUALIZATION AND MANIPULATION OF ORGANISMAL MORPHOGENESIS





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Universität Heidelberg

UNIVERSITÄT HEIDELBERG

Heidelberg University, founded in 1386, is Germany's oldest university and is one of the strongest research universities in Europe. The successes in both rounds of the Excellence Initiative and in international rankings prove its leading role in the scientific community. In terms of educating students and promoting promising young academics, Heidelberg relies on research-based teaching and a well-structured training for doctoral candidates.

Heidelberg University is a comprehensive university with the full spectrum of subjects including medicine. It aims to strengthen the individual disciplines, to further interdisciplinary cooperation and to make research results usable for society and industry.

Heidelberg also draws its strength from its cooperation with local non-university research institutions. In addition, the university is tied into a worldwide network of research and teaching collaborations which give evidence of its marked global interconnectedness.

International Profile

Heidelberg University is tied into a worldwide network of research and teaching collaborations. Exchange programmes have been established with more than 400 universities worldwide. Heidelberg's marked global interconnectedness is also evidenced by its 19 university partnerships and and three International Research Training Groups, as well as its membership in European networks such as the League of European Research Universities (LERU) and the Coimbra Group.

A myriad of research and teaching collaborations are also established at the faculty, institute and chair levels. Additionally, Heidelberg has a satellite campus in Latin America as well as liaison offices in North America and Asia. The university also offers courses in Eastern Europe.

Heidelberg's international prominence is reflected in its student popula tion: approximately 20 percent of Heidelberg's students and a third of the enrolled doctoral candidates come from abroad. According to the latest DAAD survey, Heidelberg is the favoured German university for international doctoral candidates.

SANTANDER UNIVERSIDADES

Santander, committed to Higher Education

The University plays a fundamental role in the knowledge society. It acts as a guide towards an innovative society, contributing to economic and social change and supporting scientific and technological progress.

Through its Santander Universities Global Division, Banco Santander has collaborated with universities for more than 16 years on a unique global initiative which distinguishes it from other national and international banks and financial institutions.

In 1996, Emilio Botín, Chairman of Santander, decided that the bank should be useful to the societies in which it operates. With the conviction that the university is a vital cornerstone of development and progress, it was decided that Santander's long term commitment would be materialised through creating a program to help the academic world in its role as a guardian of knowledge and a key agent in achieving progress in terms of economic competitiveness and social wellbeing.

Santander Universities maintains a stable alliance with more than 1.040 universities from America, Asia and Europe.

In 2011, through Santander Universities, Banco Santander contributed over 110 million euros to cooperation projects with universities of America, Asia and Europe.

More than 2.130 professionals coordinate and manage Santander's commitment to higher education through Santander Universities Global Division. In the words off Emilio Botín, Chairman of Santander: »increased employment and welfare provision is based on education, research and effort«.

Academic institutions receiving support from Santander for the development of academics initiatives relating to scholarships; mobility grants; research Programmes; university-Enterprise Relations; new technologies.



PROGRAMME OVERVIEW

SAT, 30.11.		Departure participants									
FRI, 29.11.	9:00-19:30 h Uni Chile	Symposium							20:00 h HCLA	:	Farewell Dinner
THU, 28.11.	9:00-19:30 h Uni Chile	Symposium		Lunch				Dinner			
WED, 27.11.	9:30-12:30 h HCLA	Tech talks Brand, Bellaiche, Friml, Whitlock		Lu	14:00-18:00 h Uni Chile	Lab work: Image Analysis		Din			
TUE, 26.11.	9:30-12:30 h HCLA	Tech talks Martínez- Morales, Laufs, Spang			14:00-18:00 h Uni Chile	Lab work: Blocks D-C*			19	Lab work:	Blocks D-C*
MON, 25.11.	9:30-12:30 h Uni Chile	Tech talks Glavic/Olguín, Norambuena Lab work: Advanced	Microscopy		13:30-18:00 h	Lab work: Blocks C-B*			19:00-22:00 h	Lab work:	Blocks C-B*
SUN, 24.11.	10:00-21:30 h	excursion to Valparaíso									
SAT, 23.11.	9:30-12:30 h HCLA	Tech talks Prud'Homme, Sarrazin, Evers, Araya			12:30-23:30 h	excursion to Cajón del Maipo					
FRI, 22.11.	9:30-12:30 h HCLA	Tech talks Wittbrodt, Allende, Evers, Schumacher		Lunch	14:00-18:00 h Uni Chile	Lab work: Blocks A-D*		Dinner	19:00-22:00 h	Posters	
тни, 21.11.	9:30-12:30 h HCLA	Introductory talks Centanin, Maizel, Lemke, Krebs		In	14:00-18:00 h Uni Chile	Lab work: Blocks A-D*		Dir	19:00-22:00 h 19:00-22:00 h	Posters	
WED, 20.11.	9:30-12:30 h HCLA 9:30 h	Poster setup 10:00 h Welcome Session 10:45 h Short talks	Glibalova, Galvez Santisteban, Urbansky, Batsivari		13:30-18:00 h Short talks Di Donato,	Lovegrove, Lust, Morales,	Vilcries Barro, Manieu Seguel, Ojeda, Ercoli, Palma		19:00-22:00 h	Short talks	Sartoretti, Lekk, Pinheiro, Torres Paz
TUE, 19.11.					15:00-18:00 h HCLA Foyer	Arrival participants /	Welcollie Desk		19:00 h HCLA		Welcome Dinner / Barbecue
MON, 18.11.									17- 19:00 h HCLA Foyer		Arrival participants / Welcome Desk

*Block A = Build your own light sheet microscope in 20 easy steps Block B = Lineage Analysis Block C = Application of the microscope Block D = Intracellular imaging in plants

SANTANDER Summer School 2013 Programme Book

DETAILED PROGRAMME

MONDAY, NOVEMBER 18, 2013, HCLA

Arrival participants

17:00 – 19:00 Welcome Desk

TUESDAY, NOVEMBER 19, 2013, HCLA

15:00 - 18:00 Welcome Desk

18:00 - 20:00 Welcome Dinner / Barbecue

WEDNESDAY, NOVEMBER 20, 2013, HCLA

09:30 - 10:00 Poster setup

10:00 **WELCOME SESSION**

Jochen Wittbrodt, Miguel Allende, Walter Eckel, Isabel Eisenmann

10:30 - 10:45 Coffee break 10:45 - 12:30 SHORT TALKS

Antonia Gibalová - Charles University in Prague:

»Role of bZIP transcription factors during male gametophyte development in Arabidopsis thaliana«

Manuel Angel Gálvez Santisteban – Universidad Autónoma de Madrid:

»Identification and characterization of novel regulators of epithelial lumen morphogenesis« Silvia Urbansky - Universität Heidelberg: »Evolution of mesoderm morphogenesis in flies«

Antoniana Batsivari – University of Edinburgh:

»The role of proliferation in haematopoietic stem cell development«

12:30 - 13:30 Lunch

13:30 - 16:00 SHORT TALKS

Vincenzo Di Donato – Institut Curie:

»Role of Reelin in zebrafish optic tectum development and retinotectal circuit formation«

Holly Lovegrove – University of Cambridge:

»Investigating integrin function in the organization of the *Drosophila* follicular epithelium«

Katharina Lust - Universität Heidelberg: »Wound response and regeneration in the retina of medaka fish«

Alexis Morales – Universidad Austral de Chile: »Zebrafish neuroepithelial morphogenesis«

Amaya Vilches Barro – Universität Heidelberg:

»Microtubules-dependent mechanical control of lateral root morphogenesis in Arabidopsis«

16:00 - 16:15Coffee break

16:15 - 18:00 SHORT TALKS

Catalina Paz Manieu Seguel – Universidad de Chile:

»Chas-Jbug/Filamin system and Myo-II cooperates to maintain the isometric tension of epithelial cells under mechanical stress during morphogenesis of Drosophila melanogaster«

Jorge Ojeda – University of Concepción: »Fz9 receptor promotes the maturation of postsynaptic apparatus at the vertebrate NMJ through Wnt/B-catenin pathway«

María Florencia Ercoli - National University of Rosario: »Function of miR396 and GROWTH REGULATING FACTOR transcription factors in Arabidopsis thaliana leaf and root development«

Karina Palma – Universidad de Chile: »Circadian Modulatíon of the Parapineal-Habenula-Interpeduncular Nucleus (Opp-H-INP) in zebrafish larvae (Danio reno)«

18:00 - 19:00 Dinner

19:00 - 22:00 SHORT TALKS

María Micaela Sartoretti – Universidad de Buenos Aires:

»Astrocytic differentiation in the developing neural tube«

Ingrid Lekk – University College London:

»Development of diencephalic asymmetries in zebrafish and chicken embryos«

Diana Pinheiro – University of Porto and University Paris VI:

»Cell division in the Drosophila epithelial tissue: How to divide with neighbors?«

Jorge Torres Paz – Unversidad de Valparaíso, Chile:

»Dissecting the roles of six4b and dlx3b during the olfactory epithelium development in zebrafish«

THURSDAY, NOVEMBER 21, 2013, HCLA

09:30 - 12:30 INTRODUCTORY TALKS

Lázaro Centanin – Universität Heidelberg: »Mechanical and Genetic Tools for Lineage Analysis « **Alexis Maizel** – Universität Heidelberg: »Build your own light sheet microscope in 20 easy steps!«

11:00 – 11:15 Coffee break

Steffen Lemke – Universität Heidelberg:

»What to do with large data microscopy recordings: introduction to automated image analysis«

Melanie Krebs – Universität Heidelberg:

»Fluorescent nanosensors for in vivo analysis of ions and metabolites«

12:30 - 13:30 Lunch

13:30 Transfer from HCLA to Universidad de Chile

14:00 – 16:00 LAB WORK: Blocks A-D*, Uni Chile

16:00 – 16:15 Coffee break

16:15 - 18:00 LAB WORK: Blocks A-D*

18:00 – 19:00 *Dinner*19:00 – 22:00 **POSTERS**

22:00 Transfer from Universidad de Chile to HCLA

FRIDAY, NOVEMBER 22, 2013, HCLA

09:30 - 12:30 TECH TALKS

Jochen Wittbrodt – Universität Heidelberg: »Light sheet microscopy, a ›historic‹ perspective« **Miguel Allende** – Universidad de Chile: »A simple, cheap and effective tool for tissue ablation and

inflammation induction in zebrafish larvae«

11:00 – 11:15 Coffee break

 $\textbf{Jan-Felix Evers} - \text{Universit\"{a}t Heidelberg: } \\ \text{ `Microscopy for developmental biology `` (Part 1)} \\$

Karin Schumacher – Universität Heidelberg: »Why study plants?«

12:30 - 13:30 Lunci

13:30 Transfer from HCLA to Universidad de Chile

14:00 - 16:00 LAB WORK: Blocks A-D*, Uni Chile

16:00 – 16:15 *Coffee break*

16:15 - 18:00 LAB WORK: Blocks A-D*

18:00 – 19:00 *Dinner*19:00 – 22:00 **POSTERS**

22:00 Transfer from Universidad de Chile to HCLA

SANTANDER Summer School 2013

Programme Book

Detailed Programme

SATURDAY, NOVEMBER 23, 2013, HCLA

09:30 - 12:30 TECH TALKS

Benjamin Prud'homme – Institut de Biologie du Développement Marseille:

»The genetic regulatory mechanisms of morphological pattern formation«

Andrés Sarrazin – Pontificia Universidad Católica de Valparaíso: »Dissecting the segmentation process:

A whole embryo culture approach to understand the relationship between the molecular mechanisms and cell

dynamics during body segmentation in the beetle Tribolium castaneum«

11:00 - 11:15 Coffee break

Jan-Felix Evers – Universität Heidelberg: »Microscopy for developmental biology« (Part 2)

Claudio Araya – Universidad Austral de Chile:

»Imaging zebrafish neural tube morphogenesis: from collective cell behavior to polarized tissue dynamics«

12:30 - 23:30 Excursion to canyon Cajón del Maipo

with Lunch package, Dinner and Wine tasting

Weather-proof clothing and adequate shoes are recommended!

SUNDAY, NOVEMBER 24, 2013, HCLA

10:00 - 21:30 Excursion to Valparaíso

Starting point: HCLA

Don't forget beach wear and a towel! (Depending on weather conditions)

MONDAY, NOVEMBER 25, 2013, UNI CHILE

09:00 – 09:30 Transfer from HCLA to Universidad de Chile

09:30 - 11:00 TECH TALKS

Alvaro Glávic, Patricio Olguín – Universidad de Chile:

»Genetic tools to study how genes control growth and form in Drosophila«

Lorena Norambuena – Universidad de Chile:

»Chemical genomics: unraveling plants endomembrane system trafficking and developmental mechanisms«

11:00 - 11:15 Coffee break

11:15 – 12:30 LAB WORK: Advanced Microscopy

12:30 - 13:30 Lunch

13:30 - 16:00 LAB WORK: Blocks C-B*

16:00 – 16:15 *Coffee break*

16:15 – 18:00 LAB WORK: Blocks C-B*

18:00 - 19:00 Dinner

19:00 - 22:00 LAB WORK: Blocks C-B*

22:00 Transfer from Universidad de Chile to HCLA

TUESDAY, NOVEMBER 26, 2013, HCLA

09:30 - 12:30 TECH TALKS

Juan Ramón Martínez Morales – Universidad Pablo de Olavide: »Live imaging of entire vertebrate organs during morphogenesis. From tissue behaviour to cell and molecular dynamics. Microscopes and limitations«

Patrick Laufs – Institut Jean-Pierre Bourgin:

»Linking gene function to morphogenesis: the example of the leaf margin«

11:00 – 11:15 Coffee break

Anne Spang – Universität Basel: »Using C. elegans to understand intracellular pathways«

12:30 – 13:30 Lunch

13:30 Transfer from HCLA to Universidad de Chile

14:00 - 16:00 LAB WORK: Blocks D-C*, Uni Chile

16:00 – 16:15 Coffee break

16:15 - 18:00 LAB WORK: Blocks D-C*

18:00 – 19:00 *Dinner*

19:00 - 22:00 LAB WORK: Blocks D-C*

22:00 Transfer from Universidad de Chile to HCLA

WEDNESDAY, NOVEMBER 27, 2013, HCLA

09:30 - 12:30 TECH TALKS

Michael Brand – Technische Universität Dresden:

»Tools for studying regeneration of the adult zebrafish brain«

Yohanns Bellaiche – Institut Curie:

»Multiscale Imaging and quantification of tissue morphogenesis: from gene to forces«

11:00 – 11:15 Coffee break

Jiří Friml – Institute of Science and Technology Austria (IST Austria):

»Imaging-assisted genetic approaches in plant cell biology«

Kate Whitlock – Universidad de Valparaíso: »Problems with Populations«

12:30 - 13:30 Lunch

13:30 Transfer from HCLA to Universidad de Chile 14:00 – 16:00 LAB WORK: Image Analysis, Uni Chile

16:00 – 16:15 Coffee break

16:15 - 18:00 LAB WORK: Image Analysis

18:00 - 19:00 Dinner

19:00 - 22:00 LAB WORK: Image Analysis

22:00 Transfer from Universidad de Chile to HCLA

INTERNATIONAL SYMPOSIUM, NOVEMBER 28 TO 29

THURSDAY, NOVEMBER 28, 2013, AUDIT. HERMANN NIEMEYER, UNIV. DE CHILE

08:30 Transfer from HCLA to Universidad de Chile

09:00 - 13:00 SESSION 1:

	Jochen Wittbrodt & Miguel Allende
09:00 - 09:10	Introductory words (Miguel Allende, Jochen Wittbrodt)
09:10 - 9:50	Jiří Friml – Institute of Science and Technology Austria (IST Austria) Wien, Austria:
	»Polarity and Patterning in Plant Development«
09:50 - 10:30	Patricio Olguín – Facultad de Medicina, University of Chile, Santiago, Chile: »Shaping the Drosophila dorsal
	thorax, the role of planar polarity and cellular and adaptation to inter-tissue mechanical stress«
10:30 - 11:00	Coffee break
11:00 - 11:40	Claudio Araya – Instituto de Ciencias
	Marinas y Limnológicas, Universidad Austral de Chile, Valdivia, Chile:
	»Regulation of cell and tissue invagination during zebrafish neurulation«
11:40 - 12:20	Patrick Laufs – Institut Jean-Pierre Bourgin, Versailles, France: »Genetic Control of Leaf Shape«
12:20 - 13:00	Alvaro Glávic - FONDAP Center for Genome Regulation, Facultad de Ciencias, Universidad de Chile,
	Santiago, Chile: »The <i>Drosophila</i> EKC/KEOPS complex: its role in protein homeostasis and animal growth«
13:00 - 14:30	Lunch and Poster viewing

14:30 - 16:30 SESSION 2:

	Alexis Maizel & Lorena Norambuena
14:30 - 15:10	Anne Spang – Biozentrum University of Basel, Switzerland:
	»Function and regulation of small GTPases in C. elegans«
15:10 - 15:50	Yohanns Bellaiche – Génétique et biologie du développement, Institut Curie, Paris, France:
	»Epithelial cell dynamics and cell division«
15:50 - 16:30	Michael Brand – Biotechnology Center, TU Dresden, Germany:
	»Regeneration of the adult zebrafish brain: an essential, positive role for inflammation«
16:30 - 17:00	Coffee break

17:00 - 19:00 SESSION 3:

Steffen Lemke & Claudio Araya

1/:00 – 1/:40	Karin Schumacher – Centre for Organismal Studies, Universität Heidelberg, Germany:
	»Same, same but different – the plant endomembrane system and its roles in growth and morphogenesis«
17:40 – 18:20	Juan Ramón Martínez Morales – Centro Andaluz de Biología del Desarrollo, Universidad Pablo de Olavide,
	Sevilla, Spain: »Optic cup morphogenesis: a model to study the cellular and molecular bases of basal

constriction«

18:20	Poster session
19:00 - 20:30	Dinner

20:30 Transfer from Universidad de Chile to HCLA

FRIDAY, NOVEMBER 29, 2013, AUDIT. HERMANN NIEMEYER, UNIV. DE CHILE

08:30 Transfer from HCLA to Universidad de Chile

09:00 - 14:30	SESSION 4:
	Karin Schumacher & Alvaro Glávic
09:00 – 9:40	Lorena Norambuena – Departamento de Biología, Universidad de Chile, Santiago, Chile:
	»Protein trafficking: Role in Plant Development«
09:40 – 10:20	Lázaro Centanin – Centre for Organismal Studies, Universität Heidelberg, Germany:
	»Life-Long Lineage Analysis of Post-Embryonic Retinal Stem Cells in Fish«
10:20 – 11:00	Alexis Maizel – Centre for Organismal Studies, Universität Heidelberg, Germany:
	»Quantitative analysis of Arabidopsis thaliana lateral root morphogenesis at cellular resolution using light
	sheet based fluorescence microscopy«
11:00 – 11:30	Coffee break
11:30 – 12:10	Jacques Dumais – Facultad de Ingeniería y Ciencias, Universidad Adolfo Ibáñez, Viña del Mar, Chile:
	»Measuring Cell Expansion in Growing Plant Organs«
12:10 – 12:50	Jan-Felix Evers – Centre for Organismal Studies, Universität Heidelberg, Germany:
	»Variability and mechanisms of plasticity during development of locomotor circuits in <i>Drosophila</i> «
12:50 – 14:30	Lunch and Poster viewing

14:30 - 16:30 SESSION 5:

Juan Ramón Martínez-Morales & Patricio Olguín

- 14:30 15:10 **Miguel Allende** FONDAP Center for Genome Regulation, Facultad de Ciencias, Universidad de Chile, Santiago, Chile: »Resilience of the zebrafish mechanosensory system: robust regenerative potential in all its cellular components«
- 15:10 15:50 **Andrés Sarrazin** Institute of Chemistry, Pontificia Universidad Católica de Valparaíso, Chile: »Evolutionary origin of segment formation mechanisms in animals«
- 15:50 16:30 **Steffen Lemke** Centre for Organismal Studies, Universität Heidelberg, Germany: »Evolution of Gastrulation«
- 16:30 17:00 Coffee break

17:00 - 19:30 SESSION 6:

Miguel Allende & Lázaro Centanin

- 17:00 17:40 **Kate Whitlock** Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), Universidad de Valparaíso, Chile: »Dissecting Development in Time and Space«
- 17:40 18:20 Siobhan Brady Department of Plant Biology and Genome Center UC Davis, USA:
 - »Mapping Spatiotemporal Gene Regulatory Networks Guiding Root Vascular Development«
- 18:20 19:00 **Jochen Wittbrodt** Centre for Organismal Studies, Universität Heidelberg, Germany:
 - »How to define a niche: Transcriptional control of stem cell features in the post-embryonic fish retina«
- 19:00 **CLOSING REMARKS** (Miguel Allende)
- 19:30 Transfer from Universidad de Chile to HCLA Dinner
- 20:00 Farewell Dinner, HCLA

SATURDAY, NOVEMBER 30, 2013

Departure of participants

SANTANDER Summer School 2013 Programme Book Coordinators List of Speakers Prof. Jochen Wittbrodt, Centre for Organismal Studies, Universität Heidelberg and Prof. Miguel Allende, FONDAP Center for Genome Regulation, Universidad de Chile

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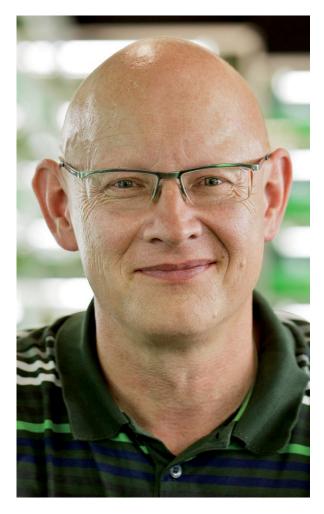
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LIST OF SPEAKERS

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SANTANDER Summer School 2013 Programme Book Abstracts of Technical Talks

ABSTRACTS OF TECHNICAL TALKS

MIGUEL ALLENDE, Universidad de Chile, FONDAP Center for Genome Regulation, Santiago de Chile, Chile

A simple, cheap and effective tool for tissue ablation and inflammation induction in zebrafish larvae

Background: Tissue injury has been employed to study diverse biological processes such as regeneration and inflammation. In addition to physical or surgical based methods for tissue injury, current protocols for localized tissue damage include laser and two-photon wounding, which allow a high degree of accuracy, but are expensive and difficult to apply. In contrast, electrical injury is a simple and inexpensive technique, which allows reproducible and localized cell or tissue damage in a variety of contexts.

Results: We describe a novel technique that combines the advantages of zebrafish for in vivo visualization of cells with those of electrical injury methods in a simple and versatile protocol which allows the study of regeneration and inflammation. The source of the electrical pulse is a microelectrode that can be placed with precision adjacent to specific cells expressing fluorescent proteins. We demonstrate the use of this technique in zebrafish larvae by damaging different cell types and structures. Axotomy can be carried out in peripheral nerves or in the spinal cord allowing the study of degeneration and regeneration of nerve fibers. We also apply this method for the ablation of single lateral line mechanosensory neuromasts, showing the utility of this approach as a tool for the study of organ regeneration. In addition, we show that electrical injury induces immune cell recruitment to damaged tissues, allowing in vivo studies of leukocyte dynamics during inflammation within a confined and localized injury. Finally, we show that it is possible to apply electroablation as a method of tissue injury and inflammation induction in adult fish. Conclusions: Electrical injury using a fine microelectrode can be used for axotomy of neurons, as a general tissue ablation tool and as a method to induce a powerful inflammatory response. We demonstrate its utility to studies in both larvae and in adult zebrafish but we expect that this technique can be readily applied to other organisms as well. We have called this method of electrical based tissue ablation, electroablation.

CLAUDIO ARAYA, Universidad Austral de Chile, Instituto de Ciencias Marinas y Limnológicas, Valdivia, Chile

Imaging zebrafish neural tube morphogenesis: from collective cell behavior to polarized tissue dynamics

Zebrafish embryos develop a neural tube by a highly complex morphogenetic process that involves the transformation of a flat sheet of cells into a mature hollow neural tube. This occurs initially by the orchestrated actions of large groups of cells from both sides of the neural plate that converge towards the dorsal midline to form a solid neural keel and neural rod. Subsequently, the neural rod cavitates to form a neural tube with a single central lumen a clear apico-basal polarity. At a cellular level, it is has been shown that the correct development of the apico-basal polarity is achieved by a combination of behaviours including cell intercalation, midline-crossing division and polarised cell behaviour. To understand cell and tissue dynamics during morphogenesis our lab use an in vivo system in which we can image neural tube morphogenesis in the transverse plane of the zebrafish embryo allowing us to observe cell behaviour throughout the superficial-basal depth of the neural tissue and at all dorso-ventral levels at high temporal resolution. In this talk you will learn how we imaging neural tube morphogenesis in zebrafish embryos. This includes; microinjection techniques to deliver construct driving expression of various fluorescent proteins transiently and mosaically in cells within developing tissues, mounting techniques for time-lapse imaging, and subsequent analysis and data visualization in available open-source softwares.

YOHANNS BELLAICHE, Institut Curie, Génétique et biologie du développement, Paris, France

Multiscale Imaging and quantification of tissue morphogenesis: from gene to forces

How proliferative tissues adopt their shape is a central question in developmental biology. Many tissues undergoing extensive proliferation concomitantly adopt their shape during development. Hence, the apparent coordination between growth and morphogenesis underlies the development of organs and tissue of defined size and shape adapted to their physiological function in the organism. The mono-layered epithelium of the Drosophila pupa undergoes extensive proliferation and morphogenesis to shape the *Drosophila* adult. To study the morphogenesis of the dorsal thorax, we implemented an innovative multi-scale imaging method to follow both cell dynamics (5 minutes time resolution, 200nm resolution) and tissue global morphogenetic (global imaging of the tissue for up to 24 hours) in a living organism. Qualitative observations suggest that the tissue undergoes extensive proliferation (up to three cell cycles) while reshaping by convergence extension movements. Image velocimetry and segmentation based image analysis allow us to describe and quantify tissue morphogenesis from the cell level to the tissue level. Using this novel model system, we have determined the role of the planar cell polarity pathway Fat-Dachsous in epithelial tissue morphogenesis. More generally, our results indicate how global gene expression patterns can trigger local changes in mechanical cell properties to drive tissue morphogenesis.

MICHAEL BRAND, Technische Universität Dresden, Biotechnology Center, Dresden, Germany

Tools for studying regeneration of the adult zebrafish brain

In contrast to mammals, adult zebrafish have a remarkable ability to regenerate their brain, retina and spinal cord following a lesion. Adult neurogenesis is likely to be linked to this ability, and in adult rodents, adult neurogenesis is limited to only two subregions of the telencephalon, whereas in adult zebrafish it occurs along the entire length of the neuraxis, suggesting a mechanistic link to its regeneration ability. The study of adult brain regeneration benefits from a panel of new technologies that are available for studying proliferation, lineage development and neuronal differentiation in normal and in lesioned brains, including thymidine incorporation studies, transgenic marker lines, Cre-loxP mediated recombination, and cerebroventricular microinjection of function-blocking morpholinos. The application of these technologies will be discussed with reference to key questions regarding adult brain regeneration.

LÁZARO CENTANIN, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Mechanical and Genetic Tools for Lineage Analysis

At the very beginning of our own history, each and every one of us was just a single cell –a zygote. That only cell massively divided, its progeny differentiated and here we are after all, multicellular animals (reasonably) gifted for a number of tasks. The path followed by that only cell (and each one of its daughters) during embryonic development has fascinated scientists over the last centuries. In these technical talks I will focus on how researchers have experimentally approached the issue of establishing lineage relation on embryos that simultaneously go through cell division and differentiation. I will review different ways of labeling and following cells in different animal models, from mechanical manipulation of the specimens (experimental embryology) to modern, interference-free genetic tools. We will perform hands-on experiments using fish (i.e. mechanical transplantation during blastula stage and colorful CRE-mediated recombination) and flies (i.e. generation of fluorescent clones by the MARCM approach). The talks will include a final discussion on how the tools we will use during the practical have changed the view on post-embryonic stem cells.

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JAN-FELIX EVERS, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Microscopy for developmental biology

To understand the mechanisms that regulate development appears impossible without the use of microscopy. The last few years have seen the arrival of many novel microscopy techniques that promise to push detection sensitivity, image resolution and acquisition speed to ever new boundaries. Which of these techniques produce sufficient quality of image data to elucidate the questions at hand, and how to analyse this data must be decided carefully before setting out to do experiments.

In this lecture I will review 1) the fundamental principle of how modern microscopes work. Here I will focus on techniques that allow 3-dimensional optical sectioning with visible light. 2) I will introduce nonlinear optics and their use for imaging deep in tissue. 3) I will discuss recent developments in super-resolution microscopy.

These lectures are intended to be interactive, such that we will be able to discuss the specific suitability of these techniques for your particular experimental questions.

JIŘÍ FRIML, Institute of Science and Technology Austria (IST Austria) Klosterneuburg, Austria

Imaging-assisted genetic approaches in plant cell biology

Coordinated, subcellular protein trafficking is one of the fundamental properties of the unicellular and multicellular eukaryotic organisms. It is crucial for regulating the amount and localization and, thus, the activity of various proteins at different subcellular destinations including cell surface. Subcellular trafficking involves a large diversity of compartments, pathways, cargo molecules, and vesicle-sorting events, but the process is still poorly genetically defined in plants.

In the past, forward genetics screens had been used to determine the function of genes by searching for a specific morphological phenotype in the organism population in which mutations had been induced chemically or by irradiation. Unfortunately, these straightforward genetic screens turned out to be limited in identifying new regulators of intracellular protein transport, because mutations affecting essential trafficking pathways often lead to lethality. In addition, the use of these approaches has been restricted by functional redundancy among trafficking regulators. Screens for mutants that rely on the observation of changes in the cellular localization or dynamics of fluorescent subcellular markers enable, at least partially, to circumvent these issues. Hence, such image-based screens provide the possibility to identify either alleles with weak effects or components of the subcellular trafficking machinery that have no strong impact on the plant growth.

An overview of current efforts and advances regarding use of imaging-assisted forward genetics and chemical genomics screening strategies will be given along with the practical experience and real outcomes of these approaches.

ALVARO GLÁVIC, Universidad de Chile, Departamento de Biología, Facultad de Ciencias, Santiago de Chile. Chile

PATRICIO OLGUÍN, Universidad de Chile, Programa de Genética Humana, ICBM, Facultad de Medicina, Santiago de Chile, Chile

Genetic tools to study how genes control growth and form in Drosophila.

Since early twenty century, *Drosophila melanogaster* has been employed to study the role of the genotype in the control of growth and form. Although a plethora of genes that control tissue morphogenesis were discovered during those early days, many remained unknown because their loss of function cause cell death and lethality. The genetic screen developed by Nusslein-Volhard and Weischaus uncovered many other genes required to establish the body plan and to shape the embryo. However, it was not until the development of techniques that allow us to manipulate gene function in a temporal and tissue/cell-specific manner, and to label cells and cellular compartments in live individuals, that we could start to unveil the role of many structural and regulatory genes in the different aspects of morphogenesis. In this talk we will review the most popular genetic techniques available in *Drosophila* to study morphogenesis, we will focus on tissue growth, cell and tissue polarity, and tissue patterning.

MELANIE KREBS, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Fluorescent nanosensors for in vivo analysis of ions and metabolites

Metabolism is a non-stationary process and cells have evolved regulatory mechanisms to adapt rapidly in response to different internal and external stimuli. To understand complex metabolic situations and follow signalling events with high temporal and spatial resolution, fluorescent nanosensors have been developed.

In this talk an overview of different classes of nanosensors will be given. Sensor design, working principles and criteria important for sensor development will be discussed. Furthermore examples for practical applications for quantitative imaging will be introduced.

PATRICK LAUFS, Institut Jean-Pierre Bourgin, AgroParisTech, Versailles, France

Linking gene function to morphogenesis: the example of the leaf margin

Leaves can show diverse levels of dissections ranging from no (entire margin), mild (serration) to strong (lobes) incisions. The leaf itself can be either simple or dissected into units called leaflets. We have identified evolutionary-conserved genetic factors the CUC genes that are required for the dissection of the leaf margin. The CUC genes are part of a network involving negative regulation by a miRNA, miR164 and possible response of the signalling molecule auxin. However, the interplay between the three actors of this network (CUC, miR164 and auxin) is not understood yet. Nor are known the cellular effects of the expression of the CUC genes and their link with differential growth of the leaf margin leading to serration.

Here, we will present current work aiming at linking the function and regulation of the CUC genes with morphogenesis of the leaf margin. We will focus on the scientific questions we want to address, the strategies we are developing and the technical solutions we are using. Three different levels will be presented:

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- At the level of the whole organ, we develop a method to automatically extract the outline
 of leaves at different stages of development and to identify automatically remarkable
 points such as tips and sinus of the teeth of the leaf margin. Methods are being developed to extract relevant quantitative data.
- At the genetic and molecular level, we use fluorescent reporters of different colours to monitor the transcriptional or translational activity of our genes of interest and the activity of auxin. Methods to quantify the level of these reporters will be presented.
- At the cellular level, we are currently developing approaches to analyse the cellular parameters of young leaves.

STEFFEN LEMKE, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

What to do with large data microscopy recordings: introduction to automated image analysis

Recording development of an entire embryo over an extended period of time at high resolution and speed, e.g. by using light sheet microscopy, leads to the accumulation of large data volumes (i.e. 5-10 terabyte for embryonic development in *Drosophila*). Conceptually, these data sets contain voxel based information about position, division, and migratory tracks for each individual cell of an organism. In order to analyze this data set quantitatively and beyond visual inspection, this voxel based information has to be extracted into a digital atlas that contains position based information for each cell and its movement in 3D over the course of time. This introduction will cover the concept of automated image analysis to handle and evaluate large data sets, with a specific focus on image segmentation and optical flow fields.

ALEXIS MAIZEL, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Build your own light sheet microscope in 20 easy steps!

Selective Plane Illumination Microscopes (SPIM) are a type of light sheet microscope. They focus a very thin light sheet that traverses the specimen, whereas fluorescent light is collected at right angle using a camera. As the sample is only exposed in the cross section defined by the illumination sheet and the fluorescence emitted from this cross section is imaged at right angles there is no out of focus signal, sample bleaching is kept at a minimum, no pinhole is required, and the whole image is captured at once, allowing unsurpassed acquisition speed of time-lapse 3D microscopy at excellent signal-to-noise ratio. SPIM is now established as the superior technique to overcome a wide range of imaging challenges in intact organisms, ranging from developmental biology to opto-physiology and 3D super-resolution. Despite the enormous success of the SPIM technique, commercial implementations are rare and have high retail prices (>250K€). To get SPIMs in reach for broader range of biologists, the OpenSPIM project has been initiated by Pavel Tomancak (MPI Dresden): it provides the community with a light sheet microscopy solution that is maximally cost-effective, technically performing, and easy to build and maintain by non-specialists after initial minimal training. The optomechanical design was optimized for a minimal footprint, and the microscope is operated by free of charge open-source software (Micromanager, based on ImageJ/Fiji). All hardware components are »off the shelf« or are straight forward to make in on-site workshops.

During the course, the students will themselves: assemble, align, calibrate and use for imaging two OpenSPIMs.

JUAN RAMÓN MARTÍNEZ MORALES, Universidad Pablo de Olavide, Centro Andaluz de Biología del Desarrollo, Sevilla, Spain

Live imaging of entire vertebrate organs during morphogenesis.

From tissue behaviour to cell and molecular dynamics Microscopes and limitations

Understanding how tissues and organs acquire their final shape is a challenging task that requires recording and integrating information from many different scales. Thus, understanding the mechanisms underlying morphogenetic events entails not only to examine molecular dynamics but also cell and tissue behaviour *in vivo*.

Translucent teleost embryos (e.g. medaka and zebrafish) are optimal vertebrate models for live imaging studies at the tissue and organ scales. In this technical talk we will address current approaches for *in vivo* imaging in teleost using conventional point-scaning confocal microscopy. Practical limitations, such as photo-toxicity, photo-beaching, and mounting of the sample for long-term recording will be discussed using practical examples from our laboratory.

Finally, the application of less invasive and powerful new imaging technologies will be examined for the particular features of the teleost models.

LORENA NORAMBUENA, Universidad de Chile, Departamento de Biología, Santiago de Chile, Chile

Chemical genomics: unraveling plants endomembrane system trafficking and developmental mechanisms

The plant endomembrane system is essential for plant viability. The endomembrane system has important roles beyond the proper delivery of cargoes, and is essential for several aspects of signal transduction and plant development. An exciting and informative area of research will be to uncover and understand how such pathways interact with each other to create functional networks. However the use of classical genetic approaches is limited due to lethality of mutants on components of these pathways and also to genetic redundancy of plants. The use of chemicals to modify or disrupt the function of specific proteins instead of classical genetics that disrupt gene function is an approach that overcomes these limitations. Useful bioactive pharmacological probes could be fruitful to identify and dissect biological processes and uncharacterized networks. The power of small bioactive molecules has been amply illustrated in plant biology however the number of compounds is extremely limited. So far chemical genomics in *A. thaliana* has yielded several new plant cell biomodulators. Cell biology, genetics and molecular biology approaches along with bioactive compounds become more powerful to unravel novel mechanisms and molecular components of endomembrane system and their role on plant development and physiology.

BENJAMIN PRUD'HOMME, Institut de Biologie du Développement de Marseille-Luminy, Marseille, France

The genetic regulatory mechanisms of morphological pattern formation

The typical pattern of morphological evolution associated with the radiation of a group of related species is the emergence of a novel trait and its subsequent diversification. From butterfly eyespots and their various colorful rings to the diversity of shapes assumed by vertebrate teeth, seashells or horn beetles, this pattern of emergence-diversification holds for countless characters across most animal groups. Yet the genetic mechanisms associated with these two evolutionary steps are poorly characterized.

We're studying the evolution of wing pigmentation patterns in flies to address from a gene regulatory perspective how morphological novelties (rarely) emerge and how they (often) diversify. We're also studying the function of wing pigmentation patterns in mating behavior in order to identify the possible selective mechanisms underlying the evolution of this morphological trait.

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ANDRÉS SARRAZIN, Pontificia Universidad Católica de Valparaíso, Institute of Chemistry, Valparaíso, Chile

Dissecting the segmentation process: A whole embryo culture approach to understand the relationship between the molecular mechanisms and cell dynamics during body segmentation in the beetle *Tribolium castaneum*

Most arthropods generate the posterior part of their bodies by adding segments sequentially from a posteriorly located region of the embryo called the "growth zone". This strategy is shared with vertebrates and it has been considered the ancestral way of segmentation. Remarkable conserved similarities have been found in the molecular mechanisms involved in the generation of a segmented body plan by these two phyla. As recently was demonstrated, arthropod and vertebrate segmentation relies on oscillatory mechanisms, where the temporal periodicity of a clock is translated into repetitive spatial pattern. Waves of gene expression pass through the growth zone determining the size and number of segments. In spite of the increasing information with respect to the molecular mechanisms involved, the behavior of cells in this zone remains poorly studied. New embryonic and imaging techniques developed in the beetle *Tribolium* (transgenic GFP animals, cell tracking, whole embryo culture, etc.), are contributing substantially to understand the contribution of cell dynamics during axis elongation and segmentation in arthropods.

KARIN SCHUMACHER, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Why study plants?

Plants are our main source of oxygen, food, fuel and fiber. Studying plants can thus not only contribute to improve and secure the food supply for an increasing world population but also to solve the challenges that mankind faces concerning energy and pollution. On top of these important issues, plants are fascinating creatures that compensate for their lack of mobility by an enormous plasticity. In my presentation, I will focus on the advantages and disadvantages of the weed *Arabidopsis* as a model system for plant cell and developmental biology.

ANNE SPANG, Universität Basel, Biozentrum, Basel, Switzerland

Using C. elegans to understand intracellular pathways

The roundworm *Caenorhabditis elegans* serves as an extremely useful tool in cell biology and genetics; most famous examples being the studies on aging and caloric restriction, as well as the discovery of RNAi. The worm is also very vital to provide understanding intracellular trafficking events *in vivo*. For example we demonstrated that transport from the early to the late endosome occurs through a maturation process. This discovery was possible because coelomocytes, which are scavenger cells, contain large endosomes that are easily followed by light microscopy, unlike the tiny endosomes in tissue culture cells. In this lecture I will provide a background on *C. elegans* development and discuss methods used in *C. elegans* cell biology and genetics.

KATE WHITLOCK, Universidad de Valparaíso, Centro Interdisciplinario de Neurociencia de Valparaíso (CINV) Valparaíso, Chile

Problems with Populations

When trying to understand mechanisms as diverse as cell movements, fish behavior and neural progenitor differentiation we are constantly confronted with the complex problem of »groups«. Cells migrate as groups, schooling fishes move as groups and progenitors change fate dependent upon the cells around them. This will be a democratically based talk where the students can vote on the topic they would like to discuss: analyzing migration of cell populations analyzing behavior of zebrafish in groups, analyzing neural stem cell populations in the adult zebrafish.

Migration of cell populations: We have developed a novel program for analyzing the movements of populations of craniofacial neural crest cells in control and ethanol exposed embryos. This analysis allows us to draw conclusions about the movements of cells in living embryos and resulting facial asymmetries (Boric et al., 2013).

Behavior of fish populations: We have provided data to develop a program to track population of adult fish in a Y-maze in order to understand olfactory-driven behaviors in zebrafish which is a schooling fish (Whitlock, unpublished).

Neural stem cell populations in the adult zebrafish: We developed a protocol to obtain and differentiate NSC (neurospheres) from the adult hypothalamus. Using markers for NSC, glial and neuronal proteins, we demonstrated that the hypothalamic-derived NS are capable of differentiating into neurons, glia and specific neuroendocrine cells.

JOCHEN WITTBRODT, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Light sheet microscopy, a »historic« perspective

A long-standing goal of biology is to map the behavior of all cells during organismal development and to correlate it with gene expression and function. So just by watching, this will address how an embryo's genes, proteins, and cells function and interact to govern morphogenesis, cell fate specification, and patterning.

These processes span very different spatial and temporal scales. Despite much progress in the field, simultaneous observation of such vastly differing scales has been beyond the scope of conventional microscopy.

We established selective plane illumination microscopy (SPIM) to generate multidimensional images of samples up to a few millimeters in size. To facilitate long term imaging with high penetration depth we developed digital scanned laser light sheet fluorescence microscopy and recorded nuclei localization and movement in entire wild-type and mutant zebrafish embryos over the first 36 hours of development. Multiview *in vivo* imaging at 1.5 billion voxels per minute provides »digital embryos, « that is, comprehensive databases of cell positions, divisions, and migratory tracks.

So light sheet microscopy fills this scale gap and is increasingly used for long-term, high-speed recordings of large specimens with high contrast and up to sub-cellular spatial resolution. I will provide an overview of applications of light sheet microscopy in developmental biology and discuss future perspectives in this field.

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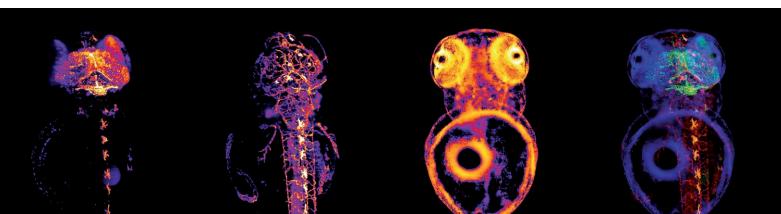
ABSTRACTS OF SYMPOSIUM SPEAKERS

MIGUEL ALLENDE, Universidad de Chile, FONDAP Center for Genome Regulation, Santiago de Chile, Chile

Resilience of the zebrafish mechanosensory system: robust regenerative potential in all ist cellular components

The mechanosensory lateral line system of zebrafish forms beginning on the second day of life and becomes functional by day three. It consists of sensory units called neuromasts, distributed over the body surface, and afferent neurons that innervate the sensory hair cells in each neuromast. The neurons have their somata in the lateral line ganglia and project their axons bundled in a lateral line nerve. We have studied the regeneration capacity of hair cells, of the entire neuromasts and of the lateral line nerve axons in three day old larvae. We damage or ablate cells with various techniques, including chemical damage, laser axotomy and electroablation. Our results show that all of these components are able to robustly regenerate. Hair cells arise from progenitors residing in a deep compartment of neuromasts. When the entire neuromast is damaged, quiescent progenitor cells from neighboring interneuromastic areas invade the vacant territory and generate neuromasts de novo. Severed axons in the lateral line nerve can also quickly regrow and innervate target hair cells, in a process that depends on an intact Schwan cell population along the pathway of regrowth. Associated with all three of these regenerative events, are strong inflammatory responses involving neutrophils and macrophages, and we have measured the contribution of inflammation to regeneration in each case. Our aim is to now identify the origin of the signals and the molecules that are responsible for inducing the regenera-

Funding: FONDAP 15090007; FONDECYT 1110275.



CLAUDIO ARAYA, Universidad Austral de Chile, Instituto de Ciencias Marinas y Limnológicas, Valdivia, Chile

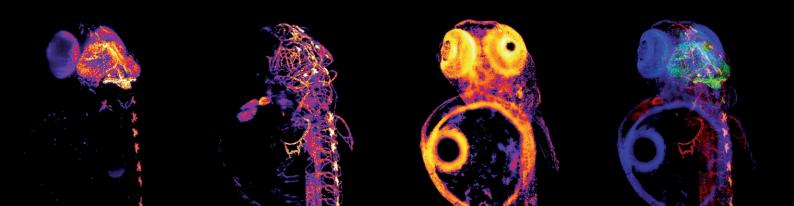
Regulation of cell and tissue invagination during zebrafish neurulation

Morphogenesis of the embryonic body plan involves the co-ordinated activities of large groups of cells within a three dimensional tissue. This often requires cells to be assigned and to maintain particular positions within the tissue. A good example of this is the highly orchestrated movements of the cells in the multi-layered zebrafish neural plate as they converge towards the dorsal midline before invaginating to form a neural keel. However, how cell and tissue dynamics are regulated to ensure invagination is unknown. By combining genetics and quantitative imaging techniques we are currently investigating the cell and molecular mechanisms underlying radial position within the zebrafish neuroectoderm. Live imaging demonstrates that the neural plate cells are tightly packed together and move as a coherent and organised sheet of cells during early convergence and this in turns depends on adjacent tissues like the mesoderm and the basal lamina. Absence of either mesoderm or basal lamina leads to severe apico-basal polarity organisation and aberrant tissue architecture. On the other hand, we find evidence that the cell-cell adhesion molecule, N-cadherin is required to complete invagination by regulating radial intercalation across the superficial-deep axis of the developing neural plate.

YOHANNS BELLAICHE, Institut Curie, Génétique et biologie du développement, Paris, France

Epithelial cell dynamics and cell division

Shape is a conspicuous and fundamental property of living multicellular organisms. Recent advances in imaging, cell biology, and active material physics phrase these questions in terms of cell dynamics and interplay between biochemical and mechanical processes associated with adherent junction remodeling. In proliferative tissue, morphogenesis is often concomitant to cell division. I will present recent results from our group showing that in epithelia tissue cell division should be view as a multicellular process, whereby the biochemical and mechanical interactions between the dividing cell and its neighbors are essential for successful daughter cell separation and junction remodeling while specifying epithelial tissue organization and preserving tissue integrity.



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SIOBHAN BRADY, University of California, Department of Plant Biology and Genome Center, Davis, USA

Mapping Spatiotemporal Gene Regulatory Networks Guiding Root Vascular Development Mallorie Taylor-Teeples, Miguel de Lucas, Allison Gaudinier, Ted Toal, Sebastian Ahnert, Francois Roudier, Siobhan M. Brady

Arabidopsis root development provides a remarkably tractable system to delineate cell type-specific, developmental gene regulatory networks and to study their functionality in a complex multicellular model system over developmental time. We present gene regulatory networks guiding two aspects of vascular cell type development, specifically xylem cell specification and differentiation and vascular proliferation. Two components of transcriptional regulation are elucidated – transcription factor-mediated regulation and Polycomb Repressive Complex 2 (PRC2)-mediated regulation. Together, these networks identify novel regulators of vascular development and provide considerable insight into the combinatorial nature of root development at cell type and temporal stage-resolution.

MICHAEL BRAND, Technische Universität Dresden, Biotechnology Center, Dresden, Germany

Regeneration of the adult zebrafish brain: an essential, positive role for inflammation Michael Brand, Nikos Kyritsis, Caghan Kizil, Sarah Zocher, Volker Kroehne, Jan Kaslin, Dorian Freudenreich, Anne Iltzsche

Severe traumatic injury to the adult mammalian central nervous system (CNS) leads to lifelong loss-of-function, and neuronal regeneration does not occur. In contrast, we find that adult zebrafish have a remarkable ability to regenerate adult brain, similar to other reports for retina and spinal cord. Neurogenesis in adult rodents is limited to only two subregions of the telencephalon, but in adult zebrafish occurs along the entire length of the neuraxis, suggesting a mechanistic link to its regeneration ability. The cellular and molecular mechanisms that enable or prevent adult CNS regeneration are largely unknown. To study these mechanisms in adult zebrafish, we developed brain lesion assays, and analyzed cellular reactions to injury. We find that adult zebrafish can efficiently regenerate brain lesions and lack permanent glial scarring. Using conditional Cre-loxP-based genetic lineage tracing, we demonstrate that a subtype of ventricular radial glial progenitor cells reacts to injury, proliferates and generates neuroblasts that migrate to the lesion site. The newly generated neurons survive for at least 3 months, are decorated with synaptic contacts and express mature neuronal markers. Thus, after traumatic lesion of the adult zebrafish brain, regeneration occurs efficiently from radial glia-type stem/progenitor cells. We used FACS sorting to isolate these progenitors from lesioned adult brains, and examined their transcriptome. This identified novel candidate genes that may function to control brain regeneration. One such candidate gene is the receptor for leukotriene lipid signaling which is expressed in adult regeneration-responsive radial glia type progenitors. Activated microglia and other immune cells accumulate around a lesion site, and generalized suppression of immune response suppresses the regeneration response. Using functional knock-down in adult brain and ventricular injection, we show that inflammation and leukotriene signaling are necessary and sufficient to elicit radial glia progenitor proliferation and neuron production, upstream of gata3 as a nuclear mediator. We currently explore the potential of these genes to stimulate regeneration also in the mammalian nervous system. Supported by the EU (Zf Health) and the DFG (SFB 655-A3).

LÁZARO CENTANIN, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Life-Long Lineage Analysis of Post-Embryonic Retinal Stem Cells in Fish

Adult stem cells have the capacity to self-renew and generate differentiated cells in a variety of mammalian tissues and organs like intestine, skin, blood or brain. Stemness is an attribute of an individual cell and, the potency of post-embryonic stem cells can only be addressed in the living organism, by labeling single cells after embryonic development and following their descendants. We have recently reported in medaka that individual retinal stem cells (RSCs) of embryonic origin located in the ciliary marginal zone (CMZ) form non-exhausting clones termed ArCoS (after arched-continuous stripe). Here we apply colorful recombination tools to address the identity, localization and potency of neural stem cells (NSC) in the retina during juvenile and adult stages by stochastic clonal labeling followed by non-invasive fate tracking. We functionally differentiate long-lasting NSCs from transient neural progenitor cells (NPCs) and show that they are located in distinct concentric domains in the CMZ. We identify retinal homeobox gene-2 (Rx2) as RSC marker and use it to stochastically label single post-embryonic RSCs. Those, intriguingly, generate ArCoS covering the entire column of neuro-retinal cell types indicating a mandatory multipotency for NSCs in the fish retina. Additionally, and in contrast to any other vertebrate stem cell system described so far, long-term analysis of clones indicates a preferential mode of asymmetric cell division. Our findings highlight the unique trade-off of studying stem cells in their natural environment at single-cell resolution to depict their genuine potential.

JACQUES DUMAIS, Universidad Adolfo Ibáñez, Facultad de Ingeniería y Ciencias, Viña del Mar, Chile

Measuring Cell Expansion in Growing Plant Organs

In plants, morphogenesis reflects the cumulative activity of cell expansion and cell division with a tissue or organ. A striking aspect of morphogenesis within plant apices is the maintenance of distinct structural and morphological features despite a continuous flux of material across the organ. In this lecture, I will discuss how time lapse imaging of marked cells can be used to map the complex relationship between cell expansion and morphogenesis. The first example will focus on the simplest apices: isolated tip-growing cells such as root hairs and pollen tubes. In these cells, a precise relation exists between the pattern of cell surface expansion and cell shape. Using this relationship, I will show how one can probe the mechanistic basis of cell expansion. The second example will be the shoot apical meristem (SAM). The reduced symmetry of meristems presents new challenges for a quantitative analysis of morphogenesis. These challenges have been met with various imaging protocols which I will describe and compare. Finally, I will describe the subtle interactions that exist between kinematics and the molecular control of development; highlighting why detailed kinematic analyses ought to be part of most morphogenetic studies.

JAN-FELIX EVERS, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

A B

Variability and mechanisms of plasticity during development of locomotor circuits in *Drosophila*

The Drosophila nervous system is well known for its stereotypic development of its constituent neurons. Much less is known about how these elements connect to form functional circuits. Recent results have shown that activity dependent mechanisms homeostatically adjust neuronal growth in the embryonic CNS and regulate the emergence of coordinated behaviour. Our aim is to study how actual patterns of synaptic connections are generated as networks develop. To be able to do this at the level of single identified neurons, we generated tools to independently label identified cholinergic inter- and sensory neurons (split-GAL4) and motorneurons (LexA). Bimolecular fluorescence complementation (GRASP) allows us to identify molecular contact between these neurons; co-localisation with presynaptic release sites (bruchpilot-mRFP) to pinpoint synaptic contacts. Using these tools we find that: 1. Variable numbers of synaptic sites form between individual pairs of inter- and motorneurons; 2. Synapse numbers between connecting neurons increase with developmental age; 3. Connections between sensory and motor neurons are highly variable at larval hatching, but this variability decreases during larval development. Our data suggest that synaptogenesis in the embryonic and larval nervous system may be rather opportunistic, and that the levels of synaptic activity received is specified primarily at the level of the postsynaptic neuron. We speculate that the amount of overlap of projection areas is an important regulator of the number of synaptic contacts formed.

JIŘÍ FRIML, Institute of Science and Technology Austria (IST Austria), Klosterneuburg, Austria

Polarity and Patterning in Plant Development

In plants, more than in other eukaryotes, establishment of cell polarity is one of the major developmental themes. The process of tissue polarization inevitably encompasses de novo specification of individual cell polarities in cells within a polarizing tissue. The connection between cellular polarizing events and macroscopic manifestation of polarity such as specification of different cell types along the axis, depend on an action of the signalling molecule auxin. Auxin is a prominent intercellular signal in plants and acts as a versatile trigger of developmental change in multitude of processes. Directional, active transport between cells mediates differential auxin distributions within tissues (so called auxin gradients) that are underlying many patterning processes, including apical-basal axis formation during embryogenesis, organogenesis, vascular tissue formation and tropisms. Environmental and endogenous signals can be integrated into changes in auxin distribution through their effects on auxin transport, specifically on the cellular distribution of PIN auxin transporters. Differentially expressed PIN proteins, each with specific polar, subcellular localization form a network mediating directional auxin fluxes through different tissues for formation of auxin activity gradients. Within cell, PIN proteins undergo constitutively cycles of a clathrin-dependent endocytosis and ARF GEF-dependent recycling. Various endogenous and external signals can regulate this subcellular dynamics, thus changing polarity of PIN localization and controlling their directional activity. In this view, the PIN-dependent auxin transport network, whose directional throughput is modulated by both endogenous and exogenous signals, provides one of the mechanisms underlying the plasticity and adaptability of plant development.

ALVARO GLÁVIC, Universidad de Chile, Departamento de Biología, Facultad de Ciencias, Santiago de Chile, Chile

The *Drosophila* EKC/KEOPS complex: its role in protein homeostasis and animal growth Alvaro Glávic, Diego Rojas-Benitez and Consuelo Ibar

The size of organisms is the resultant of coordinated proliferation, cell death and cell growth. Together they establish the final number of cells and their sizes, thereby defining tissue dimensions. Nutrients and hormonal signals influence cell and tissue growth. Both signals are transduced by integrative machinery to assemble a systemic response, which improves the translational capacity to sustain cell and animal growth. TOR pathway is crucial in the translation of nutritional inputs into protein synthesis machinery regulation. We recently identified Prpk (p53-related protein kinase) in Drosophila as a regulator of TOR kinase activity. PRPK is an ancient protein conserved from Archeae to humans. Together with Kae1p (ATPase), Cgi-121 and Pcc2p it forms in yeast the KEOPS (Kinase, putative Endopeptidase and Other Proteins of Small size) complex, implicated in telomere maintenance, transcriptional regulation, bud site selection and chemical modification of transfer RNAs (tRNAs). The synthesis of N6-threonylcarbamoyladenosine (t6A), a chemical modification that occurs at position 37 of tRNAs that pair A-starting codons, is dependent on Kae1 and PRPK and required for proper translation in most species. Here, we present our findings regarding the role of this complex in animal growth in *Drosophila*. We suggest that KEOPS complex could be integrating t6A-modified tRNA availability with translational rates, which are ultimately reflected in animal growth.

PATRICK LAUFS, Institut Jean-Pierre Bourgin, AgroParisTech, Versailles, France

Leaves show a tremendous diversity in their sizes and shapes. Though, they all originate as small, finger-shaped primordia at the flanks of stem cells-containing groups of undifferentiated cells, the meristem. Leaf shape is established later during development, mainly as a result of differential growth of their margins. The formation of complexe shapes, such as those found in compound leaves that are formed by several leaflets, requires a coordinated delay of cell differentiation and the initiation of new growth axes in the young leaf primordium. Here, we will present recent advances in the understanding of the regulatory networks controlling leaf development and how variations in these networks may have contributed to changes in leaf shape. We will exemplify this by looking at the roles of the CUP-SHAPED COTYLEDON genes during the development of simple and compound leaves.

SANTANDER Summer School 2013 Programme Book Abstracts of Symposium Speakers

STEFFEN LEMKE, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Evolution of fly gastrulation

Morphological differences between two species are shaped by diverging developmental trajectories. To assess molecular principles contributing to the evolution of form, we are using gastrulation in flies as a genetically tractable model of (transient) morphogenesis. Flies are long-germband insects and most aspects of their early embryonic development are comparable and thought to be highly conserved. Recent studies that analyzed early embryonic patterning and selected aspects of gastrulation in different fly species, however, have revealed a significant degree of divergence on the level of developmental genetic networks and morphogenesis. To systematically explore the evolution of gastrulation in flies, we have generated transgenic tools that allow us to compare early embryonic development in toto between *Drosophila melanogaster* and selected satellite fly species. I will present results of this initial comparison, which will be complemented by functional data that aims to link genetic and morphological evolution.

ALEXIS MAIZEL, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Quantitative analysis of *Arabidopsis thaliana* lateral root morphogenesis at cellular resolution using light sheet based fluorescence microscopy

In plants, the root system is responsible for the uptake of all nutrients and water the plants needs to sustain viability and growth. In Arabidopsis thaliana, it consists of an embryo-derived primary root, from which a variable number of lateral roots branches. The lateral root primordia (LRP) originate from pericycle cells located deep within the parental root and have to emerge through several cell layers of the main root. We use light sheet based fluorescence microscopy to capture with subcellular resolution the entirety of lateral root morphogenesis from initiation to emergence. Quantitative analysis and generation of virtual lateral roots from these dataset allow to study with unprecedented details how patterns of cell division, organ growth and overlaying tissues integrate during LRP morphogenesis. In particular, we observed that early stage LRP exhibit tangential divisions that create a ring of cells corralling a population of rapidly dividing cells at its centre and the patterns of division in the latter population of cells during LRP morphogenesis are not stereotypical. We tested the relative importance of cell division pattern versus overlaying tissues on LRP morphogenesis using mutant and transgenic approaches. In a mutant with disrupted pattern of cell divisions the evolution of LRP shape is not affected. In contrast, manipulating the properties of overlaying tissues disrupted LRP morphogenesis.

JUAN RAMÓN MARTÍNEZ MORALES, Universidad Pablo de Olavide, Centro Andaluz de Biología del Desarrollo, Sevilla, Spain

Optic cup morphogenesis: a model to study the cellular and molecular bases of basal constriction

Abstract: Shaping the vertebrate eye into an hemispherical organ requires the inward folding of the polarized retinal neuroepithelium. Optic cup morphogenesis is however an atypical model for epithelial morphogenesis for, in contrast to well-known apical constrictions described mainly in *Drosophila* epithelia, it involves the constriction of the tissue towards its basal surface. Understanding which cellular and molecular aspects of basal constriction are specific and which are shared with apical constrictions, is one of our long-term objectives. In particular we focus on developmental regulators that, operating directly on basic cell properties, such as cell adhesion, cell shape or cell contractility, control eye morphogenesis. One of these developmental effectors, the transmembrane regulator of polarized integrin endocytosis Opo, plays an essential role in optic cup formation and hence it has been the topic of several studies in our group. Through a combination of transcriptomic, genetic, and cell biological approaches, we are currently identifying novel components of the molecular machinery involved in optic cup folding. In addition, we are exploring the biophysical aspects of the morphogenetic process using live imaging and mathematical modelling.

LORENA NORAMBUENA, Universidad de Chile, Departamento de Biología, Santiago de Chile, Chile

Protein trafficking: Role in Plant Development

Plants developmental plasticity plays a pivotal role to respond to environmental conditions. The root system is the most plastic plant structure. Root developmental plasticity integrates dynamically different stimulus such as nutrients and water abundance as well as soil aeration and salinity. The root system modifies its structure by inducing root growth and developing lateral roots in a process called root branching. The extension of this process depends of the environmental conditions and plant status. Root branching contributes to root spatial distribution and also to increase surface area improving water and nutrients absorption. It has been shown that the hormone auxin tunes lateral roots development and components for its signaling pathway have been identified. Our lab has revealed a distinctive role for cellular protein trafficking in the promotion of lateral root formation via a process that does not rely on the already described auxin-induced lateral roots molecular pathway. Using chemical biology, we have described an Arabidopsis thaliana lateral root formation mechanism which is independent of the key player for lateral root formation, the auxin receptor SCFTIR. Furthermore our evidences substantiate the independency of this mechanism of transcriptional activation downstream of SCFTIR. Protein endocytic trafficking of Late Endosome towards the vacuole is pivotal for SCFTIR-independent lateral root formation. The involvement of endosomal trafficking on lateral roots development has been completely unexplored in plants even though endosomes has been described as a site of intracellular signaling for several processes. Now we are in the process of unravel molecular components in this novel mechanism of plant development using genetics and molecular biology approaches including the advantages of chemical genomics. We expect to reach a further step on the comprehension of this novel molecular mechanism of lateral roots formation.

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PATRICIO OLGUÍN, Universidad de Chile, Programa de Genética Humana, ICBM, Facultad de Medicina, Santiago de Chile, Chile

Shaping the *Drosophila* dorsal thorax, the role of planar polarity and cellular adaptation to inter-tissue mechanical stress.

The shape and polarity of cells and tissues depends on the interplay between molecular patterning signals and the ability of cells to respond to intrinsic and extrinsic mechanical cues, for example, to the interaction with other tissues. The *Drosophila* dorsal thorax (notum) is formed early during metamorphosis by the fusion of the notum region of the wing imaginal discs at the midline. Planar polarity is established before the fusion and is morphologically evident at later stages by the formation of a single trichome at the posterior side of each epithelial cell. After fusion, a patterned group of epithelial cells, specified as tendons, make contact with the underlying flight muscles. After 24 hours of metamorphosis, indirect flight muscles shorten, pulling the tendon cells inside the thorax. In response, tendon cells extend cellular processes maintaining the attachment to the muscles and the shape of the notum. Using cellular, molecular genetics and imaging approaches we study the role of the actin cytoskeleton and planar polarity signaling pathways in the adaptation of the notum epithelium to the tension generated by the shortening of the flight muscles and their role in shaping the notum and notum cells.

ANDRÉS SARRAZIN, Pontificia Universidad Católica de Valparaíso, Institute of Chemistry, Valparaíso, Chile

Evolutionary origin of segment formation mechanisms in animals

Most arthropods generate the posterior part of their bodies by adding segments sequentially from a posteriorly located region of the embryo called the growth zone (GZ). This strategy is shared with vertebrates and it has been considered the ancestral way of segmentation. Vertebrate segmentation relies on oscillatory mechanisms, where the temporal periodicity of a clock is translated into repetitive spatial patterns. Waves of gene expression pass through the presomitic mesoderm (the equivalent of the GZ in vertebrates) determining the size and number of segments. Whether this mechanism is used by other segmented animals has been controversial and there is no rigorous demonstration of cyclic expression during arthropod segmentation. Using embryo culture, transgenic markers, live imaging and cell tracking in the beetle Tribolium castaneum and in situ hybridization in the ctenophore Pleurobrachia pileus, we showed that the segmentation gene odd-skipped oscillates with a period of about 95 minutes at 30° C. We demonstrated for the first time in arthropods that these oscillations are due to temporal changes in expression levels and not explained by cell movements in the GZ. As a comparative approach, we found the repetitive expression of Hes gene orthologs in a ctenophore (early divergent animal phylum), proposing the possibility of a common origin of the molecular mechanism underlying the formation of repetitive patterns instead of a segmented ancestor of all bilaterian animals.

KARIN SCHUMACHER, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Same, same but different – the plant endomembrane system and its roles in growth and morphogenesis

Productivity of higher plants as our major source of food and many renewable resources is linked to their ability to buffer changes in essential and toxic ion concentrations. The plant endomenbrane system is specifically tailored to meet the requirements of the sessile lifestyle and the continuous formation of organs that goes along with it. Although many of the key players involved in vesicle trafficking are conserved between plants, yeast and mammals they are not necessarily used in the same context. In my presentation I will focus on the organell-specific isoforms of the V-ATPase that highlight two hallmarks of the plant endomembrane system, the presence of a hybrid trans-Golgi network/early endosomal compartment (TGN/EE) that serves as the central hub for protein trafficking and the large lytic vacuoles that allow plants to produce large cells at low cost.. In particular, I will foucs on recent data based on genetic and pharmacological inhibition combined with high-resolution imaging wshowing that a subdomain of the ER serves as the membrane source during vacuole biogenesis will be presented.

ANNE SPANG, Universität Basel, Biozentrum, Basel, Switzerland

Function and regulation of small GTPases in C. elegans

Small GTPases of the ras and rab family are key regulators of intracellular transport events. While Arf/Sar subfamily GTPases are essential in the generation of transport containers throughout the secretory pathway, rab family GTPases are involved in fusion of transport containers and they mark domains on different intracellular compartments. Both types of GTPases play also pivotal role in organellar homeostasis.

In the first part of my talk I will discuss novel roles of Arf/Sar GTPases in the function of mitochondria. These findings were unexpected because mitochondria are not part of the secretory pathway. However it has been appreciated over the last couple of years that the endoplasmic reticulum and mitochondria form interaction sites through which probably molecules can be exchanged.

The second part of my talk will deal with the regulation of rab GTPases in the endosomal system in different *C. elegans* tissues and elucidate the role of tethering factors in transport from the cell surface to lysosomes.

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Abstracts of Symposium Speakers Abstracts of Doctoral Students

KATE WHITLOCK, Universidad de Valparaíso, Centro Interdisciplinario de Neurociencia de Valparaíso (CINV), Valparaíso, Chile

Dissecting Development in Time and Space

Vertebrate sensory organs originate from both cranial neural crest cells (CNCCs) and placodes. Previously we have shown that the olfactory placode (OP) forms from a field of cells that migrates rostrally. Concurrently CNCCs also migrate rostrally to populate the frontal mass. Little is known about the interactions between CNCCs and the placodes that form the olfactory sensory system. In order to understand the initial development of the olfactory organs when the neuronal precursors are being delineated we analyzed the interaction of the cells that form structural elements of the nose as well the olfactory epithelia. In order to do so we made a fluorescent reporter line that express red fluorescence in the precursors of the olfactory placode. Using animals epressing a six4b:mCherry (OP precursors) and sox10:egfp (CNCCs) to follow cell migration we showed that CNCCs associate with and eventually surround the forming OP. In spite of the close association between the CNCCs and OP fields, little cell mixing occurs during this process. Furthermore the OP cells expressing six4b:mCherry move caudally away from the adenohypophyseal anlagen during early somitogenesis.

Originally the olfactory sensory system was proposed to be a source of the neuroendocrine Gonadotropin Releasing-Hormone (GnRH) cells essential for puberty. We have used genetic, molecular and imaging techniques to show that the endocrine GnRH cells arise from regions outside the olfactory sensory system, and that the adult hypothalamus has the ability to generate new GnRH cells thus opening the door to therapeutic treatment of human disease.

JOCHEN WITTBRODT, Universität Heidelberg, Centre for Organismal Studies, Heidelberg, Germany

Transcriptional control of stem cell features in the post-embryonic fish retina Robert Reinhardt, Daigo Inoue, Lazaro Centanin and Jochen Wittbrodt

Postembryonic neurogenesis relies on the activity of neural stem cells (NSCs) defined by their multipotency and unique ability to self-renew. Despite their importance for the homeostasis of the central nervous system, the transcriptional network governing stemness in adult NSCs is largely unknown. We establish the transcription factor (TF) Rx2 as proxy for retinal stem cells (RSCs) in the post-embryonic retina of the teleost medaka (O. latipes). By interrogating the regulatory input of the Rx2 promoter we identify four TFs, which distinctly modulate stem cell features. Conditional mosaic analysis *in vivo* characterizes Sox2 and Tlx as activators of Rx2, sufficient to trigger de-differentiation of post-mitotic neurons and to induce stem cell features therein. Conversely, sustained repression of Rx2 in RSCs by ectopic Gli3 or Her9, arrests cell cycle progression and stem cell proliferation. Their combinatorial input confines Rx2 expression specifically to the stem cell domain of

The experimental approach and the biological implications will be discussed in detail.

the post-embryonic neural retina.

ABSTRACTS OF DOCTORAL STUDENTS

ANTONIANA BATSIVARI, University of Edinburgh

The role of proliferation in haematopoietic stem cell development

This project is aiming to address whether cell cycle status can be used to identify and discriminate developing HSCs from more committed progenitors in the embryo *in vivo*. The Fucci reporter mouse is used to visualize *in vivo* the cell cycle status. Immunohistochemical techniques reveal the localization and cell cycle status of the haematopoietic clusters, while functional assays are used tho characterize the different haematopoietic populations.

VINCENZO DI DONATO, Institut Curie

Role of Reelin in zebrafish optic tectum development and retinotectal circuit formation

Neuronal connections in the retina as well in retino-recipient nuclei are arranged in layers. Axon guidance cues play a crucial role in the formation of synaptic layers. During the past few years Reelin, an extracellular matrix protein, has been intensively studied in neuronal migration. Our interest is to investigate the involvement of this protein in the process of lamination, axon guidance, and dendritic growth during vertebrate CNS early development, using as a model the zebrafish larval optic tectum.

MARÍA FLORENCIA ERCOLI, National University of Rosario

Function of miR396 and GROWTH REGULATING FACTOR transcription factors in Arabidopsis thaliana leaf and root development

MiRNAs are important regulators of gene expression that affect various aspects of plant biology. In particular, our work is focused on the characterization of the role of miR396 and their targets, the GROWTH REGULATING FACTOR transcription factors in *Arabidopsis* leaf and root development. We found that miR396 restricts the expression of GRFs to the meristem, where these transcription factors promote cell proliferation.

MANUEL ANGEL GÁLVEZ SANTISTEBAN, Universidad Autónoma de Madrid

Identification and characterization of novel regulators of epithelial lumen morphogenesis

Formation of epithelial tissues requires the generation of apico-basal polarity and the coordination of this polarity between adjacent cells to form a central lumen. Vectorial membrane transport is critical in this process. A transcriptional and functional screen has revealed key roles for Synaptotagmin-like proteins 2/4 in the lumenogenesis process in 3D cultures. Moreover, these genes are also necessary to generate the zebrafish pronephros architecture.

ANTONIA GIBALOVÁ, Charles University in Prague

Role of bZIP transcription factors during male gametophyte development in Arabidopsis thaliana

Molecular mechanisms underlying many developmental processes, including the production of both male and female gametes, remain largely unknown. To uncover such mechanisms, our approach is to identify and characterize transcription factors (TFs) taking part in the haploid regulatory networks that governs gamete production in flowering plants.

INGRID LEKK, University College London

Development of diencephalic asymmetries in zebrafish and chicken embryos

Lateralisation of brain structure and function is an evolutionary conserved mechanism to establish a more diverse pattern of neuronal circuits underlying lateralized behavior and cognitive functions. Using zebrafish and chicken as model organisms, we study how asymmetries develop in the dorsal diencephalon during embryogenesis and to what extent these asymmetries and the underlying molecular mechanisms are conserved between species.

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HOLLY LOVEGROVE, University of Cambridge

Investigating integrin function in the organization of the Drosophila follicular epithelium

In order to carry out specialized functions, epithelial cells are organized into layers of polarized cells. One model for investigating epithelial tissue are the *Drosophila* follicle cells, a simple, single-layered epithelium that surrounds the developing female germline. Loss of integrin function in follicle cells results in a dramatic disorganization of the tissue, but the etiology of this phenotype remains unclear. This project aims to elucidate the way in which integrin signaling is required to establish and/or maintain tissue integrity.

KATHARINA LUST, Universität Heidelberg

Wound response and regeneration in the retina of medaka fish

Teleost fish posess the ability to regenerate their retina after injury and recover visual function. It is known that Müller glia cells can dedifferentiate into multipotent progenitors upon injury which can give rise to all neuronal subtypes. So far, most studies on retinal regeneration in fish were done in adult animals where live imaging is challenging. We are using juvenile medaka fish to perform live imaging and ablation of cells with a 2-photon laser to investigate the wound response of the retina.

CATALINA PAZ MANIEU SEGUEL, Universidad de Chile

Chas-Jbug/Filamin system and Myo-II cooperates to maintain the isometric tension of epithelial cells under mechanical stress during morphogenesis of *Drosophila melanogaster*

During morphogenesis, notum cells adapt to the mechanical stress generated by the indirect flight muscles in order to maintain the polarity and shape of the notum. This process requires Myosin-II and jitterbug/Filamin, along with chascon. The aim of our study is how Chas-Jbug/Filamin system and Myo-II work at different levels contributing to the architecture of the cotyskeleton in order to maintain the mechanical homeostasis of tendon cells, elucidating the molecular and cellular mechanism of cell adaptation to mechanical stress during development.

ALEXIS MORALES, Universidad Austral de Chile

Zebrafish neuroepithelial morphogenesis

The initial stages of zebrafish neural formation are characterized by the coordinated action of large group of cells towards the dorsal midline before undergo invagination. This project aims to dissect the role of the cell-cell adhesion during the cell and tissue invagination *in vivo* during zebrafish neuroepithelial morphogenesis.

JORGE OJEDA, University of Concepción

Fz9 receptor promotes the maturation of postsynaptic apparatus at the vertebrate NMJ through Wnt/B-catenin pathway

An archetypal model to study synaptic formation, maturation and maintenance is the vertebrate NMJ, a peripheral cholinergic synapse formed by motoneurons, muscle fibers and glial Schwann cells. Growing evidence reveals that pathways activated by Wnt ligands regulate key aspects of synaptogenesis during NMJ development of invertebrate and vertebrate models. Based on our recent findings revealing that the Wnt receptor Fzd9 promotes the maturation of the NMJ, we currently analyze the possible molecular mechanisms involved.

KARINA PALMA, Universidad de Chile

Circadian Modulation of the Parapineal-Habenula-Interpeduncular Nucleus (Opp-H-INP) in zebrafish larvae (Dan;o reno)

The Opp-Hab-IPN circuit in zebrafish has been linked to various physiological functions, including circadian rhythm. The genetic/molecular mechanisms of the clock are well known, but there is little evidence of how this affects complex neural structures. Here we propose the use of transgenesis, microscopy and image analysis *in vivo* to study the presence of a circadian rhythmicity in the Opp-Hab-IPN circuit in larval zebrafish.

DIANA PINHEIRO, University of Porto and University Paris VI

Cell division in the Drosophila epithelial tissue: How to divide with neighbors?

Epithelial tissues act as barriers between body compartments. Thus, epithelial cells are tighly adhered and mechanically coupled to their neighbors, through a series of specialized junctions, namely the adherens junctions. Interestingly, upon cell division, a new junction is formed between the daughter cells. During my PhD project, we aim to understand how neighboring cells sense and respond to cell division and how the new interface formed between the daughters expands and re-polarizes.

MARÍA MICAELA SARTORETTI, Universidad de Buenos Aires

Astrocytic differentiation in the developing neural tube

Mechanisms underlying astrocyte diversity in the central nervous system are not well understood. Using mouse genetics, we traced a restricted group of progenitors of the embryonic spinal cord which gives rise to a defined set of astrocytes. Their precursors follow a precise radial pathway of migration, probably through nuclear translocation, while proliferating in the lateral spinal cord, distal from their origin in the ventricular zone. We found that the transcription factor Dbx1 and Notch signaling are involved to control the region-specific allocation of astrocytic precursors.

JORGE TORRES PAZ, Unversidad de Valparaíso, Chile

Dissecting the roles of six4b and dlx3b during the olfactory epithelium development in zebrafish

The diverse types of cells found in the olfactory epithelium (OE) arise from a pair of embryological structures called olfactory placodes. Different homeotic genes participate in the genetic network controlling morphogenesis and differentiation of the olfactory sensory tissue. We are using zebrafish as a model to study the roles of six4b and dlx3b; two of these homeotic controllers involved in the OE development.

SILVIA URBANSKY, Universität Heidelberg

Evolution of mesoderm morphogenesis in flies

Morphogenesis of mesoderm during gastrulation constitutes one of the earliest events in the development of multi-cellular organisms. It is generally comparable among flies and provides sufficient morphological diversity. We study these gastrulation movements in the nematoceran midge *Chironomus riparius* and functionally test for puptative genetic changes leading to a novel morphology.

AMAYA VILCHES BARRO, Universität Heidelberg

Microtubules-dependent mechanical control of lateral root morphogenesis in Arabidopsis

In *A. thaliana*, lateral root primordia (LRP) originate deep within the primary root and grow across different cell layers until they emerge. Genetic and pharmacological disturbance of microtubule dynamics during LRP formation presumptively alters LRP shape, cell organization and emergence. Further analysis will include light-sheet based microscopy in combination with tissue specific gene silencing and overexpression.

SANTANDER Summer School 2013 Programme Book Suggested Reading List

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