

1st Joint Meeting of the British & Spanish Developmental Biology Societies

Seville, Spain, 24-27 September 2008

The first joint meeting of the Spanish Society for Developmental Biology (*Sociedad Española de Biología del Desarrollo*, SEBD) and the British Society for Developmental Biology (BSDB) was held last September 2008 in the city of Seville (Spain). This was to follow on the footsteps of the previous, hugely successful "Biology on the Beach" meeting in Nice, joint between the French and British Societies for Developmental Biology, and the equally popular SEBD international meeting in Barcelona some years back. The standards to meet were high, and organising this event was nerve-racking a lot of the time, a pleasure some times too. Finally, when the time came, we all convened in the large, splendid, majestic, *Al Andalus* Hotel. There were over 300 delegates from around the world. It was international, the speakers and their talks were superb, and the environment was both vibrant and relaxed. The meeting was divided into ten short, intense sessions, each with a combination of invited speakers and others selected from abstract submissions. The sessions were: Stem cells, Model systems for human pathologies, Functional genomics and evolution, Systems biology, Cell proliferation and apoptosis, Organogenesis and morphogenesis, The polarised cell in development, Migrating cells and folding tissues, Cell communication and Architecture of the nervous system. There was also a helpful talk on how to write a paper entitled "On the Conception, Gestation & Parturition of a scientific manuscript" by David J. Fogarty, Managing Editor of *The International Journal of Developmental Biology*. There were two lively poster sessions, with altogether 250 posters. We also had a gala dinner, where we enjoyed a flamenco "fiesta rociera". So this is how it went.

The physics and maths of biology

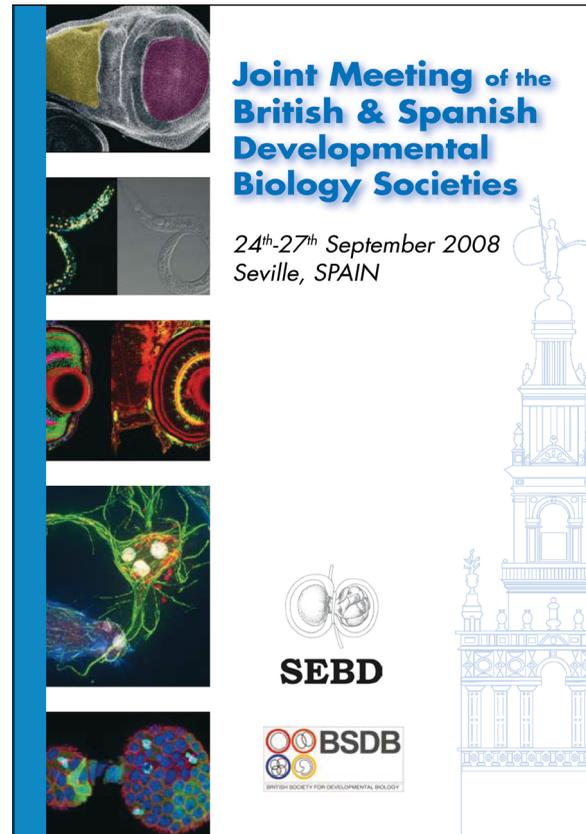
Sevilla, city of wonders. And wonders we saw. There was the *Alcazar* and *La Giralda*, the bar-crawling, the many warm friends, the delicious sea-food and *pescadito*, and the blue, still, waters of the hotel pool. But among the greatest wonders was Damian Brunner's movie of the yet undiscovered amnioserosa sea. The amnioserosa cells continuously pulsate as if in the last storm; with incredible resolution, these large hexagonal cells with hairy long thin thready filopodia (who said cells are round and smooth?) pulsated and pulsated, and this pulsation is one of the main sources required for dorsal closure. There were in fact several waves sweeping through the Meeting.

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There was a prevalent revival of the old idea that physical forces contribute to morphogenesis, now with the help of computer simulation and fancy technology. Damian Brunner has been modelling the pulsation of *Drosophila* amnioserosa cells by generating mathematical models to reproduce, and hence try to understand, the rhythmic and coupled beautiful movements. He found that cell pulsation is regular and oscillatory and requires tissue tension. Carl Philip Heisenberg went about it with the idea that tissues behave like oil and water. He used atomic force microscopy to measure cell cortex tension and cell adhesion during zebrafish gastrulation. He showed that, again, cell cortex tension plays a leading role in establishing germ layer tissue surface tension and that differences in germ layer tissue surface tensions are the main driving force for zebrafish germ layer sorting and positioning. By combining live imaging analysis with automated cell tracking, Nicole Gorfinkiel, from the lab of Alfonso Martinez-Arias, showed us that the geometry of the embryo

Abbreviations used in this paper: BSDB, British Society for Developmental Biology; SEBD, Sociedad Española de Biología del Desarrollo.

imposes mechanical constraints that result in a differential spatial pattern of apical cell contractions, which drive dorsal closure. Dealing with the plant world, Andrew Fleming used a combination of experiments and computer modelling, to explore the involvement of the cell wall in constraining leaf morphogenesis. While increasing cell proliferation did not affect leaf morphology, loosening the plant cell wall by Expansin proteins did. Furthermore, the size and the rigidity of cells at the leaf margin influenced the growth properties of the leaf. It is interesting how science moves along spirals through time, in which questions remain while technology grows.

There were waves on this splendid, large, curved pool surrounded by the green lawn of the hotel gardens, with gentle steps that led you straight from the water into the bar! All of it placed there to put us to the test. It was impressive to see the lecture theatre constantly full. Such was the excitement of the science.

Systems Biology came with a splash: “All models are wrong, some models are useful”. Ben Lehner is navigating the agitated waters of predictive genetics: without doing any crosses, he wants to predict phenotypes and genetic interactions with a computer. He made interesting remarks of relevance for everyone doing gain of function experiments, such as the fact that over-expression of any protein will force unnatural binding between proteins leading to harmful consequences; that most house-keeping proteins have tissue-specific interactions and that tissue specific protein-protein interactions are more informative than the actual proteins themselves. Continuing on the subject of *in silico* genetics, Sarah Teichmann and Jussi Taipale spoke about how one can infer how many transcription factors there are in a genome, or how to predict the target genes of oncogenic transcription factors. Thomas Becker reported the use of Genomic Regulatory Blocks (GRBs), combined with genome wide association studies (GWAs) and transgenesis in the zebrafish, to help identifying likely culprits of human genetic diseases for which no clear candidate (or perhaps even the wrong candidate) gene has been defined. These GRBs are genomic regions, usually of low gene density, that contain a major regulatory gene plus all the cis-regulatory elements responsible for its complex pattern of expression. Thus, T. Becker proposed that certain SNPs linking the FTO gene to diabetes just by proximity, were instead associated to regulatory regions of the *Irx3* gene. By means of functional studies in the zebrafish, it was shown that indeed, at least in this model, *Irx3* was required for the development of insulin-producing cells in the pancreas, thus pointing to regulatory mutation in the *Irx3* locus as the diabetes risk factor previously assigned to FTO. From more familiar grounds and into stem cell biology, Elaine Dzierzak presented the “gestation” and “birth” of the hematopoietic stem cells, amongst the most paradigmatic during mouse embryo development. Using transgenic embryos for the stem cell marker Ly6AGFP, she showed us impressive three-dimensional projections of the dorsal aorta and demonstrated the dramatic effects that genes such as *Runx1*, *BMP4* and *Hedgehog* have in the generation of the aortic cell clusters, on the differentiation of stem cells and on the generation of the blood system.

Movement, cell migration and cancer

After the splash came the gentle sweeping of normal cell movements. Enrique Martin-Blanco analysed the movement of

Drosophila histoblasts (small clusters of abdominal larval cells) as they replace the larval epidermal cells to form the adult abdominal epidermis during metamorphosis. By using live imaging techniques and clonal genetic interference, he found that Dpp secreted from the larval epidermis leads to the graded activation of different pathways that activate the invasive capacity of histoblasts. And with more traditional technologies such as biochemistry and *in vitro* experiments to show gels (which didn't move), James Nelson convinced us that the transition from mature quiescent contacts to active lamellipodia can be regulated by the ability of α -Catenin to function as a molecular switch, binding to either the Cadherin- β -catenin complex as a monomer or to actin as a dimer. Angela Nieto presented the first, impressive, plenary talk, discussing her laboratory's contribution to the understanding of the Snail protein family and their roles in the epithelial-mesenchymal transition (EMT) of the neural crest. She spoke of Snail targets, noting how E-Cadherin is repressed by Snail, but emphasising the broad range of target genes affecting cell shape and movement that underlie Snail-mediated EMT. She took us all the way from the evolution of the Snail family to the link between Snails and cancer, showing how the roles of Snails in development - EMT, cell cycle control and resistance to apoptosis - were all co-opted by tumour cells to promote metastasis and tissue invasion.

And with that came the tumorous wave. Tano Gonzalez showed amazing time-lapse movies tracking the centrosomes exploring the cells prior to establishing the position of the spindles before mitosis. Using a classical transplantation approach in flies, he showed that larval brain tissue carrying neuroblasts with mutations in genes controlling asymmetric cell division transplanted into the abdomen of the adult fly induced extraordinary tumours, which would fill up the whole adult abdomen. He addressed the question of whether aneuploidy due to centrosomal dysfunction was the cause of the observed tumorigenesis. For this, he analysed multiple mutants affecting chromosome segregation without affecting centrosomal function. He showed that, contrary to Boveri's hypothesis of tumorigenesis induced by aneuploidy, centrosomal dysfunction results in tumorigenesis by impairing asymmetric cell division, which eventually can result in aneuploidy. Tumorous growth can also result from failed alterations to the endogenous mechanism of cell competition, as shown by Ginés Morata. He used clonal analysis to show that tumorous progression relies on the ability of tumorous cells to outcompete non-tumorous cells, reminiscent of normal cell competition. To complete the picture, Nicolas Tapon gave a molecularly meticulous dissection of a new function of dASPP in maintaining epithelial integrity, as a tumour suppressor in the negative regulation of Src together with dCSK and Boa.

There was food. A feast for breakfast – there was so much to choose from, one just couldn't – then a copious lunch with wine, and multiple delicate snacks at coffee breaks with chocolate truffles. Couldn't see the drinks during the poster session, but not even this deficiency put people off. The poster room was bustling, hot, alive. People would not give up the science. It was fun.

Evo-devo

Then there was the evo-devo wave. Michalis Averof and colleagues have made it possible for many of the old *Drosophila* tricks to be applied to crustaceans of choice: transposable ele-



ments, wonderful fluorescent green or red eye transformation reporters, transgenesis, heat-shock inducible misexpression and gene trapping – all of which will enable them and the community to make a wide range of functional experiments in crustaceans, better suited than flies for certain questions. And one can always eat the surplus. Juan Pablo Couso taught us how to build a Cambrian bomb with Notch and a clock, and that Notch is at the base of an ancestral mechanism of segmentation, even prior to Engrailed, common to all bilaterians. Emili Saló carried out functional analyses using RNAi interference experiments in planarians to test whether the molecular mechanisms responsible for axis establishment are conserved. He showed that while the role of the TGF β signalling pathway in the maintenance of the dorsoventral (DV) axis is conserved, the striking body transformation from bilateral to radial-like upon inhibition of β Catenin function supports a conserved role for Wnt signalling in anteroposterior (AP) but not in DV axis specification. Thierry Lepage showed how the good old reaction-diffusion mechanism by Nodal and Lefty drives the establishment of the DV axis during sea urchin development. His findings reinforce the idea that the ventral ectoderm of the sea urchin embryo acts as an organizing center that patterns the three germ layers along the DV axis.

And then there was this exquisite cocktail amongst lush trees and fountains, followed by dinner and flamenco dancing. Please contact Benedicte Sanson for a report on this point.

Cell communication and the nervous system

The meeting was closed with two excellent sessions and five rather impressive talks. Marcos Gonzalez-Gaitán spoke about how the trafficking of internalized Notch/Delta molecules to Sara endosomes prior to signalling can lead to directional signalling during SOP asymmetric cell division. Astounding cell biology and superb, wonderful microscopy. Michael Bate showed how the nervous system begins to function in early development. Whereas muscle movements start before neurons fire, coordinated muscle movement requires patterned neuronal activity. In essence, the motor system is ready to go as soon as it is made, and it is the firing activity of neurons that ultimately sets in coordinated, functional movement. The dendritic arborisations of the motoneurons respond in a plastic manner to the influence of neuronal activity. Oscar Marín spoke about novel roles for Robo receptors in neural

development, which include the involvement of these receptors in regulating cell proliferation during early stages of brain development. Alberto Pascual, by conditional ablation of GDNF expression in mice, re-established the importance of GDNF as a survival factor for adult catecholaminergic neurons. Following a late Spanish lunch timetable, before a hungry audience, Christine Holt gave the final splendid plenary talk on how local protein synthesis and degradation at the growth cone induces turning during axon guidance. They used laser capture to isolate 1000 tiniest little growth cones from which to extract mRNA and carry out a microarray analysis! Amongst ribosomal proteins and transcription factors (!) at the growth cone, they also found β Actin. They visualised protein translation with a fluorescent reporter in time-lapse at the growth cone and saw how interfering with β Actin translation affected Netrin-mediated growth cone turning. Netrin in fact causes asymmetric translation by inducing the polarised transport of mRNA into the filopodia. The mRNA specific regulation of translation leads to the differential translation at the growth cone, whereby new production of β Actin results in attraction and new production of Actin disassembly proteins results in repulsion. With that, we were all sad that it had all ended, we ate some more canapés and wonderful tiny cups of *salmorejo*, and as we said *adiós* to all our friends, watched the last marvel, the rain falling in the city of Sevilla, as it created on the pool the faintest tiny waves.

We hope everyone enjoyed this meeting as much as we did. It was for us a great challenge to match previous successful meetings, and we hope now to have established the tradition of the trans-European joint meetings. We are very grateful to all those people who impeccably helped make this a fun, exciting, scientifically vibrant, pleasant occasion (speakers and attendants, all the poster presenters and their enthusiasm, audiovisual technicians, conference and hotel staff, all involved in organising the Meeting, and the cooks who made for us such nice food). We would like to thank our generous sponsors, who in various ways enabled us to hold this Meeting: Spanish Ministry for Science and Education, Consejo Superior de Investigaciones Científicas (CSIC), Junta de Andalucía, Universidad Pablo de Olavide, Genoma España, EMBO, Astra Zeneca, Leica, *The International Journal of Developmental Biology*, Emage, Yorkshire Biosciences and Intavis. We very much look forward to many more future joint meetings. Next stop, the Franco-Spanish meeting coming soon. See you there!

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