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5th Congress of the Spanish Society of Developmental Biology

Alicante, 21-23 September 2006

MEETING REPORT

The Spanish Society of Developmental Biology (Sociedad Española de Biologia del Desarrollo - SEBD) has been organizing periodic meetings for over 10 years now, since its first Congress in 1996 (Leioa, Vizcaya). The objective of these Congresses is to gather Developmental Biology researchers from Spain and different parts of the world, for interaction and exchange of ideas. After the successful meetings in Leioa (1996), Barcelona (1999, the only all-English one so far), Málaga (2001) and Santander (2004), it was time to hold the 5th venue.

From 21st to 23rd September (2006), the Spanish community of developmental biologists converged on Alicante for the 5th Meeting (see photos at: http://www.sebd.ehu.es/congresos.htm). Held at the Hotel Melià just by the sea, the location provided a nice and self contained atmosphere where most activities (talks, poster sessions, meals, drinks and rest) had adecuate time to be celebrated. The venue was sponsored by the Miguel Hernández University at Elche (Alicante), together with other institutions including the Spanish Ministry of Education and Science, Bancaja and the Generalitat Valenciana. The meeting was organized by José Luis Micol with the help of a small but dedicated and efficient team of supporting people. As it could not have been otherwise, given the gastronomic fame of the city and the organizer, outside activities nucleated inside good to very good restaurants, where all sorts of rice, good wine and other delicatessen from the Alicante cuisine were served. In addition, a handful of discos and bars were at reach for young, and not so young, attendants. A night tour to the Santa Barbara castle offered a breathtaking view of the city and the Mediterranean Sea, which was followed by a standing buffet served indoors. That closed the official outdoor activities of the Congress.

The meeting was organized around seven sessions, with two invited lectures and 3-4 shorter oral communications each. A round table and a mini-symposium were interspersed within the meeting, which closed with very emotive tributes to two outstanding figures in the field, Antonio García-Bellido (CBM-CSIC, Madrid) and Eric H. Davidson (Caltech, USA).

Plant Development

The conference kicked off with development in plants, the main subject of the organizer and his research team. No wonder most talks focused on *Arabidopsis thaliana*. P. Mas (Instituto de Biología Molecular de Barcelona-CSIC) summarized the most recent data



on circadian rhythms in A. thaliana and the key role of the gene toc1 (Timing of CAB Expression 1) which is driven by the rhythmic activities of acetylation-deacetylation of histone H3 and CCA1 (a sort of acetyltransferase) binding at the toc promoter. F. Madueño (Instituto de Biología Molecular y Celular de Plantas, Universidad Politécnica de Valencia-CSIC), in a somewhat lengthy talk, instilled new data on the genetic control of inflorescence architecture, focusing on the role of the tf/1 gene in different species and the whereabouts of a new gene veg1, found in pea. This gene is important to give identity to I2 secondary meristems in complex inflorescences. From the open communications, two are particularly worth mentioning: P. Robles (Universidad Miguel Hernandez, Elche) on the genetics of leaf development, focused on the gene ron1 (currently known as fry1). Using microarrays, they found that ron1 mutants deregulate genes involved in different metabolic processes, auxin transport and circadian rhythms, which explained some of the phenotypic effects of the mutant. Finally, V. Aguilera, from the same research Institute in Elche, went into the new and hot topic of microRNAs (miRNAs). Mutants of the main genes involved in the biosynthesis and processing of miRNAs led

Abbreviations used in this paper: A-P, antero-posterior; CBM, Centro de Biología Molecular; C/E, convergence/extension; CIB, Centro de Investigaciones Biológicas; CNB, Centro Nacional de Biotecnología; CSIC, Consejo Superior de Investigaciones Científicas; D-V, dorso-ventral; FGF, fibroblast growth factor; GRN, gene regulatory network; HSPG, heparan sulphate proteoglycan; ISI, Institute for Scientific Information; miRNA, microRNA; PKC, protein kinase C; SCI, Science Citation Indices; SEBD, Sociedad Española de Biología del Desarrollo; UAM, Universidad Autonóma de Madrid; UPO, Universidad Pablo Olavide.

them to find scores of up and downregulated genes using microarrays. Among the plethora of phenotypic changes caused by these mutants, the effects on the proximodistal and vein patterning of the leaf are their next concern.

Evolution and Development

Next was the session on Evo-Devo, which covered a broad sample of subjects and species. I personally found the invited talks extremely good. The first, in charge of R. Muñoz-Chápuli (Málaga University) dealt with the origin and evolution of the vascular endothelium, a characteristic feature of vertebrates, but absent as such in invertebrates. A first stumbling block is the uncertain origin of endothelial cells during ontogeny in vertebrates. As a way out, he suggested a phylogenetic origin of these cells from hemocytes of invertebrates. Further, because the hemal or blood vascular system in invertebrates seems to originate from the embryonic coelom, this might be the ontogenetic precursor of the vascular endothelium. He traced interesting parallelisms of amebocytes and coelomocytes from annelids to the endothelial cells and made interesting speculations on the pervasive presence of endothelium in vertebrates. The next invited talk by U. Technau (SARS Centre, Bergen, Norway) on Cnidaria and the evolution of bilaterian body plans was thrilling. After a detour on the functional Evo-Devo of 'mesodermal' genes in cnidarians showing their role in gastrulation, he went on to tackle the presumed homologies between the antero-posterior (A-P) and dorso-ventral (D-V) body axes of bilateral organisms and the oral-aboral axis of cnidarians. Asymmetric expression of cnidarian genes, orthologous to bilaterian D-V genes, were shown to back the claim of a true D-V axis in cnidarians orthogonal to the A-P axis, which turns them into true 'bilateral' organisms. Finally, he discussed the cnidarian Hox complement and made the strong claim of independent Hox cluster evolution in chidarians and bilaterians from a minimal ProtoHox cluster. From the oral communications, a mention of M. Crespo (Instituto de Investigaciones Biomédicas Alberto Sols, CSIC-UAM, Madrid) with first data tracking the evolutionary conservation of genes involved in early lineage determinations of extra-embryonic structures between mouse and chicken embryos, and C. Minguillón (National Institute of Medical Research, London, U.K.) who reported sophisticated experiments to sort out whether the duplication of the Tbx4/5gene of amphioxus into separate Tbx4 and Tbx5 genes in vertebrates played a role in the origin of vertebrate appendages.

Stem Cells

The afternoon session on the newcomer topic of Stem Cells included talks by three invited speakers and two additional short intermingled oral presentations. The talks were largely devoted to adult somatic stem cells, but this did not make the whole topic less developmental because issues as fundamental in developmental

biology as fate determination, self-renewal and proliferation or differentiation were the main focus. I. Fariñas (Valencia University) talked about regulation of stem cell renewal in adult neurogenic niches and described the identification of a vasculature-derived molecule (PEDF) which induces the symmetrical division of neural stem cells, providing the first molecular specific regulator of self-renewal in the already proposed framework concept of the "neuro-angiogenic niche". P. Herrera (Geneva University, Switzerland) gave a great, very comprehensive presentation on cell lineage relationships in the developing and regenerating pancreas. Following toxigen-mediated ablation of specific cell populations in islets of Langerhans, the response of genetically marked hormone-producing cell populations is followed to understand cellular relationships in the construction of the endocrine pancreas. The session had almost run out of time but stemness was king again in an outstanding presentation by A. Ruiz i Altaba (Geneva University, Switzerland) which captivated most of the audience who gaily refused coffee and remained seated during break time to hear about the regulation of stem cell attributes by SHH. Most interestingly, a specific stemness-related signature and self-renewal regulation by elements of the HH pathway was reported for tumor-inducing cancer stem cells as those found in the devastating most-feared gliomas.

Round Table Discussion of the Social Impact of Stem Cell Research

Late afternoon witnessed the first out of session activity: a round table. Two stem-cell experts,'Anna Veiga (Centro de Medicina Regenerativa, Barcelona) and Ariel Ruiz i Altaba (Geneva University, Switzerland), and a journalist in charge of the science section of a local newspaper, José María Perea, concurred to introduce laymen to the main topics and worries of this hot and debated topic. As such, it was advertised as open to the general public. At this level, the result fell very short of expectations as only congress people attended. As regards the speakers, Anna Veiga delivered a somewhat protracted and very general talk on stem cells to a relatively well prepared audience. Ariel Ruiz i Altaba gave a short but very informative talk on the Swiss Program on Stem Cells built on a general consensus of labs and model systems, whereas José-María Perea's long dissertation dealt with the problems and difficulties of scientific journalism in Spain. The main casualties were questions and answers, which was reduced to a mere 10 minutes. Even so, this brief period generated a heated crisscross of questions and answers between audience and speakers. The principal concerns seemed to be the more than modest state of stem cell research in Spain, its apparent concentration to a mere very well provided 2-3 labs, and the uncritical propaganda they get from most Spanish newspapers. The mounting frustration of the audience witnessing a shortened debate, which was terminated all too quickly, was dispelled with

Moments during the Fifth SEBD Congress (opposite). (A) Morning views from the breakfast room of the Hotel Melià. (B) Eric Davidson and Antonio Garcia-Bellido. (C) The Congress organizer, José Luis Micol. (D) Lunch break. (E) Speakers at the discussion on the social impact of stem cell research. (F) Paola Bovolenta. (G) Comfortable conference room. (H) The V SEBD Family Photo. (I) Acaimo González-Reyes, organizer of the next SEBD-BSDB joint meeting in 2008 in Seville. (J) Poster session. (K) Coffee break. (L) Isabel Fariñas and Pedro Herrera. (M) Nocturnal fiesta at the Santa Barbera Castle. (N) Two of the three winners of the IJDB Golden Anniversary Awards for excellence in science communication, Pedro Robles and Aitana Perea-Gomez with Juan Aréchaga and David J. Fogarty.



a visit to the Santa Barbara Castle and the following open buffet.

Organogenesis

Next day, 22nd September, came the 4th session on Organogenesis. It opened with a very good and authoritative talk delivered by L. Puelles (Murcia University) on a classical subject: segmentation of the nervous system. From the title on, there was no alternative: segmentation is true and segments are already there in the embryo. No way out. To back it, a deluge of data, both from morphology and molecules, poured over the audience. After this overwhelming experience came the main open question: are there 6 prosomeres or just 4? The answer will likely come at the next SEBD venue in Seville 2008. Upcoming talks dwarfed after such a display of evidence. To be mentioned, those by J.A. Montero (Cantabria University) on the ontogenetic origin of the muscles in the palm of the hand, indicating an important role for apoptosis to dwindle the excess of muscles produced, and a new tour de force on the *snail* gene delivered by C. Alvarez (Alicante Neuroscience Institute, Universidad Miguel Hernández-CSIC). Using a sophisticated transgenic mouse, they overexpressed snail to test its role in mammalian chondrogenesis and to analyze the interplay between the Fibroblast Growth Factor (FGF) pathway and snail in proliferation and differentiation.

Development of the Nervous System

After coffee break came the 5th session on one of the usually exciting and recurrent topics in any Developmental Biology meeting, the development of the nervous system. The first invited talk, by P. Bovolenta (Cajal Institute, CSIC, Madrid), summarized the roles of BMP7 and Shh on the origin and morphogenesis of the optic disc using mutants of Bmp7 and rescue experiments. Briefly, BMP7 has an early role, whereas Shh acts at later stages. Next invited talk by P. Boya (CIB-CSIC, Madrid) dealt with a new entry into mechanisms of cell death or cell turnover: cell autophagy. This process has a protracted history with scarce data and few known specific molecular mechanisms. Strangely, the talk went shorter than expected and merely summarized what was known in other organisms, namely at the level of the Atg gene family, with very scant references to their own work. Hopefully, Seville 2008 will be the place to learn the rest of the story. The remaining talks dealt with determination of the proneural otic domain in chicken, quail/chick chimaeras to track cell migration in the telencephalon, neurogenic patterns and cell viability in the weaver mutant, and DNA breaks and apoptosis in the mouse retina.

Symposium on The International Journal of Developmental Biology

This seminar was intended to discuss the main trends in science publishing and how the *Int. J. Dev. Biol.* fares in it, together with useful tips to write better papers. Contributors were Juan Aréchaga, Editor-in-Chief of the *Int. J. Dev. Biol.* and David J. Fogarty, its Managing Editor. After a historical account of the rambling whereabouts of the journal, Juan Aréchaga went into bibliometric indices, the ISI and the SCI, how the Int. J. Dev. Biol. fared and fares compared to other journals (e.g. Development), and described the rather gloomy situation of scientific journals in Spain (of 1,250)

journals, a mere 30 are included in the ISI database), namely in terms of lack of money invested and aggressive competition from multinational oligopolies such as Springer, Elsevier or Blackwell. Then, he changed gears to ask how to make the Int. J. Dev. Biol. a more attractive and saleable journal. Main suggestions were electronic edition, a better Web page, use of professional editing services, etc. The next contribution by David J. Fogarty was great! Its title was "Trends in Publishing Science", in short, TIPS and was addressed to students and postdocs as guidelines for successful writing, editing and publishing of scientific papers. It was divided into three parts: writing tips, choosing a journal, and recent tendencies in science publishing. As time was running out, he concentrated on the first, by far most interesting section, which I consider a compulsory lecture for students, postdocs, lecturers and professors trying to write and publish a good paper in proper English. For Spanish scientists, besides nice tips to organize concepts, methods, results and discussion into a proper paper, the talk showed how to imitate the usually short, clear, and concise Anglo-Saxon style of writing and to avoid the more usual verbose, repetitive and intricate phrasing. As it was for the Round Table, time ran out and the upcoming open discussion was not held. This should be avoided and mended at the next venue.

Signaling

Without pause, the 6th session on signaling took place. The first invited talk dealt with how the Hedgehog gradient is made, and was delivered by I. Guerrero (CBM-UAM, Madrid). She traveled through the dense jungle of hedgehog (Hh) secretion, modification and reception which involves lipids, cholesterol, palmitic acid, extracellular matrix heparan sulphate proteoglycans (HSPG) until it binds to its receptor Patched. The story turned more dense with *shifted*, a gene coding for a product involved in Hh and HSPG interaction and modulating the stability and extracellular distribution (that is, the gradient) of Hh in Drosophila. I am confident that Seville 2008 will be the place to learn whether they are still inside the jungle or have made its way out to a clearing. E. Amaya (The Healing Foundation Centre, London) gave an extremely nice summary of FGF signaling in early vertebrate development taking *Xenopus* tropicalis as a model system. Using a vast display of techniques, they set out to disentangle how mesoderm specification and convergence/extension (C/E) movements are coordinated during gastrulation and, in particular, the roles of Sprouty and Spred protein families and FGF signaling. Whereas Sprouty inhibits C/E movements, through protein kinase C (PKC) and Ca2+ signaling, leaving mesoderm specification intact, the converse is true for Spred acting through the MAPK pathway. These antagonistic molecules switch FGFR signal interpretation to activate mesoderm formation first, under Sprouty modulation, and later C/E movements under the influence of Spred. Of the oral communications, two in particular are very worth mentioning. H. Herranz (Institució Catalana de Recerca i Estudis Avancats, Institut de Recerca Biomèdica-PCB, Barcelona) introduced the first Systems Biology talk into the meeting, combining in silico and in vivo experiments on the dorso-ventral (D/V) gene regulatory network of the Drosophila wing disc. He showed how short-range cell interactions mediated by Notch and its ligands and long-range cell interactions mediated by the wingless pathway shape the D/V boundary and restrict gene expression there. From these data, he set up a model which

predicts most phenotypes found and anticipates novel properties to be validated experimentally. Cell polarity in epithelial cells and the role of JAK/STAT signaling was dealt by S. Sotillos (Centro Andaluz de Biologia del Desarrollo, CSIC-UPO, Seville). In several cell types, cell polarity is established by the specific segregation of aPKC, Par-6, Par-3, Crb and Stardust in the apical part and Par-1, Dlg, Lgl and Scribble in the baso-lateral part. Par-1 and Lgl have an additional role: to modulate some signaling pathways (e.g. Wnt and Notch). Using the *Drosophila*spiracle as a model, they showed that the JAK/STAT pathway localizes in the apical part of the cells where it forms complexes with aPKC, Par-3, Par-6 and Crb, suggesting a complementary role to Wnt and Notch to coordinate signaling and cell polarity.

A Tribute to Eric H. Davidson

Late afternoon-early evening was time to pay due tribute to Prof. Eric H. Davidson, professor at the California Institute of Technology (Caltech, Pasadena, USA) and a towering figure in Developmental Biology. Antonio García-Bellido introduced to the audience Eric Davidson's main achievements from his early days at the Rockefeller Institute, going through his DNA-DNA hybridization and Cot and Rot 1960s period, his Jacob-Monod-like model, theorizing about gene regulation in late 60s-early 70s, and from the 1970s settling down to start his seminal and far-reaching work on gene regulation and gene regulatory networks (GRN) using sea urchins as models. As it could not be otherwise, Eric Davidson's talk was thrillingly spectacular. He started by outlining the problem: to work out in detail the GRN of the sea urchin endomesoderm, containing around 50 genes, from prior knowledge of developmental processes, spatial and temporal patterns of gene expression, and large-scale perturbation analysis. The outcome followed soon: a computational model of the GRN that permits prediction of cisregulatory inputs at the nodes and gene regulatory transactions, active or inactive in given spatial domains of the embryo at specific times. These predictions have in many cases been experimentally validated. Two main principles emerge from GRNs: the fastforward principle, enforced by auto-activating and cross-activating positive feed-back loops among genes, which makes development proceed, and the principle of exclusion of alternative states, implemented by cross-inhibitory feed-back loops, to ensure that specific genes of a tissue or cell type are not expressed in other tissue and viceversa. Finally, he mentioned two recent developments from GRNs; first, gene network comparison among phylogenetically distant groups by interspecific sequence comparisons (e.g. sea urchins and sea stars which split around 500 million years ago) to identify their conserved elements which will enable insightful advances in functional Evo-Devo. Secondly, the ability to reprogram GRNs to produce cell fate changes at will, which will lead in the future to a re-engineering of life forms. At the end, the audience stood up and broke into a long, loud applause, the best tribute to such an outstanding and still active scientific life.

Other Aspects of Development

At the eve of day three, everybody was pretty exhausted, not to mention those still in bed! The title of the last session, Other Aspects of Development, did not help to keep eyes open or wake up those in the arms of Morpheus [Ed. The principal god of dreams

in Greek mythology]. The session focused on less conventional topics in a development meeting, such as cell cycle control and aging. David Gems (University College, London, U.K.) talked about how mutants in the insulin-signaling pathway can affect lifespan in different species. By using DNA microarrays and proper statistical analysis, he found that many genes involved in cell protection are overexpressed in the long-lived Caenorhabditis elegans nematode mutants. Interestingly, genes of the phase 1 and phase 2 of the detoxification system are among them (what he call "the green theory of aging"). José Perez (CNB-CSIC, Madrid) presented the involvement of Cdk2, a member of the PHO85 CDK family, in the control of polar growth in *Ustilago* maydis. The speaker gave an interesting point of view of how molecular mechanisms governing polar growth in these fungi are common to those regulating axon formation in neurons. The next speaker was Rafael R. Daga (Centro Andaluz de Biologia del Desarrollo, CSIC-UPO, Seville), who described the basic mechanism of how a single cell is able to identify the cell centre. By using an ingenious mixture of genetic methods and in vivo imaging systems, he demonstrated that in the end, microtubules by themselves are sufficient to establish the location of the cell centre in fission yeast. M. J. Muñoz (Centro Andaluz de Biologia del Desarrollo, CSIC-UPO, Seville) delivered an interesting talk on the role of PKC in longevity processes in the worm C. elegans. They set up a mutation screen for suppressors of long-lived phenotypes and entry to dauer larva (a resistant larval stage) produced by alleles of daf-2, the homolog of the insulin receptor in C. elegans. One of the genes found, asu-1, was shown by positional cloning to be the gene coding for PKC. This signifies a new role for this kinase in the complex gene network coordinating growth, metabolism, and longevity in C. elegans. M.C. Risueño (CIB-CSIC, Madrid) presented her observations about the role of programmed cell dead during pollen development in Nicotiana tabacum. Exhaustive histochemical analysis showed interesting similarities between this process and conventional apoptotic steps in animal cells. The final talk was from M. Mari-Beffa (Málaga University). He presented his book to the audience, entitled Key Experiments in Practical Developmental Biology: A teaching experience co-edited with J. Knight and published by Cambridge University Press (2005) and made an intense defense of it. Painstakingly assembled over several years from the answers of 47 developmental biologists, this book intends to bridge experimental labs in Developmental Biology and lab practical sessions for undergraduates and post-graduate levels. One of the bonus of this book is that many of the 27 chapters are personal accounts by first-class scientists who developed the concepts and provided the foundation of key experiments in Developmental Biology. Worth buying indeed.

A Tribute to Antonio García-Bellido

After the last coffee break, it was time to pay tribute to Prof. Antonio García-Bellido, research professor at the Centro de Biologia Molecular (CSIC-UAM, Madrid), and another world-towering figure in Developmental Biology, specifically in Developmental Genetics. In due exchange, he was introduced by Eric H. Davidson (Caltech, USA). He illustrated García-Bellido's main achievements giving a long list of topics to which he contributed, some of which are nowadays commonplace names in all text-

books in Developmental Biology and Developmental Genetics. To name the main ones: clonal analysis, compartments and selector genes. He also praised very highly his work on such different items like homeotic genes, maternal effects, transvection, estimates of the number of genes and number of lethals in Drosophila, analysis of scores of genes and gene complexes (e.g. achaete-scute, Notch,...), gene interactions in the wing and vein formation, to end with his current topic: how local cell interactions control organ size and shape. Antonio Garcia-Bellido's talk was on Control of size and shape in imaginal discs of Drosophila melanogaster which has been the underlying topic throughout his scientific life from early clonal analysis to the current use in the last decade of sophisticated genetic, cellular and molecular tools in cells. His talk was a fascinating, all-embracing journey to illustrate the relationships between gene expression patterns in cells and cell proliferation together with cell arrangement in developing organs; the stuff of how size and shape are attained in tissues and organs. As could not have been otherwise, his talk was a strong apologia of the "internalistic" view on how cells acquire positional identity in contrast to the "externalistic" view which assumes that cells acquire positional identity according to levels of external signals and morphogens. His talk ended with his current "Entelechia Model", [Ed. Greek for perfection, completion or totality] still under elaboration, which tries to capture an internalistic explanation of how organs grow and, what is even more important, when, why and how they stop growing. At the end, the audience stood up and broke again into a big, long applause as a tribute to an exceptionally gifted thinker in Developmental Biology and Developmental Genetics.

Int. J. Dev. Biol. Golden Anniversary Awards

Before going home, *The International Journal of Developmental Biology* presented its young scientist Golden Anniversary Awards for excellence in science communication. The objective of these awards was to celebrate over 50 years of independent scholarly publishing (the journal is now the most highly cited scientific journal produced in Spain) and to distinguish young researchers for the quality of the presentation of their work and their capacity to convey its significance to others. The First Prize was awarded to Dr. Aitana Perea-Gómez, from the Institut Jacques Monod, in the University of Paris (France) and her award-winning presentation was entitled *Formation and growth dynamics of mouse extra-embryonic tissues*. The Second Prize went to Dr. Pedro Robles for work carried out at the Division of Genetics and Institute of Bioengineering of the Miguel Hernández University (Alicante, Spain). His distinguished presentation was entitled

Pleiotropic effects of ron1 mutations in Arabidopsis thaliana. Finally, the Third Prize was awarded to Dr. Juan Montero who is working at the Dept. of Anatomy and Cell Biology of the University of Cantabria (Santander, Spain). His spectacularly illustrated work was entitled Morphogenesis of limb muscular bellies during development. Congratulations to these young winners! We wish them every success with their careers as scientists and look forward to publishing exceptional Developmental Biology papers by them in the future.

For photos of the presentations, see http://www.sebd.ehu.es/vcsebd/index.html

Conclusion

The 5th Meeting of the SEBD turned out to be a success in providing a platform for presenting recent advances in the wide spectrum of topics of Developmental Biology, and a calm and attractive atmosphere for the celebration of the meeting. Local organizers deserve full merit on both counts. The next meeting of the SEBD will be in Seville in 2008, to be held together with the British Society for Developmental Biology in an all-English speaking meeting. Attracting the best from here, there and everywhere (apologies to "The Beatles") is undoubtedly the best strategy for inspiring scientific excellence and enhancing relationships and collaboration among developmental biologists from different countries and from our national scientific societies.

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