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Meeting Report

1st Joint Meeting of the French & Spanish Developmental Biology Societies (2009)

Toulouse (France) 7-10 November 2009

The first joint meeting of the Spanish and French Societies for Developmental Biology (*Sociedad Española de Biología del Desarrollo,* SEBD and *Société Française de Biologie du Développement,* SFBD) was held in November 2009 in the city of Toulouse (France). International Joint Developmental Biology meetings have now become a tradition within Europe. The most recent were organised by SFBD with the British, Swiss and Japenese Societies for Developmental Biology, and by the SEBD with the British Society (Hidalgo and Martín-Bermudo, 2009). This year, two other large European meetings, the International Society of Developmental Biologists (ISDB) Meeting in Edinburgh, and the European Drosophila Conference in Nice, influenced the attendance of the SFBD/SEBD meeting, such that attendance was slightly lower than at previous joint meetings, making it perfect for both a friendly and studious meeting. It fostered fruitful discussion between students/post-docs and group leaders, often a challenge in large meetings. Over 150 conference delegates from around Europe, with 24 invited speakers, including a keynote speaker, all presented very high quality, largely unpublished data. The meeting was divided into 6 sessions with a combination of invited speakers and selected speakers from abstract submissions. The sessions were: Tissue regeneration in Evo/Devo models, Metabolism and Tissue Growth, Tissue patterning, Hematopoieisis, Myogenesis and Neurogenesis, all linked by a strong focus on stem cell biology, in animal and plant model organisms. There was a very stimulating keynote address by Andreas Trumpp, Heidelberg, on Cancer Stem Cells: concepts, facts and prospects for therapies. There were three poster sessions, with altogether 75 poster presentations.

Apoptosis and regeneration in diploblastic and triploblastic animals

The nature of stemness, cell plasticity and reprogramming is at the forefront of today biology. The molecular era of Evo-Devo has brought classical embryological models for studying tissue regeneration back into the limelight. Brigitte Galliot, University of Geneva, described how head and tail regeneration in the Hydra are dramatically different at both cellular and molecular levels. Head regeneration involves apoptosis, engulfment and cell proliferation of distinct subpopulations of cells, leading to the complete generation of the missing structures in less than 3 days (Chera *et al.*, 2009). Activation of Wnt signalling by early apoptotic cells promotes compensatory proliferation of "dormant" progenitors, suggesting possible evolutionarily conserved mechanisms of epimorphic regeneration between cnidarians and bilaterians. Evelyn Houliston, Observatoire 0céanologique, Villefranche-sur-mer, also reported on the key role of Wnt signalling, in embryonic patterning of another cnidarian, the medusa *Clytia hemisphaerica* (Amiel *et al.*, 2009). In this case, asymmetric Wnt signalling is initiated by the vegetal localisation of the inhibitory Wnt receptor Fz3 mRNAs during meiosis completion. Wnt and Fz1 mRNAs are localised at the animal pole by independent processes. Thus, like in bilaterians, temporally and mechanistically distinct RNA localisation pathways direct cnidarian body plan development. Planarians can undergo dramatic changes in body size and also regenerate their entire body plan from small pieces after cutting (Salo *et al.*, 2009). Emili Saló, University of Barcelona, told us about his most recent characterisation of the involvement of the BMP and Wnt pathways in re-establishing the dorso-ventral and

Abbreviations used in this paper: BSDB, British Society for Developmental Biology; SEBD, Spanish Society of Developmental Biology; SFBD, French Society of Developmental Biology.

***Address correspondence to:** Alain Vincent or Eric Agius. Centre de Biologie du Développement, UMR 5547 CNRS/UPS, 118 route de Narbonne, F-31062 Toulouse cedex 9, France. e-mail: agius@cict.fr or vincent@cict.fr

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antero-posterior polarity, respectively, during regeneration of the planarian *Schmidtea mediterranea*. Vincent Laudet, IGF, Lyon, reported specific adaptation of retinoic acid (RA) signalling during tooth development in cypriniform fishes which, in contrast to many other fish species, contain pharyngeal teeth but lack oral teeth. Comparison of the respective roles of RA and FGF signalling in inducing the pharyngeal tooth program in zebrafish and the Mexican *tetra* and *medaka* species suggests a new evolutionary scenario in which the gene network controlling tooth development gained RA-dependency in the lineage leading to the Cypriniforms.

Food for thought and the humoral control of growth in *Drosophila*

In metazoans, tissue growth relies on the availability of nutrients and the activation of insulin signalling. Likewise, Drosophila larval growth is mediated by insulin-like peptides (Dilps) produced by the brain which couple nutrient uptake with systemic growth (Slaidina *et al.*, 2009). Pierre Leopold, IRSBDC, Nice, reported that during metamorphosis, when feeding has stopped, a specific Dilp, Dilp6 is produced by the fat body and relays the growth signal. Dilp6 expression is controlled by steroid hormones, revealing a tight link between control of growth and developmental timing. Moderate nutrient deprivation during development can result in undersized adults. Not all organs, however, scale down proportionately. For example, sparing of the newborn brain is observed when pregnancy occurs in dietary restriction conditions. Alex Gould, NIMR, London, reported that when *Drosophila* larvae are starved during the late phase of growth, the CNS reaches a near-normal size within a half-size larva. Surprisingly, unlike most larval cell types, neural progenitors (neuroblasts) can divide in the absence of Insulin Receptor or the amino-sensing TOR kinase. Instead, neuroblast divisions are dependent upon an atypical PI-3 kinase pathway that is active under both fed and starved conditions. *Drosophila* thus appears as an interesting model in which to study the mechanisms sparing brain growth under nutrient stress.

The control of trichome patterns in plants and flies

The formation of leaf hairs (trichomes) of Arabidopsis thaliana is a model to address general questions in cell and developmental biology. A. Schnittger, IBMP, Strasbourg, reported how endoreplication controls the trichome fate. A reduction of endoreplication results in both reduced trichome numbers and loss of trichome identity, revealing that cells committed to a trichome fate revert to epidermal fate. Conversely, promoting endoreplication in glabrous patterning mutants restores trichome fate. Endoreplication, a special cell cycle variant, is thus a new important determinant of *Arabidopsis* cell identity. Patterning the trichome field of *Drosophila* embryos is another classical developmental problem. The transcription factor Shavenbaby (Svb) plays a key role in this patterning by directly controlling the expression of a wide range of effectors of cell shape remodelling (Fernandes *et al.*, 2010). Evolution of the trichome pattern between distantly related flies is intimately linked to modifications of *svb* expression. François Payre, CNRS, Toulouse, now reported another, novel level of regulation of Svb activity, by evolutionarily conserved small peptides encoded by polycistronic mRNA.

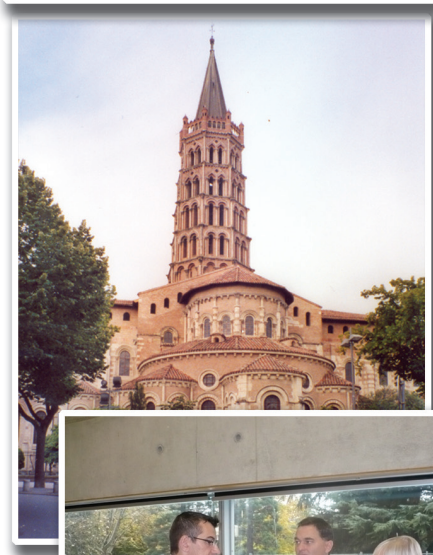
Vessel maturation and the evolution of branching patterns in plants

Xylem differentiation, required for water and solute transport in plants, is initiated from the stem cells that constitute the procambium and vascular cambium and invariably culminates with cell death. The analysis of *Arabidopsis acaulis5* (*acl5*) mutants suggested that ACL5 participates in a safeguard mechanism that maintains differentiating xylem cells alive until xylem differentiation is finished. From an EMS-mutagenesis screen for *acl5* suppressors, Miguel A. Blazquez, CSIC-UPV, Valencia, identified three “AJAX” bHLH transcription factors which may control the expression of genes involved in xylem maturation, for instance those encoding nucleases and proteases involved in cell death. Branching patterns are also major determinants of plant architecture. They depend both on leaf phyllotaxy and on the decision of buds to grow out to give a branch or to remain dormant. In *Arabidopsis*, another plant-specific bHLH transcription factor belonging to the TCP family, BRANCHED1 (BRC1) (Martin-Trillo and Cubas, 2010), is specifically expressed in buds. Loss of *BRC1* function leads to precocious progression of bud development and excess of shoot branching. *BRC1* function within axillary buds mediates the response to endogenous and environmental signals controlling branching. Pilar Cubas, Madrid reported at the meeting her analysis of *BRC1*-like genes in several *Solanaceae* species which suggest that *BRC1*-like genes have played a key role in the evolution of branching patterns and the evolution of tomato and potato.

Dormant, activated and malignant stem cells in mice

In his keynote address, Andreas Trumpp, DFKZ and HI-STEM, Heidelberg, Germany, drove to the heart of the most recent research on hematopoietic stem cells (HSC), as a model for understanding other stem cells, including cancer stem cells present in the mammalian body. He first described evidence that a long-term dormant population of HSC harbors the vast majority of multi-lineage long-term self-renewal activity and that these cells can reversibly switch from dormancy to self-renewal under conditions of hematopoietic stress. Relative dormancy is one reason why cancer stem cells are thought to escape anti-proliferative chemotherapy. A. Trumpp then reported that treatment of mice with the cytokine Interferon (IFN)-alpha leads to the “activation“ and proliferation of dormant HSC (Essers *et al.*, 2009), which simultaneously sensitizes them to chemotherapy drugs. The observation that STAT-1 and Sca-1 mediate IFN-alpha induced proliferation raises the possibility to design novel concepts to target and eliminate chemotherapy resistant cancer stem cells.

It is essential to maintain a balance between renewal and differentiation of muscle progenitors during skeletal muscle development and renewal and differentiation of adult (satellite) muscle stem cells during muscle growth or following injury. Margaret Buckingham, Institut Pasteur, Paris, told us her most recent work on the role of mouse Pax3/7 in controlling the myogenic program. More specifically, she described that a negative feedback loop between Pax3 on Foxc2 expression is implicated in cell fate decisions of the multipotent Pax3/7 positive stem

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cells of the dermomyotome. Up-regulation of Foxc2 promotes endothelial and smooth muscle fates whereas Pax3/7 promotes myogenesis (Lagha *et al.*, 2009). Understanding the molecular details of how signalling from adjacent tissues effects the equilibrium between between Pax3/7 and Foxc2 expression and fate choice of multipotent progenitors is underway.

Peripheral and central nervous stem cells and adult neurogenesis

Ricardo Pardal, IBiS, Sevilla, introduced the audience to the carotid body, a peripheral chemoreceptor in mammals whose major role is to detect oxygen tension in the arterial blood and evoke hyperventilation in response to acute hypoxemia. His group has previously shown that growth of the carotid body which allows adaptation of the organism in situation of chronic hypoxia, as experienced by people who live at high altitudes, depends on the activation of neural progenitors able to proliferate and differentiate into new neuronal cells (Lopez-Barneo *et al.*, 2009). Here, he reported that carotid body stem cells change their phenotype from quiescence to proliferation and back to quiescence, in response to signalling from their niche, another example of intimate communications between stem cells and their microenvironnement. This communication was also stressed by Hernan López-Schier, CRG-PRBB, Barcelona, in his description of the regeneration of mechanosensory hair cells in the lateral line of zebrafish. He provided evidence for the existence of resident hair-cell progenitors and described the choreographed set of steps of the regenerative process leading from a hair-cell progenitor to a functional mechano-sensory organ. Emergence of oligodendrocyte precursors in the embryonic ventral spinal cord takes place at the same time as ventral neural progenitors stop producing neurons. Previous work by Cathy Soula, CBD, Toulouse, has shown that an increased concentration of the morphogen Sonic Hedgehog determines the timing of this transition. At this meeting, she described parallel experiments in chicken and mice suggesting that the Sulfatase 1 secreted enzyme, a regulator of the sulfation state of HSPGS, is a positive regulator of Shh signalling responsible for this ventroneuroglial switch. The balance between quiescence of neural stem cells and their recruitment to differentiate sets the limit to generation of neurons during adulthood. Laure Bally-Cuif, Hemholtz Zentrum, Munich and CNRS, Gif-sur-Yvette, reported that in the germinal zone of the zebrafish adult telencephalon neural progenitors transit back and forth between the quiescent and dividing states according to varying levels of Notch activity. Notch induction which drives progenitors to quiescence appears to be imposed by newly recruited progenitors on their neighbours, suggesting a self-limiting mechanism of neurogenesis in adult germinal zones. This work suggests for the first time that the equilibrium between quiescence and neurogenesis in the adult brain is controlled by fluctuations of Notch activity, via a lateral inhibition-like mechanism.

Beside invited speakers, there were very interesting short talks selected on abstracts. For example, Jennifer Croce, Villefranche-sur-mer, reported on the timing and molecular dynamics of endoderm segregation in the sea urchin embryo and the importance of a continuous Delta/Notch input in converting endomesodermal cells to a mesoderm fate (Croce and McClay, 2010). Daniel Mesnard, EPFL, Lausanne, described the role of proprotein convertase, furin and PACE4, provided by the extraembryonic ectodem in activating Nodal signalling in the adjacent epiblast during mouse gastrulation. By using a combination of furin-GFP expression and a protein convertase biosensor, he provided new evidence for the importance of paracrine protein convertase activity in the instructive extra-embryonic ectoderm to epiblast signalling. Myriam Roussigné, UCL, London, reported that FGF signalling functions during the establishment of left/right asymmetry in the brain by promoting the migration on the left side of the parapineal gland (Roussigne *et al.*, 2009).

Finally, 3 posters prizes, sponsored by the *Company of Biologists*, were awarded from the generally excellent presentations : Marie le Bouteiller, Institut Pasteur, Paris: Notchless regulation of adult HSC homeostasis in mice; Marie-Anaïs Tiberghien, CBD, Toulouse: Modulation of cell adhesion and segregation by the Hox protein Deformed in the Drosophila eye-antennal imaginal disc; Veronica Uribe, CNIC, Madrid: The role of Arid3 in heart development in mouse.

In summary, the SFBD/SEBD *Development Stem cells and Evolution* meeting yielded a stimulating synthesis of multiple and varied efforts aimed at understanding stem-cell properties in an Evo/Devo perspective.

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Alain Vincent and Eric Agius

Centre de Biologie du Développement, UMR 5547 CNRS/UPS, Toulouse, France

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