

# G·A·B·B·A

## DEVELOPMENTAL BIOLOGY MODULE INSTITUTO DE MEDICINA MOLECULAR, FAC. MEDICINA UNIV. LISBOA

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	Monday, 25 <sup>th</sup> March	Tuesday, 26 <sup>th</sup> March	Wednesday, 27 <sup>th</sup> March	Thursday, 28 <sup>th</sup> March
10-12h	Domingos Henrique <a href="http://imm.fm.ul.pt/web/imm/developmentalbiology">http://imm.fm.ul.pt/web/imm/developmentalbiology</a> Notch and neurogenesis	Leonor Saúde ( <a href="http://imm.fm.ul.pt/web/imm/udev">http://imm.fm.ul.pt/web/imm/udev</a> ) Left-Right asymmetry	1- A.Jacinto ( <b>9-11h!!</b> ) <a href="http://cedoc.unl.pt">http://cedoc.unl.pt</a> Tissue Morphogenesis and Repair  2- Diogo Castro ( <b>11-13h</b> ) <a href="http://www.igc.gulbenkian.pt/">http://www.igc.gulbenkian.pt/</a> Molecular Neurobiology	Tristan Rodriguez <a href="http://www1.imperial.ac.uk/medicine/people/tristan.rodriguez">http://www1.imperial.ac.uk/medicine/people/tristan.rodriguez</a> Axis establishment in the mouse embryo
14-17h	Fernando Giraldez <a href="http://www.upf.edu/devbiol/">http://www.upf.edu/devbiol/</a> Specification of sensory cells in the inner ear	José A. Belo ( <a href="http://www.cbme.ualg.pt/jbelo_cbme.html">http://www.cbme.ualg.pt/jbelo_cbme.html</a> ) Gastrulation	Élio Sucena <a href="http://www.igc.gulbenkian.pt/">http://www.igc.gulbenkian.pt/</a> Evolution and Development	Moisés Mallo <a href="http://www.igc.gulbenkian.pt/">http://www.igc.gulbenkian.pt/</a> Patterning and Morphogenesis

Location – Sala 6, Piso 0, Edifício Egas Moniz, Faculdade de Medicina da Universidade de Lisboa, Hospital Santa Maria, Av. Prof Egas Moniz, 1649-028, Lisboa. (See Map - do not pay attention to Meeting Point!).

**Please, be punctual for Lectures !!!**

This Developmental Biology Course is aimed at discussing some relevant topics in the field, with national and foreign speakers who will cover a broad range of themes and models. You can find information on the speakers and their research interests in the website addresses above.

## ABSTRACT FOR FERNANDO GIRALDEZ

### Signals and Factors in Ear Development

The function of the brain relies on the activity of an enormous number of different neurones that establish stereotyped connections. The generation of such diversity arises during embryonic development and depends on a precise allocation of competence states to cell progenitors and their development into precise cellular fates. The diversification of neuronal subtypes results from the combination of autonomous and cell-to-cell communication factors that act on neural progenitors. The developing inner ear is an interesting model system to address these questions. The basic functional unit of the ear consists of three elements of neural origin: the mechano-transducing hair-cells (HCs), the supporting cells (SCs), and the primary afferent neurons that connect hair cells to central neurones. All three elements derive from the otic vesicle, which in turn is the result of the proliferation, growth and invagination of the *otic placode*. The generation of hair cells, and otic neurons follows a stereotyped spatial and temporal pattern by which otic neurons become specified prior to hair cells and supporting cells.

How sensory patches develop? Sensory patches arise from a common neurosensory competent field that split into prosensory domains. Notch signalling is required for the specification of sensory organs and for the determination of hair cells. The latter function results from lateral inhibition, whereby Notch ligands are expressed in hair cells and signal to neighboring cells to prevent their differentiation. However, the prosensory function of Notch seems to operate through a different mechanism that is called lateral induction in which Notch signaling is propagated into a coherent field. By this mechanism, Notch activity restricts *Sox2* function and sensory competence to the sensory patches, providing an example of coupling between patterning and cell fate in development. But, how the same Notch signaling pathway operates both for lateral induction and lateral inhibition? We shall discuss some theoretical possibilities and experimental evidence that may shed some light on how this occurs.

How otic progenitors commit to hair cell fate? The commitment to the sensory fate is associated with the expression of *Atoh1*, a bHLH transcription factor that behaves as a master gene for hair cell fate specification. Therefore, the understanding of hair cell development is very much that of the onset and regulation of *Atoh1* expression. *Sox2* is a High Mobility Group (HMG) box domain transcription factor, belonging to the B1 subfamily of Sox proteins that are crucial for neural development. *Sox2* shows two seemingly contradictory functions: to promote neural competence of progenitors and at the same time to prevent their differentiation. In the inner ear, *Sox2* directly activates *Atoh1* through a transcriptional activator function. But besides, *Sox2* also promotes de expression of *Atoh1* inhibitors through an incoherent feed-forward loop that transiently silences *Atoh1* expression. The indication is that sensory competence is established very early in otic development by the activation of *Atoh1*. However, the incoherence in the *Sox2* response results in the procrastination of hair cell differentiation until later stages of development.

Reading:

Sarah Bray (2006) Notch signalling: a simple pathway becomes complex  
<http://www.nature.com/nrm/journal/v7/n9/full/nrm2009.html>

Neves et al., (2012) The Prosensory Function of Sox2 in the Chicken Inner Ear Relies on the Direct Regulation of *Atoh1*  
<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0030871>

See also

<http://www.ncbi.nlm.nih.gov/pubmed/23252974>

<http://www.ncbi.nlm.nih.gov/pubmed/23154195>

<http://www.ncbi.nlm.nih.gov/pubmed/21266409>