



Signalling in morphogenesis

Our research focuses on the genetic control of development, and in particular the role of cell communication mechanisms in development in the context of the whole organism. The work of many laboratories has allowed us to begin to understand the genetic logic behind development. We are now attempting

*to explain how these mechanisms impinge on cell behaviour and how changes in individual cells sum up to generate organs and the whole organism. For this purpose, we analyse these mechanisms in two model systems in *Drosophila*, namely Torso RTK signalling and the formation of the trachea. In particular, we have begun our studies at the interface between development and cell biology using tracheal development as a tool to unveil how transcription factors and signalling pathways regulate the mechanisms responsible for changes in the cell, such as migration, invagination and shape.*

The major outcomes of our research in 2009 can be broken into the following sections:

A functional antagonism between the *pgc* germline repressor and *torso* in the development of somatic cells

Segregation of the germline is a fundamental event during early development. In *Drosophila*, germ cells are specified at the posterior pole of the embryo by the germplasm. As zygotic expression is activated, germ cells remain transcriptionally silent owing to the polar granule component (Pgc), a small peptide present in germ cells. Somatic cells at both embryonic ends are specified by the torso (Tor) receptor tyrosine kinase, and in *tor* mutants the somatic cells closest to germ cells fail to cellularise correctly. We have shown that extra wild-type gene copies of *pgc* cause a similar cellularisation phenotype, and that both excessive *pgc* and a lack of *tor* are associated with impaired transcription in somatic cells. Moreover, a lack of *pgc* partly ameliorates the cellularisation defect of *tor* mutants, thus revealing a functional antagonism between *pgc* and *tor* in the specification of germline and somatic properties. As transcriptional quiescence is a general feature of germ cells, similar mechanisms might operate in many organisms to ‘protect’ somatic cells that adjoin germ cells from inappropriately succumbing to such quiescence.

Closca, a new gene required for both Torso RTK activation and vitelline membrane integrity. Germline proteins contribute to *Drosophila* eggshell composition

The *Drosophila* eggshell is a specialised extracellular matrix (ECM) that surrounds and protects the oocyte and the embryo until its eclosion. In addition, the vitelline membrane, the innermost layer of the eggshell, holds the local determinant required to activate the Torso RTK pathway, which establishes the embryonic terminal regions. We have identified and char-

acterised *closca*, a gene encoding a new member of a group of proteins which act non-redundantly in vitelline membrane biogenesis and in Torso signalling. We have also found that the Nasrat protein, another member of this group, is incorporated into the vitelline membrane, thereby indicating that the eggshell is a shared ECM that receives contributions from follicle cells and the germline. This observation also provides a new scenario that accounts for the long-known contribution of germline products to vitelline membrane biogenesis and to the follicle cell-dependent activation of the Torso receptor.

In vivo coupling of cell elongation and lumen formation in a single cell

Fine tubes form inside cells as they reach their target tissues in epithelial ducts and in angiogenesis. Although a very suggestive model of cell hollowing proposes that intracellular lumen arise

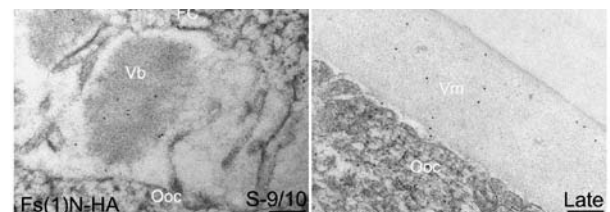


Figure 1. Immunoelectron microscopy of egg chambers bearing a *fs(1)Nasrat-HA* construct fixed with high pressure freezing (HPF) and stained with an anti-HA antibody (3F10). In stage 9/10 egg chamber staining is detected mainly in the vitelline bodies. In late egg chambers, labelling is detected in the vitelline membrane. Control egg chambers show no significant staining. Ooc, oocyte; FC, follicle cells; Vb, vitelline bodies; Vm, vitelline membrane. Bars, 200 nm. (image obtained at the Electron Microscopy facility, SCT-UB).

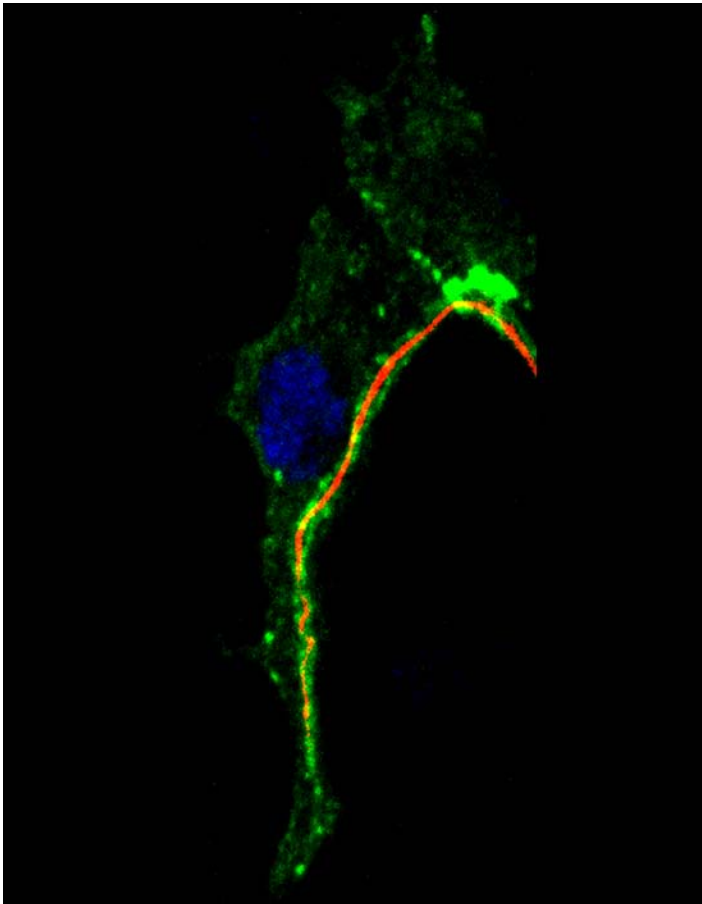
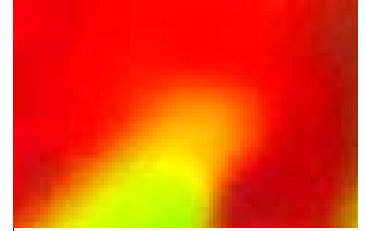


Figure 2. Confocal image of the terminal cell of a dorsal branch of the *Drosophila* embryonic tracheal system (nucleus of the terminal cell is detected by DSRF expression in blue). Baz-YFP expression (green) labels the apical membrane and lower green staining allows observation of cell shape. The intracellular lumen is detected by CBP (in red; image from L Gervais, obtained at IRB Barcelona's Advanced Digital Microscopy Core Facility).



Research Group Members

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by coalescence of intracellular vacuoles, how these tubes form *in vivo* remains an open question. We have addressed this issue by examining intracellular lumen formation in the *Drosophila* trachea. The main branches of the *Drosophila* tracheal system have an extracellular lumen, as their cells fold to form a tube. However, terminal cells, specialised cells in some of the main branches, form unicellular branches by generating an intracellular lumen. In contrast to the above-mentioned model, we have found that the intracellular lumen arises when an apical mem-

brane grows inwards the cell. In support of this observation, we have detected an appropriate subcellular compartmentalisation of distinct components of the intracellular trafficking machinery. We have also shown that both cellular elongation and lumen formation depend on a mechanism that is based on asymmetric actin accumulation and microtubule network organisation. Given the similarities in the formation of fine respiratory tubes and capillaries, we propose that an inward membrane growth model could account for lumen formation in these two processes.

Scientific output

Publications

De las Heras JM, Martinho RG, Lehmann R and Casanova J. A functional antagonism between the *pgc* germline repressor and *torso* in the development of somatic cells. *EMBO Rep*, **10**(9), 1059-65 (2009)

Research networks and grants

Ajuts per a grups de recerca reconeguts
Agency for Administration of University and Research Grants (AGAUR), SGR2008-00343 (2009-2013)
Principal investigator: Jordi Casanova

Cellular properties and morphogenesis. From genes to shape: analysis of morphogenesis in Drosophila and vertebrates
Spanish Ministry of Science and Innovation, Consolider CSD 2007-0008 (2007-2012)
Principal investigator: Jordi Casanova

Mecanismos de señalización celular y morfogénesis en el desarrollo de Drosophila
Spanish Ministry of Science and Innovation, Plan Nacional BFU2006-01935/BMC (2007-2009)
Principal investigator: Jordi Casanova

Regulación de los mecanismos celulares en la morfogénesis de Drosophila
Spanish Ministry of Science and Innovation, BFU2009-07629 (2009-2011)
Principal investigator: Jordi Casanova

Collaborations

*A functional antagonism between the *pgc* and *torso**
Ruth Lehmann, New York University (New York, USA) and Rui Martinhol, Gulbenkian Institute (Lisbon, Portugal)

*Identification and characterization of the gene *cloaca**
Vitor Barbosa, Gulbenkian Institute (Lisbon, Portugal)

Morphogenesis of the Drosophila tracheal tube
Veronique Brodu and Antoine Guichet, Institut Jacques Monod-CNRS (Paris, France)

New elements in the Drosophila terminal system
Stephan Luschnig, University of Zurich (Zurich, Switzerland)