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 elucidate the genetic logic behind development and we are now addressing how these mechanisms impinge on cell behaviour and how changes in individual cells sum up to generate organs and the whole organism. We are analysing these mechanisms in two model systems in *Drosophila*, namely Torso RTK signalling and the formation of the trachea. In particular, we have begun our work at the interphase between development and cell biology using tracheal formation to study how transcription factors and signalling pathways regulate the cellular mechanisms responsible for changes in cell shape and cell behaviour such as migration and invagination.

The major outcomes of our research in 2008 can be broken down into the following sections:

**Modulation of intracellular trafficking regulates cell intercalation in the *Drosophila* trachea**

Epithelial cells exchange places in a spatially oriented manner by means of intercalation, a fundamental mechanism underlying elongation during morphogenesis (Pilot and Lecuit, 2005). Epithelial cells are tightly coupled through distinct intercellular junctions, including adherens junctions. Whether trafficking-mediated regulation of adhesion through adherens junctions modulates intercalation *in vivo* remains controversial (Pilot and Lecuit, 2005; D'Souza-Schorey, 2005). In *Drosophila melanogaster*, cells in most branches intercalate during tracheal development. However, Wingless (Wg)-promoted expression of the transcription factor Spalt (Sal) in the dorsal trunk inhibits intercalation (Ribeiro et al., 2004) by an unknown mechanism.

In collaboration with Marta Llimargas (at IBMB-CSIC), we have examined the role of trafficking in tracheal intercalation and found that it requires endocytosis, whereas it is opposed by *Rab11*-mediated recycling in the dorsal trunk. Subapical *Rab11* accumulation is enhanced by *sal* and elevated *Rab11*-mediated recycling occurs in the dorsal trunk, thereby suggesting that upregulation of *Rab11* is one way in which *sal* inhibits intercalation. We found that *dRip11*, which regulates *Rab11* localisation and function (Ribeiro et al., 2004), is regulated by *sal* and can modulate intercalation. Finally, we observed that expression of E-cadherin (DE-cad), an
adherens junction component (Oda et al., 1994), and Rab11-compartment cargo (Classen et al., 2005; Langevin, 2005; Lock et al., 2005) are dynamically regulated by trafficking during tracheal development, and that such regulation modulates intercalation. Our work points to a mechanism by which trafficking of adhesion molecules regulates intercalation and shows how this mechanism is modulated in vivo to influence cell behaviour (Figure 1).

A functional antagonism between the pgc germ-line repressor and torso in the development of somatic cells

Segregation of the germ-line is a fundamental event during early development (see Strome and Lehmann 2007). In Drosophila, germ cells are specified at the posterior pole of the embryo by germplasm, and as zygotic expression is activated germ cells remain transcriptionally silent (Van Doren et al., 1998) owing to Polar granule component (Pgc), a small peptide present in germ cells (Martinho et al., 2004; Hanyu-Nakamura et al., 2008). Somatic cells at both embryonic ends are specified by the Torso (Tor) RTK and in tor mutants the somatic cells closest to the germ cells do not cellularise properly (Schüpbach and Wieschaus, 1986; Degelmann et al., 1986). In collaboration with Rui Martinho (Gulbenkian Institute) and Ruth Lehman (New York University), we have shown that extra wild-type gene copies of pgc cause a similar cellularisation phenotype and that both excessive pgc and lack of tor are associated with an impairment of transcription in somatic cells. Moreover, lack of pgc partially ameliorates the cellularisation defect of tor mutants, thus unveiling functional antagonism between pgc and tor in the specification of germ-line 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 abut germ cells from inappropriately succumbing to such quiescence (Figure 2).
Figure 2. Posterior poles of wild-type (A,D,G), 6x[pgc] (B,E,H) and tor (C,F,I) embryos. In red, anti-Neurotactin (Nrt) labels somatic but not germ cells; DAPI labels nuclei; in green, anti-Vas labels germ-cells. Groups of nuclei fall into the yolk in 6x[pgc] and tor mutants (arrows in E and F), some cells fail to complete cellularisation as shown by the lack of a basal membrane (ie, see arrowhead in E) and many cells have lost the typical epithelial elongated shape. Occasionally, a few nuclei fall into the yolk in wild-type. In 6x[pgc] (H) and tor (I) embryo, germ cells are found in the 'hole' between the somatic cells (figure from Jose M de las Heras).