Année de publication : 2012

Floris Bosveld, Isabelle Bonnet, Boris Guirao, Sham Tlili, Zhimin Wang, Ambre Petitalot, Raphaël Marchand, Pierre-Luc Bardet, Philippe Marcq, François Graner, Yohanns Bellaïche (2012 Apr 14)

Mechanical control of morphogenesis by Fat/Dachsous/Four-jointed planar cell polarity pathway.

Science (New York, N.Y.) : 724-7 : DOI : 10.1126/science.1221071

Résumé

During animal development, several planar cell polarity (PCP) pathways control tissue shape by coordinating collective cell behavior. Here, we characterize by means of multiscale imaging epithelium morphogenesis in the Drosophila dorsal thorax and show how the Fat/Dachsous/Four-jointed PCP pathway controls morphogenesis. We found that the proto-cadherin Dachsous is polarized within a domain of its tissue-wide expression gradient. Furthermore, Dachsous polarizes the myosin Dachs, which in turn promotes anisotropy of junction tension. By combining physical modeling with quantitative image analyses, we determined that this tension anisotropy defines the pattern of local tissue contraction that contributes to shaping the epithelium mainly via oriented cell rearrangements. Our results establish how tissue planar polarization coordinates the local changes of cell mechanical properties to control tissue morphogenesis.

Bertrand Jauffred, Yohanns Bellaiche (2012 Jan 6)

Analyzing frizzled signaling using fixed and live imaging of the asymmetric cell division of the Drosophila sensory organ precursor cell.

Methods in molecular biology (Clifton, N.J.) : 19-25 : DOI : 10.1007/978-1-61779-510-7_2

Résumé

When you look at the dorsal thorax of a fruitfly, you can easily get fascinated by the high degree of alignment of the bristles that show a strong polarization in their surface organization. This organization of cells in the plane of the epithelium is known as planar cell polarity (PCP), and was initially characterized in Drosophila melanogaster. This process is important in a broad variety of morphological cellular asymmetries in various organisms. In Drosophila, genetic studies of PCP mutants showed that the asymmetric division of the sensory organ precursor cell (pI cell) is polarized along the anterior-posterior axis by Frizzled receptor signaling. Here, we described two methods to image and analyze the PCP in the pI cell model.

Année de publication : 2011

Xavier Morin, Yohanns Bellaïche (2011 Jul 19)

Mitotic spindle orientation in asymmetric and symmetric cell divisions during

animal development.
Developmental cell : 102-19 : DOI : 10.1016/j.devcel.2011.06.012

Résumé

The orientation of the mitotic spindle has been proposed to control cell fate choices, tissue architecture, and tissue morphogenesis. Here, we review the mechanisms regulating the orientation of the axis of division and cell fate choices in classical models of asymmetric cell division. We then discuss the mechanisms of mitotic spindle orientation in symmetric cell divisions and its possible implications in tissue morphogenesis. Many recent studies show that future advances in the field of mitotic spindle orientation will arise from combinations of physical perturbation and modeling with classical genetics and developmental biology approaches.

Année de publication : 2010

Juliette D Godin, Kelly Colombo, Maria Molina-Calavita, Guy Keryer, Diana Zala, Bénédicte C Charrin, Paula Dietrich, Marie-Laure Volvert, François Guillemot, Ioannis Dragatsis, Yohanns Bellaiche, Frédéric Saudou, Laurent Nguyen, Sandrine Humbert (2010 Aug 11)
Huntingtin is required for mitotic spindle orientation and mammalian neurogenesis.
Neuron : 392-406 : DOI : 10.1016/j.neuron.2010.06.027

Résumé

Huntingtin is the protein mutated in Huntington's disease, a devastating neurodegenerative disorder. We demonstrate here that huntingtin is essential to control mitosis. Huntingtin is localized at spindle poles during mitosis. RNAi-mediated silencing of huntingtin in cells disrupts spindle orientation by mislocalizing the p150(Glued) subunit of dynactin, dynein, and the large nuclear mitotic apparatus NuMA protein. This leads to increased apoptosis following mitosis of adherent cells in vitro. In vivo inactivation of huntingtin by RNAi or by ablation of the Hdh gene affects spindle orientation and cell fate of cortical progenitors of the ventricular zone in mouse embryos. This function is conserved in Drosophila, the specific disruption of Drosophila huntingtin in neuroblast precursors leading to spindle misorientation. Moreover, Drosophila huntingtin restores spindle misorientation in mammalian cells. These findings reveal an unexpected role for huntingtin in dividing cells, with potential important implications in health and disease.

Marion Ségalen, Christopher A Johnston, Charlotte A Martin, Julien G Dumortier, Kenneth E Prehoda, Nicolas B David, Chris Q Doe, Yohanns Bellaïche (2010 Apr 19)
The Fz-Dsh planar cell polarity pathway induces oriented cell division via Mud/NuMA in Drosophila and zebrafish.
Developmental cell : 740-52 : DOI : 10.1016/j.devcel.2010.10.004

Résumé

The Frizzled receptor and Dishevelled effector regulate mitotic spindle orientation in both vertebrates and invertebrates, but how Dishevelled orients the mitotic spindle is unknown. Using the Drosophila S2 cell « induced polarity » system, we find that Dishevelled cortical polarity is sufficient to orient the spindle and that Dishevelled's DEP domain mediates this function. This domain binds a C-terminal domain of Mud (the Drosophila NuMA ortholog), and Mud is required for Dishevelled-mediated spindle orientation. In Drosophila, Frizzled-Dishevelled planar cell polarity (PCP) orients the sensory organ precursor (pI) spindle along the anterior-posterior axis. We show that Dishevelled and Mud colocalize at the posterior cortex of pI, Mud localization at the posterior cortex requires Dsh, and Mud loss-of-function randomizes spindle orientation. During zebrafish gastrulation, the Wnt11-Frizzled-Dishevelled PCP pathway orients spindles along the animal-vegetal axis, and reducing NuMA levels disrupts spindle orientation. Overall, we describe a Frizzled-Dishevelled-NuMA pathway that orients division from Drosophila to vertebrates.

Maria-Isabel Yuseff, Anne Reversat, Danielle Lankar, Jheimmy Diaz, Isabelle Fanget, Paolo Pierobon, Violaine Randrian, Nathanael Larochette, Fulvia Vascotto, Chantal Desdouets, Bertrand Jauffred, Yohanns Bellaiche, Stéphane Gasman, François Darchen, Claire Desnos, Ana-Maria Lennon-Duménil (2010 Mar 11)

Polarized secretion of lysosomes at the B cell synapse couples antigen extraction to processing and presentation.

Immunity : 361-74 : DOI : 10.1016/j.immuni.2011.07.008

Résumé

Engagement of the B cell receptor (BCR) by surface-tethered antigens (Ag) leads to formation of a synapse that promotes Ag uptake for presentation onto major histocompatibility complex class II (MHCII) molecules. We have highlighted the membrane trafficking events and associated molecular mechanisms involved in Ag extraction and processing at the B cell synapse. MHCII-containing lysosomes are recruited to the synapse where they locally undergo exocytosis, allowing synapse acidification and the extracellular release of hydrolases that promote the extraction of the immobilized Ag. Lysosome recruitment and secretion results from the polarization of the microtubule-organizing center (MTOC), which relies on the cell division cycle (Cdc42)-downstream effector, atypical protein kinase C (aPKCζ). aPKCζ is phosphorylated upon BCR engagement, associates to lysosomal vesicles, and is required for their polarized secretion at the B cell synapse. Regulation of B lymphocyte polarity therefore emerges as a central mechanism that couples Ag extraction to Ag processing and presentation.

Année de publication : 2008

Pierre Fichelson, Clara Moch, Kenzo Ivanovitch, Charlotte Martin, Clara M Sidor, Jean-Antoine

Lepesant, Yohanns Bellaiche, Jean-René Huynh (2008 Nov 14)
Live-imaging of single stem cells within their niche reveals that a U3snoRNP component segregates asymmetrically and is required for self-renewal in Drosophila.
Nature cell biology : 685-93 : DOI : 10.1038/ncb1874

Résumé

Stem cells generate self-renewing and differentiating progeny over many rounds of asymmetric divisions. How stem cell growth rate and size are maintained over time remains unknown. We isolated mutations in a Drosophila melanogaster gene, wicked (wcd), which induce premature differentiation of germline stem cells (GSCs). Wcd is a member of the U3 snoRNP complex required for pre-ribosomal RNA maturation. This general function of Wcd contrasts with its specific requirement for GSC self-renewal. However, live imaging of GSCs within their niche revealed a pool of Wcd-forming particles that segregate asymmetrically into the GSCs on mitosis, independently of the Dpp signal sent by the niche. A fraction of Wcd also segregated asymmetrically in dividing larval neural stem cells (NSCs). In the absence of Wcd, NSCs became smaller and produced fewer neurons. Our results show that regulation of ribosome synthesis is a crucial parameter for stem cell maintenance and function.

Andrea Leibfried, Robert Fricke, Matthew J Morgan, Sven Bogdan, Yohanns Bellaiche (2008 Nov 4)
Drosophila Cip4 and WASp define a branch of the Cdc42-Par6-aPKC pathway regulating E-cadherin endocytosis.
Current biology : CB : 1639-48 : DOI : 10.1016/j.cub.2008.09.063

Résumé

Integral to the function and morphology of the epithelium is the lattice of cell-cell junctions known as adherens junctions (AJs). AJ stability and plasticity relies on E-Cadherin exocytosis and endocytosis. A mechanism regulating E-Cadherin (E-Cad) exocytosis to the AJs has implicated proteins of the exocyst complex, but mechanisms regulating E-Cad endocytosis from the AJs remain less well understood.

Année de publication : 2007

Andrea Leibfried, Yohanns Bellaïche (2007 Jul 27)
Functions of endosomal trafficking in Drosophila epithelial cells.
Current opinion in cell biology : 446-52

Résumé

The mechanisms underlying endosomal trafficking have been mostly dissected in yeast and mammalian tissue culture cells. Here, we review recent advances in the understanding of the role of endosomal trafficking in Drosophila epithelial cells. We focus on endosomal pathways that control cell polarization, cell growth, cell fate and epithelial cell rearrangement. We expect that mechanistic studies in mammalian cells and functional studies in invertebrates will continue to synergize to provide a comprehensive view of the role of endosomal trafficking in epithelial tissue organization and functions.

Année de publication : 2006

Maria Balakireva, Carine Rossé, Johanna Langevin, Yu-chen Chien, Michel Gho, Geneviève Gonzy-Treboul, Stéphanie Voegeling-Lemaire, Sandra Aresta, Jean-Antoine Lepesant, Yohanns Bellaiche, Michael White, Jacques Camonis (2006 Sep 25)

The Ral/exocyst effector complex counters c-Jun N-terminal kinase-dependent apoptosis in Drosophila melanogaster.

Molecular and cellular biology : 8953-63

Résumé

Ral GTPase activity is a crucial cell-autonomous factor supporting tumor initiation and progression. To decipher pathways impacted by Ral, we have generated null and hypomorph alleles of the Drosophila melanogaster Ral gene. Ral null animals were not viable. Reduced Ral expression in cells of the sensory organ lineage had no effect on cell division but led to postmitotic cell-specific apoptosis. Genetic epistasis and immunofluorescence in differentiating sensory organs suggested that Ral activity suppresses c-Jun N-terminal kinase (JNK) activation and induces p38 mitogen-activated protein (MAP) kinase activation. HPK1/GCK-like kinase (HGK), a MAP kinase kinase kinase kinase that can drive JNK activation, was found as an exocyst-associated protein in vivo. The exocyst is a Ral effector, and the epistasis between mutants of Ral and of msn, the fly ortholog of HGK, suggest the functional relevance of an exocyst/HGK interaction. Genetic analysis also showed that the exocyst is required for the execution of Ral function in apoptosis. We conclude that in Drosophila Ral counters apoptotic programs to support cell fate determination by acting as a negative regulator of JNK activity and a positive activator of p38 MAP kinase. We propose that the exocyst complex is Ral executioner in the JNK pathway and that a cascade from Ral to the exocyst to HGK would be a molecular basis of Ral action on JNK.

Sébastien Courty, Camilla Luccardini, Yohanns Bellaiche, Giovanni Cappello, Maxime Dahan (2006 Jul 13)

Tracking individual kinesin motors in living cells using single quantum-dot imaging.

Nano letters : 1491-5

Résumé

We report a simple method using semiconductor quantum dots (QDs) to track the motion of intracellular proteins with a high sensitivity. We characterized the in vivo motion of individual QD-tagged kinesin motors in living HeLa cells. Single-molecule measurements provided important parameters of the motor, such as its velocity and processivity, as well as an estimate of the force necessary to carry a QD. Our measurements demonstrate the importance of single-molecule experiments in the investigation of intracellular transport as well as the potential of single quantum-dot imaging for the study of important processes such as cellular trafficking, cell polarization, and division.

Année de publication : 2005

Nicolas B David, Charlotte A Martin, Marion Segalen, François Rosenfeld, François Schweisguth, Yohanns Bellaïche (2005 Oct 18)

Drosophila Ric-8 regulates Galphai cortical localization to promote Galphai-dependent planar orientation of the mitotic spindle during asymmetric cell division.

Nature cell biology : 1083-90

Résumé

Localization and activation of heterotrimeric G proteins have a crucial role during asymmetric cell division. The asymmetric division of the Drosophila sensory precursor cell (pI) is polarized along the antero-posterior axis by Frizzled signalling and, during this division, activation of Galphai depends on Partner of Inscuteable (Pins). We establish here that Ric-8, which belongs to a family of guanine nucleotide-exchange factors for Galphai, regulates cortical localization of the subunits Galphai and Gbeta13F. Ric-8, Galphai and Pins are not necessary for the control of the anteroposterior orientation of the mitotic spindle during pI cell division downstream of Frizzled signalling, but they are required for maintainance of the spindle within the plane of the epithelium. On the contrary, Frizzled signalling orients the spindle along the antero-posterior axis but also tilts it along the apico-basal axis. Thus, Frizzled and heterotrimeric G-protein signalling act in opposition to ensure that the spindle aligns both in the plane of the epithelium and along the tissue polarity axis.

Johanna Langevin, Matthew J Morgan, Jean-Baptiste Sibarita, Sandra Aresta, Mala Murthy, Thomas Schwarz, Jacques Camonis, Yohanns Bellaïche (2005 Oct 15)

Drosophila exocyst components Sec5, Sec6, and Sec15 regulate DE-Cadherin trafficking from recycling endosomes to the plasma membrane.

Developmental cell : 365-76

Résumé

The E-Cadherin-catenin complex plays a critical role in epithelial cell-cell adhesion, polarization, and morphogenesis. Here, we have analyzed the mechanism of Drosophila E-Cadherin (DE-Cad) localization. Loss of function of the Drosophila exocyst components sec5,

sec6, and sec15 in epithelial cells results in DE-Cad accumulation in an enlarged Rab11 recycling endosomal compartment and inhibits DE-Cad delivery to the membrane. Furthermore, Rab11 and Armadillo interact with the exocyst components Sec15 and Sec10, respectively. Our results support a model whereby the exocyst regulates DE-Cadherin trafficking, from recycling endosomes to sites on the epithelial cell membrane where Armadillo is located.

Johanna Langevin, Roland Le Borgne, François Rosenfeld, Michel Gho, François Schweisguth, Yohanns Bellaïche (2005 May 27)
Lethal giant larvae controls the localization of notch-signaling regulators numb, neuralized, and Sanpodo in Drosophila sensory-organ precursor cells.
Current biology : CB : 955-62

Résumé

Asymmetric distribution of fate determinants is a fundamental mechanism underlying the acquisition of distinct cell fates during asymmetric division. In Drosophila neuroblasts, the apical DmPar6/DaPKC complex inhibits Lethal giant larvae (Lgl) to promote the basal localization of fate determinants. In contrast, in the sensory precursor (pI) cells that divide asymmetrically with a planar polarity, Lgl inhibits Notch signaling in the anterior pI daughter cell, pIIb, by a yet-unknown mechanism. We show here that Lgl promotes the cortical recruitment of Partner of Numb (Pon) and regulates the asymmetric distribution of the fate determinants Numb and Neuralized during the pI cell division. Analysis of Pon-GFP and Histone2B-mRFP distribution in two-color movies confirmed that Lgl regulates Pon localization. Moreover, posterior DaPKC restricts Lgl function to the anterior cortex at mitosis. Thus, Lgl functions similarly in neuroblasts and in pI cells. We also show that Lgl promotes the acquisition of the pIIb cell fate by inhibiting the plasma membrane localization of Sanpodo and thereby preventing the activation of Notch signaling in the anterior pI daughter cell. Thus, Lgl regulates cell fate by controlling Pon cortical localization, asymmetric localization of Numb and Neuralized, and plasma-membrane localization of Sandopo.

Année de publication : 2004

Stéphane Audebert, Christel Navarro, Claire Nourry, Sylvette Chasserot-Golaz, Patrick Lécine, Yohanns Bellaïche, Jean-Luc Dupont, Richard T Premont, Christine Sempéré, Jean-Marc Strub, Alain Van Dorsselaer, Nicolas Vitale, Jean-Paul Borg (2004 Jun 9)
Mammalian Scribble forms a tight complex with the betaPIX exchange factor.
Current biology : CB : 987-95

Résumé

Drosophila Scribble is implicated in the development of normal synapse structure and epithelial tissues, but it remains unclear how it plays a role and which process it controls. The mammalian homolog of Scribble, hScrib, has a primary structure and subcellular

localization similar to that of its fly homolog, but its function remains unknown. Here we have used tandem mass spectrometry to identify major components of the hScrib network. We show that it includes betaPIX (also called Cool-1), a guanine nucleotide exchange factor (GEF), and its partner GIT1 (also called p95-APP1), a GTPase activating protein (GAP). betaPIX directly binds to the hScrib PDZ domains, and the hScrib/betaPIX complex is efficiently recovered in epithelial and neuronal cells and tissues. In cerebellar granule cell cultures, hScrib and betaPIX are both partially localized at neuronal presynaptic compartments. Furthermore, we show that hScrib is required to anchor betaPIX at the cell cortex and that dominant-negative betaPIX or hScrib proteins can each inhibit Ca2+-dependent exocytosis in neuroendocrine PC12 cells, demonstrating a functional relationship between these proteins. These data reveal the existence of a tight hScrib/betaPIX interaction and suggest that this complex potentially plays a role in neuronal transmission.