Année de publication : 2017

Jérémy Magescas, Lucie Sengmanivong, Amandine Viau, Adeline Mayeux, Tien Dang, Martine Burtin, Ulf J Nilsson, Hakon Leffler, Françoise Poirier, Fabiola Terzi, Delphine Delacour (2017 May 5)

Spindle pole cohesion requires glycosylation-mediated localization of NuMA.

Scientific reports : 1474 : DOI : 10.1038/s41598-017-01614-6

Résumé

Glycosylation is critical for the regulation of several cellular processes. One glycosylation pathway, the unusual O-linked β-N-acetylglucosamine glycosylation (O-GlcNAcylation) has been shown to be required for proper mitosis, likely through a subset of proteins that are O-GlcNAcylated during metaphase. As lectins bind glycosylated proteins, we asked if specific lectins interact with mitotic O-GlcNAcylated proteins during metaphase to ensure correct cell division. Galectin-3, a small soluble lectin of the Galectin family, is an excellent candidate, as it has been previously described as a transient centrosomal component in interphase and mitotic epithelial cells. In addition, it has recently been shown to associate with basal bodies in motile cilia, where it stabilizes the microtubule-organizing center (MTOC). Using an experimental mouse model of chronic kidney disease and human epithelial cell lines, we investigate the role of Galectin-3 in dividing epithelial cells. Here we find that Galectin-3 is essential for metaphase where it associates with NuMA in an O-GlcNAcylation-dependent manner. We provide evidence that the NuMA-Galectin-3 interaction is important for mitotic spindle cohesion and for stable NuMA localization to the spindle pole, thus revealing that Galectin-3 is a novel contributor to epithelial mitotic progress.

Julie Salomon, Cécile Gaston, Jérémy Magescas, Boris Duvauchelle, Danielle Canioni, Lucie Sengmanivong, Adeline Mayeux, Grégoire Michaux, Florence Campeotto, Julie Lemale, Jérôme Viala, Françoise Poirier, Nicolas Minc, Jacques Schmitz, Nicole Brousse, Benoit Ladoux, Olivier Goulet, Delphine Delacour (2017 Jan 14)

Contractile forces at tricellular contacts modulate epithelial organization and monolayer integrity.

Nature communications : 13998 : DOI : 10.1038/ncomms13998

Résumé

Monolayered epithelia are composed of tight cell assemblies that ensure polarized exchanges. EpCAM, an unconventional epithelial-specific cell adhesion molecule, is assumed to modulate epithelial morphogenesis in animal models, but little is known regarding its cellular functions. Inspired by the characterization of cellular defects in a rare EpCAM-related human intestinal disease, we find that the absence of EpCAM in enterocytes results in an aberrant apical domain. In the course of this pathological state, apical translocation towards tricellular contacts (TCs) occurs with striking tight junction belt displacement. These unusual cell organization and intestinal tissue defects are driven by the loss of actomyosin network

homoeostasis and contractile activity clustering at TCs, yet is reversed by myosin-II inhibitor treatment. This study reveals that adequate distribution of cortical tension is crucial for individual cell organization, but also for epithelial monolayer maintenance. Our data suggest that EpCAM modulation protects against epithelial dysplasia and stabilizes human tissue architecture.

Année de publication : 2016

Selma Maacha, Océane Anezo, Malika Foy, Géraldine Liot, Laurence Mery, Cécile Laurent, Xavier Sastre-Garau, Sophie Piperno-Neumann, Nathalie Cassoux, Nathalie Planque, Simon Saule (2016 Apr 21)

Protein Tyrosine Phosphatase 4A3 (PTP4A3) Promotes Human Uveal Melanoma Aggressiveness Through Membrane Accumulation of Matrix Metalloproteinase 14 (MMP14).

Investigative ophthalmology & visual science : 1982-90 : DOI : 10.1167/iovs.15-18780

Résumé

To study PTP4A3 phosphatase and MMP14 metalloprotease synergy in uveal melanoma aggressiveness.

Tao Zou, Fatimata Dembele, Anne Beugnet, Lucie Sengmanivong, Ario de Marco, Min-Hui Li (2016 Mar 24)

Nanobody-functionalized polymersomes.

Journal of controlled release : official journal of the Controlled Release Society : e79-80 : DOI : 10.1016/j.jconrel.2015.05.132

Résumé

Carlos A Niño, David Guet, Alexandre Gay, Sergine Brutus, Frédéric Jourquin, Shweta Mendiratta, Jean Salamero, Vincent Géli, Catherine Dargemont (2016 Jan 20)

Posttranslational marks control architectural and functional plasticity of the nuclear pore complex basket.

The Journal of cell biology : 167-80 : DOI : 10.1083/jcb.201506130

Résumé

The nuclear pore complex (NPC) serves as both the unique gate between the nucleus and the cytoplasm and a major platform that coordinates nucleocytoplasmic exchanges, gene expression, and genome integrity. To understand how the NPC integrates these functional constraints, we dissected here the posttranslational modifications of the nuclear basket

protein Nup60 and analyzed how they intervene to control the plasticity of the NPC. Combined approaches highlight the role of monoubiquitylation in regulating the association dynamics of Nup60 and its partner, Nup2, with the NPC through an interaction with Nup84, a component of the Y complex. Although major nuclear transport routes are not regulated by Nup60 modifications, monoubiquitylation of Nup60 is stimulated upon genotoxic stress and regulates the DNA-damage response and telomere repair. Together, these data reveal an original mechanism contributing to the plasticity of the NPC at a molecular-organization and functional level.

Cédric Delevoye, Xavier Heiligenstein, Léa Ripoll, Floriane Gilles-Marsens, Megan K Dennis, Ricardo A Linares, Laura Derman, Avanti Gokhale, Etienne Morel, Victor Faundez, Michael S Marks, Graça Raposo (2016 Jan 4)

BLOC-1 Brings Together the Actin and Microtubule Cytoskeletons to Generate Recycling Endosomes.

Current biology : CB : 1-13 : DOI : 10.1016/j.cub.2015.11.020

Résumé

Recycling endosomes consist of a tubular network that emerges from vacuolar sorting endosomes and diverts cargoes toward the cell surface, the Golgi, or lysosome-related organelles. How recycling tubules are formed remains unknown. We show that recycling endosome biogenesis requires the protein complex BLOC-1. Mutations in BLOC-1 subunits underlie an inherited disorder characterized by albinism, the Hermansky-Pudlak Syndrome, and are associated with schizophrenia risk. We show here that BLOC-1 coordinates the kinesin KIF13A-dependent pulling of endosomal tubules along microtubules to the Annexin A2/actin-dependent stabilization and detachment of recycling tubules. These components cooperate to extend, stabilize and form tubular endosomal carriers that function in cargo recycling and in the biogenesis of pigment granules in melanocytic cells. By shaping recycling endosomal tubules, our data reveal that dysfunction of the BLOC-1-KIF13A-Annexin A2 molecular network underlies the pathophysiology of neurological and pigmentary disorders.

Topkaya D., Lafont D., Poyer F., Garcia G., Albrieux F., Maillard P., Bretonniere Y., Dumoulin F. (2016 Jan 1)

Design of an amphiphilic porphyrin exhibiting high in vitro photocytotoxicity

NEW JOURNAL OF CHEMISTRY : 40 : 2044-2050 : DOI : 10.1039/c5nj02716k

Résumé

A porphyrin monosubstituted by three triethyleneglycol chains grafted on a pentaerythritol skeleton was designed to display an optimized amphiphilicity for an enhanced cellular uptake and thus to exert enhanced photocytotoxicity. This porphyrin proved to be an excellent photosensitiser with submicromolar IC50.

Année de publication : 2015

Velot L., Molina A., Rodrigues-Ferreira S., Nehlig A., Bouchet B.P., Morel M., Leconte L., Serre L., Arnal I., Braguer D., Savina A., Honore S., Nahmias C. (2015 Dec 22)

Negative regulation of EB1 turnover at microtubule plus ends by interaction with microtubule-associated protein ATIP3.

Oncotarget : 6 : 43557-70 : DOI : 10.18632/oncotarget.6196

Résumé

The regulation of microtubule dynamics is critical to ensure essential cell functions. End binding protein 1 (EB1) is a master regulator of microtubule dynamics that autonomously binds an extended GTP/GDP-Pi structure at growing microtubule ends and recruits regulatory proteins at this location. However, negative regulation of EB1 association with growing microtubule ends remains poorly understood. We show here that microtubule-associated tumor suppressor ATIP3 interacts with EB1 through direct binding of a non-canonical proline-rich motif. Results indicate that ATIP3 does not localize at growing microtubule ends and that in situ ATIP3-EB1 molecular complexes are mostly detected in the cytosol. We present evidence that a minimal EB1-interacting sequence of ATIP3 is both necessary and sufficient to prevent EB1 accumulation at growing microtubule ends in living cells and that EB1-interaction is involved in reducing cell polarity. By fluorescence recovery of EB1-GFP after photobleaching, we show that ATIP3 silencing accelerates EB1 turnover at microtubule ends with no modification of EB1 diffusion in the cytosol. We propose a novel mechanism by which ATIP3-EB1 interaction indirectly reduces the kinetics of EB1 exchange on its recognition site, thereby accounting for negative regulation of microtubule dynamic instability. Our findings provide a unique example of decreased EB1 turnover at growing microtubule ends by cytosolic interaction with a tumor suppressor.

Rogov A., Irondelle M., Gomes F.R., Bode J., Staedler D., Passemard S., Courvoisier S., Yamamoto Y., Waharte F., Ciepielewski D., Rideau P., Gerber-Lemaire S., Alves F., Salamero J., Bonacina L., Wolf J.P. (2015 Oct 1)

Simultaneous Multiharmonic Imaging of Nanoparticles in Tissues for Increased Selectivity

ACS Photonics : 2 : pp 1416-1422

Résumé

We investigate the use of bismuth ferrite (BFO) nanoparticles for tumor tissue labeling in combination with infrared multiphoton excitation at 1250 nm. We report the efficient and simultaneous generation of second- and third-harmonic signals by the nanoparticles. On this basis, we set up a novel imaging protocol based on the co-localization of the two harmonic signals and demonstrate its benefits in terms of increased selectivity against endogenous background sources in tissue samples. Finally, we discuss the use of BFO nanoparticles as mapping reference structures for correlative light-electron microscopy.

Jani R.A., Purushothaman L.K., Rani S., Bergam P., Setty S.R.G. (2015 Sep 1)
STX13 regulates cargo delivery from recycling endosomes during melanosome biogenesis.
Journal of cell science : 128 : 3263-76 : DOI : 10.1242/jcs.171165

Résumé

Melanosomes are a class of lysosome-related organelles produced by melanocytes. Biogenesis of melanosomes requires the transport of melanin-synthesizing enzymes from tubular recycling endosomes to maturing melanosomes. The SNARE proteins involved in these transport or fusion steps have been poorly studied. We found that depletion of syntaxin 13 (STX13, also known as STX12), a recycling endosomal Qa-SNARE, inhibits pigment granule maturation in melanocytes by rerouting the melanosomal proteins such as TYR and TYRP1 to lysosomes. Furthermore, live-cell imaging and electron microscopy studies showed that STX13 co-distributed with melanosomal cargo in the tubular-vesicular endosomes that are closely associated with the maturing melanosomes. STX family proteins contain an N-terminal regulatory domain, and deletion of this domain in STX13 increases both the SNARE activity in vivo and melanosome cargo transport and pigmentation, suggesting that STX13 acts as a fusion SNARE in melanosomal trafficking pathways. In addition, STX13-dependent cargo transport requires the melanosomal R-SNARE VAMP7, and its silencing blocks the melanosome maturation, reflecting a defect in endosome-melanosome fusion. Moreover, we show mutual dependency between STX13 and VAMP7 in regulating their localization for efficient cargo delivery to melanosomes.

Ahmed S.S., Messali Z., Ouahabi A., Trepout S., Messaoudi C., Marco S. (2015 Jan 1)
Nonparametric Denoising Methods Based on Contourlet Transform with Sharp Frequency Localization: Application to Low Exposure Time Electron Microscopy Images
Entropy : 17 : 3461 : DOI : 10.3390/e17053461

Résumé

Image denoising is a very important step in cryo-transmission electron microscopy (cryo-TEM) and the energy filtering TEM images before the 3D tomography reconstruction, as it addresses the problem of high noise in these images, that leads to a loss of the contained information. High noise levels contribute in particular to difficulties in the alignment required for 3D tomography reconstruction. This paper investigates the denoising of TEM images that are acquired with a very low exposure time, with the primary objectives of enhancing the quality of these low-exposure time TEM images and improving the alignment process. We propose denoising structures to combine multiple noisy copies of the TEM images. The structures are based on Bayesian estimation in the transform domains instead of the spatial domain to build a novel feature preserving image denoising structures; namely: wavelet domain, the contourlet transform domain and the contourlet transform with sharp frequency localization. Numerical image denoising experiments demonstrate the performance of the Bayesian approach in the contourlet transform domain in terms of improving the signal to noise ratio (SNR) and recovering fine details that may be hidden in the data. The SNR and

the visual quality of the denoised images are considerably enhanced using these denoising structures that combine multiple noisy copies. The proposed methods also enable a reduction in the exposure time.

Année de publication : 2012

Song W., Zukor H., Lin S.H., Liberman A., Tavitian A., Mui J., Vali H., Fillebeen C., Pantopoulos K., Wu T.D., Guerquin-Kern J.L., Schipper H.M. (2012 Oct 1)

Unregulated brain iron deposition in transgenic mice over-expressing HMOX1 in the astrocytic compartment.

Journal of neurochemistry : 123 : 325-36 : DOI : 10.1111/j.1471-4159.2012.07914.x

Résumé

The mechanisms responsible for pathological iron deposition in the aging and degenerating mammalian CNS remain poorly understood. The stress protein, HO-1 mediates the degradation of cellular heme to biliverdin/bilirubin, free iron, and CO and is up-regulated in the brains of persons with Alzheimer&aquote;s disease and Parkinson&aquote;s disease. HO-1 induction in primary astroglial cultures promotes deposition of non-transferrin iron, mitochondrial damage and macroautophagy, and predisposes cocultured neuronal elements to oxidative injury. To gain a better appreciation of the role of glial HO-1 in vivo, we probed for aberrant brain iron deposition using Perls&aquote; method and dynamic secondary ion mass spectrometry in novel, conditional GFAP.HMOX1 transgenic mice that selectively over-express human HO-1 in the astrocytic compartment. At 48 weeks, the GFAP.HMOX1 mice exhibited increased deposits of glial iron in hippocampus and other subcortical regions without overt changes in iron-regulatory and iron-binding proteins relative to age-matched wild-type animals. Dynamic secondary ion mass spectrometry revealed abundant FeO^- signals in the transgenic, but not wild-type, mouse brain that colocalized to degenerate mitochondria and osmiophilic cytoplasmic inclusions (macroautophagy) documented by TEM. Sustained up-regulation of HO-1 in astrocytes promotes pathological brain iron deposition and oxidative mitochondrial damage characteristic of Alzheimer&aquote;s disease-affected neural tissues. Curtailment of glial HO-1 hyperactivity may limit iron-mediated cytotoxicity in aging and degenerating neural tissues.

Bosak T., Liang B., Wu T.D., Templer S.P., Evans A., Vali H., Guerquin-Kern J.L., Klepac-Ceraj V., Sim M.S., Mui J. (2012 Sep 1)

Cyanobacterial diversity and activity in modern conical microbialites.

Geobiology : 10 : 384-401 : DOI : 10.1111/j.1472-4669.2012.00334.x

Résumé

Modern conical microbialites are similar to some ancient conical stromatolites, but growth, behavior and diversity of cyanobacteria in modern conical microbialites remain poorly characterized. Here, we analyze the diversity of cyanobacterial 16S rRNA gene sequences in

conical microbialites from 14 ponds fed by four thermal sources in Yellowstone National Park and compare cyanobacterial activity in the tips of cones and in the surrounding topographic lows (mats), respectively, by high-resolution mapping of labeled carbon. Cones and adjacent mats contain similar 16S rRNA gene sequences from genetically distinct clusters of filamentous, non-heterocystous cyanobacteria from Subsection III and unicellular cyanobacteria from Subsection I. These sequences vary among different ponds and between two sampling years, suggesting that coniform mats through time and space contain a number of cyanobacteria capable of vertical aggregation, filamentous cyanobacteria incapable of initiating cone formation and unicellular cyanobacteria. Unicellular cyanobacteria are more diverse in topographic lows, where some of these organisms respond to nutrient pulses more rapidly than thin filamentous cyanobacteria. The densest active cyanobacteria are found below the upper 50 µm of the cone tip, whereas cyanobacterial cells in mats are less dense, and are more commonly degraded or encrusted by silica. These spatial differences in cellular activity and density within macroscopic coniform mats imply a strong role for diffusion limitation in the development and the persistence of the conical shape. Similar mechanisms may have controlled the growth, morphology and persistence of small coniform stromatolites in shallow, quiet environments throughout geologic history.

Année de publication : 2011

Gardette M., Papon J., Bonnet M., Desbois N., Labarre P., Wu T.D., Miot-Noirault E., Madelmont J.C., Guerquin-Kern J.L., Chezal J.M., Moins N. (2011 Dec 1)

Evaluation of new iodinated acridine derivatives for targeted radionuclide therapy of melanoma using 125I, an Auger electron emitter.

Investigational new drugs : 29 : 1253-63 : DOI : 10.1007/s10637-010-9471-x

Résumé

The increasing incidence of melanoma and the lack of effective therapy on the disseminated form have led to an urgent need for new specific therapies. Several iodobenzamides or analogs are known to possess specific affinity for melanoma tissue. New heteroaromatic derivatives have been designed with a cytotoxic moiety and termed DNA intercalating agents. These compounds could be applied in targeted radionuclide therapy using (125)I, which emits Auger electrons and gives high-energy, localized irradiation. Two iodinated acridine derivatives have been reported to present an in vivo kinetic profile conducive to application in targeted radionuclide therapy. The aim of the present study was to perform a preclinical evaluation of these compounds. The DNA intercalating property was confirmed for both compounds. After radiolabeling with (125)I, the two compounds induced in vitro a significant radiotoxicity to B16F0 melanoma cells. Nevertheless, the acridine compound appeared more radiotoxic than the acridone compound. While cellular uptake was similar for both compounds, SIMS analysis and in vitro protocol showed a stronger affinity for melanin with acridone derivative, which was able to induce a predominant scavenging process in the melanosome and restrict access to the nucleus. In conclusion, the acridine derivative with a higher nuclear localization appeared a better candidate for application in targeted radionuclide therapy using (125)I.

Petroff A.P., Wu T.D., Liang B., Mui J., Guerquin-Kern J.L., Vali H., Rothman D.H., Bosak T. (2011 Nov 21)

Reaction-diffusion model of nutrient uptake in a biofilm: theory and experiment.

Journal of theoretical biology : 289 : 90-5 : DOI : 10.1016/j.jtbi.2011.08.004

Résumé

Microbes in natural settings typically live attached to surfaces in complex communities called biofilms. Despite the many advantages of biofilm formation, communal living forces microbes to compete with one another for resources. Here we combine mathematical models with stable isotope techniques to test a reaction-diffusion model of competition in a photosynthetic biofilm. In this model, a nutrient is transported through the mat by diffusion and is consumed at a rate proportional to its local concentration. When the nutrient is supplied from the surface of the biofilm, the balance between diffusion and consumption gives rise to gradients of nutrient availability, resulting in gradients of nutrient uptake. To test this model, a biofilm was incubated for a fixed amount of time with an isotopically labeled nutrient that was incorporated into cellular biomass. Thus, the concentration of labeled nutrient in a cell is a measure of the mean rate of nutrient incorporation over the course of the experiment. Comparison of this measurement to the solution of the reaction-diffusion model in the biofilm confirms the presence of gradients in nutrient uptake with the predicted shape. The excellent agreement between theory and experiment lends strong support to this one-parameter model of reaction and diffusion of nutrients in a biofilm. Having validated this model empirically, we discuss how these dynamics may arise from diffusion through a reactive heterogeneous medium. More generally, this result identifies stable isotope techniques as a powerful tool to test quantitative models of chemical transport through biofilms.