Année de publication : 2021

Ana Martins Figueiredo, Pedro Barbacena, Ana Russo, Silvia Vaccaro, Daniela Ramalho, Andreia Pena, Aida Pires Lima, Rita Rua Ferreira, Marta Alves Fidalgo, Fatima El-Marjou, Yulia Carvalho, Francisca Ferreira Vasconcelos, Ana-Maria Lennon-Duménil, Danijela Matic Vignjevic, Claudio Areias Franco (2021 Apr 27)

Endothelial cell invasion is controlled by dactylopodia.

Proceedings of the National Academy of Sciences of the United States of America : DOI : e2023829118

Résumé

Sprouting angiogenesis is fundamental for development and contributes to cancer, diabetic retinopathy, and cardiovascular diseases. Sprouting angiogenesis depends on the invasive properties of endothelial tip cells. However, there is very limited knowledge on how tip cells invade into tissues. Here, we show that endothelial tip cells use dactylopodia as the main cellular protrusion for invasion into nonvascular extracellular matrix. We show that dactylopodia and filopodia protrusions are balanced by myosin IIA (NMIIA) and actin-related protein 2/3 (Arp2/3) activity. Endothelial cell-autonomous ablation of NMIIA promotes excessive dactylopodia formation in detriment of filopodia. Conversely, endothelial cell-autonomous ablation of Arp2/3 prevents dactylopodia development and leads to excessive filopodia formation. We further show that NMIIA inhibits Rac1-dependent activation of Arp2/3 by regulating the maturation state of focal adhesions. Our discoveries establish a comprehensive model of how endothelial tip cells regulate its protrusive activity and will pave the way toward strategies to block invasive tip cells during sprouting angiogenesis.

Shanna L Bowman, Linh Le, Yueyao Zhu, Dawn C Harper, Anand Sitaram, Alexander C Theos, Elena V Sviderskaya, Dorothy C Bennett, Graça Raposo-Benedetti, David J Owen, Megan K Dennis, Michael S Marks (2021 Apr 22)

A BLOC-1-AP-3 super-complex sorts a cis-SNARE complex into endosome-derived tubular transport carriers.

The Journal of cell biology : DOI : e202005173

Résumé

Membrane transport carriers fuse with target membranes through engagement of cognate vSNAREs and tSNAREs on each membrane. How vSNAREs are sorted into transport carriers is incompletely understood. Here we show that VAMP7, the vSNARE for fusing endosome-derived tubular transport carriers with maturing melanosomes in melanocytes, is sorted into transport carriers in complex with the tSNARE component STX13. Sorting requires either recognition of VAMP7 by the AP-3δ subunit of AP-3 or of STX13 by the pallidin subunit of BLOC-1, but not both. Consequently, melanocytes expressing both AP-3δ and pallidin variants that cannot bind their respective SNARE proteins are hypopigmented and fail to sort BLOC-1-dependent cargo, STX13, or VAMP7 into transport carriers. However, SNARE binding

does not influence BLOC-1 function in generating tubular transport carriers. These data reveal a novel mechanism of vSNARE sorting by recognition of redundant sorting determinants on a SNARE complex by an AP-3-BLOC-1 super-complex.

Markus Frederik Schliffka, Anna Francesca Tortorelli, Özge Özgüç, Ludmilla de Plater, Oliver Polzer, Diane Pelzer, Jean-Léon Maître (2021 Apr 19)

Multiscale analysis of single and double maternal-zygotic and mutants during mouse preimplantation development.

eLife : DOI : 10.7554/eLife.68536

Résumé

During the first days of mammalian development, the embryo forms the blastocyst, the structure responsible for implanting the mammalian embryo. Consisting of an epithelium enveloping the pluripotent inner cell mass and a fluid-filled lumen, the blastocyst results from a series of cleavage divisions, morphogenetic movements, and lineage specification. Recent studies have identified the essential role of actomyosin contractility in driving cytokinesis, morphogenesis, and fate specification, leading to the formation of the blastocyst. However, the preimplantation development of contractility mutants has not been characterized. Here, we generated single and double maternal-zygotic mutants of non-muscle myosin II heavy chains (NMHCs) to characterize them with multiscale imaging. We found that (NMHC II-A) is the major NMHC during preimplantation development as its maternal-zygotic loss causes failed cytokinesis, increased duration of the cell cycle, weaker embryo compaction, and reduced differentiation, whereas (NMHC II-B) maternal-zygotic loss is much less severe. Double maternal-zygotic mutants for and show a much stronger phenotype, failing most of the attempts of cytokinesis. We found that morphogenesis and fate specification are affected but nevertheless carry on in a timely fashion, regardless of the impact of the mutations on cell number. Strikingly, even when all cell divisions fail, the resulting single-celled embryo can initiate trophectoderm differentiation and lumen formation by accumulating fluid in increasingly large vacuoles. Therefore, contractility mutants reveal that fluid accumulation is a cell-autonomous process and that the preimplantation program carries on independently of successful cell division.

D Hequet, G Harrissart, D Krief, L Maumy, F Lerebours, E Menet, C Callens, R Rouzier (2021 Apr 16)

Prosigna test in breast cancer: real-life experience.

Breast cancer research and treatment : 141-147 : DOI : 10.1007/s10549-021-06191-x

Résumé

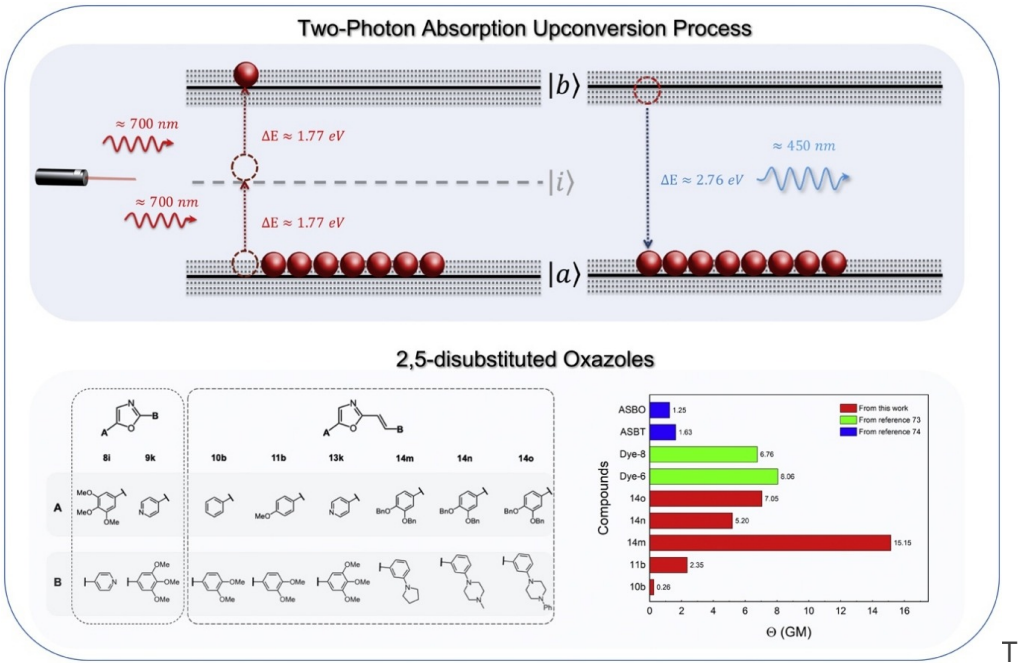
Genomic tests can guide the decision to administer adjuvant chemotherapy in women with hormone receptor (HR)-positive, Human Epidermal growth Factor 2 (HER2)-negative breast cancer (BC) at intermediate risk of recurrence. We assessed the decision-making and economic impact of the Prosigna test in a real-life setting.

Abegão L.M., Santos F.A., Piguel S., Rodrigues J.J., Mendonça C.R., De Boni L. (2021 Apr 15)

The ability of 2,5-disubstituted oxazole dyes derivatives to generate two-photon upconversion photoluminescence and its brightness evaluation

Journal of Photochemistry and Photobiology A: Chemistry : 411 : 113214 : DOI : 10.1016/j.jphotochem.2021.113214

Résumé



The brightness study of emissive compounds is one of the fundamental spectroscopic characterizations. In this work, we assessed the brightness values of eight 2,5-disubstituted oxazole dyes derivatives by combining linear and nonlinear spectroscopic parameters. The range of the brightness values obtained is from 0.26 GM to 15.15 GM. The highest value belongs to compound 14 m, which, compared to previously investigated compounds of similar π-conjugation length, is at least two times higher. Brightness values were determined in the spectral region between 700 nm–720 nm, revealing this class of dyes' potential to be used as photoluminescence bioprobes excited by two-photons.

Patrick T Rudak, Joshua Choi, Katie M Parkins, Kelly L Summers, Dwayne N Jackson, Paula J Foster, Anton I Skaro, Ken Leslie, Vivian C McAlister, Vijay K Kuchroo, Wataru Inoue, Olivier Lantz, S M Mansour Haeryfar (2021 Apr 14)

Chronic stress physically spares but functionally impairs innate-like invariant T cells.

Cell reports : 108979 : DOI : S2211-1247(21)00293-X

Résumé

The deleterious effects of psychological stress on mainstream T lymphocytes are well documented. However, how stress impacts innate-like T cells is unclear. We report that long-term stress surprisingly abrogates both T helper 1 (T1)- and T2-type responses orchestrated by invariant natural killer T (iNKT) cells. This is not due to iNKT cell death because these cells are unusually refractory to stress-inflicted apoptosis. Activated iNKT cells in stressed mice exhibit a « split » inflammatory signature and trigger sudden serum interleukin-10 (IL-10), IL-23, and IL-27 spikes. iNKT cell dysregulation is mediated by cell-autonomous glucocorticoid receptor signaling and corrected upon habituation to predictable stressors. Importantly, under stress, iNKT cells fail to potentiate cytotoxicity against lymphoma or to reduce the burden of metastatic melanoma. Finally, stress physically spares mouse mucosa-associated invariant T (MAIT) cells but hinders their T1-/T2-type responses. The above findings are corroborated in human peripheral blood and hepatic iNKT/MAIT cell cultures. Our work uncovers a mechanism of stress-induced immunosuppression.

Ophélie Lautier, Arianna Penzo, Jérôme O Rouvière, Guillaume Chevreux, Louis Collet, Isabelle Loïodice, Angela Taddei, Frédéric Devaux, Martine A Collart, Benoit Palancade (2021 Apr 10)

Co-translational assembly and localized translation of nucleoporins in nuclear pore complex biogenesis.

Molecular cell : DOI : S1097-2765(21)00225-2

Résumé

mRNA translation is coupled to multiprotein complex assembly in the cytoplasm or to protein delivery into intracellular compartments. Here, by combining systematic RNA immunoprecipitation and single-molecule RNA imaging in yeast, we have provided a complete depiction of the co-translational events involved in the biogenesis of a large multiprotein assembly, the nuclear pore complex (NPC). We report that binary interactions between NPC subunits can be established during translation, in the cytoplasm. Strikingly, the nucleoporins Nup1/Nup2, together with a number of nuclear proteins, are instead translated at nuclear pores, through a mechanism involving interactions between their nascent N-termini and nuclear transport receptors. Uncoupling this co-translational recruitment further triggers the formation of cytoplasmic foci of unassembled polypeptides. Altogether, our data reveal that distinct, spatially segregated modes of co-translational interactions foster the ordered assembly of NPC subunits and that localized translation can ensure the proper delivery of proteins to the pore and the nucleus.

Tsai Feng-Ching, Simunovic Mijo, Sorre Benoit , Bertin Aurélie, Manzi John, Callan-Jones Andrew, Bassereau Patricia (2021 Apr 6)

Comparing physical mechanisms for membrane curvature-driven sorting of BAR-domain proteins

Soft Matter : DOI : 10.1039/D0SM01573C

Résumé

Protein enrichment at specific membrane locations in cells is crucial for many cellular functions. It is well-recognized that the ability of some proteins to sense membrane curvature contributes partly to their enrichment in highly curved cellular membranes. In the past, different theoretical models have been developed to reveal the physical mechanisms underlying curvature-driven protein sorting. This review aims to provide a detailed discussion of the two continuous models that are based on the Helfrich elasticity energy, (1) the spontaneous curvature model and (2) the curvature mismatch model. These two models are commonly applied to describe experimental observations of protein sorting. We discuss how they can be used to explain the curvature-induced sorting data of two BAR proteins, amphiphysin and centaurin. We further discuss how membrane rigidity, and consequently the membrane curvature generated by BAR proteins, could influence protein organization on the curved membranes. Finally, we address future directions in extending these models to describe some cellular phenomena involving protein sorting.

Heltberg Mathias, Miné-Hattab Judith, Taddei Angela , Walczak Aleksandra M. , Mora Thierry (2021 Apr 2)
Physical observables to determine the nature of membrane-less cellular sub-compartments
preprint. : DOI : 10.1101/2021.04.01.438041

Résumé

Abstract

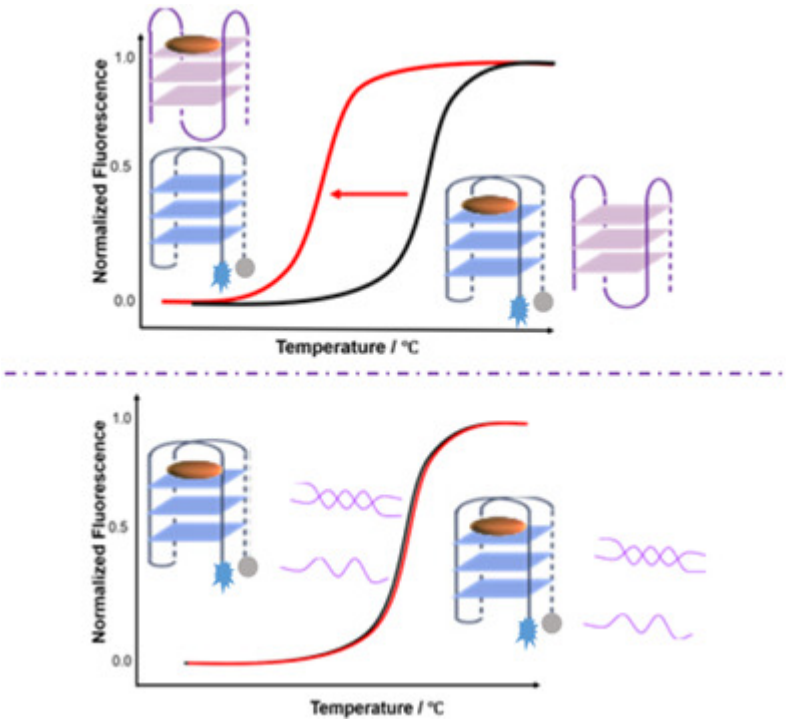
The spatial organization of complex biochemical reactions is essential for the regulation of cellular processes. Membrane-less structures called foci containing high concentrations of specific proteins have been reported in a variety of contexts, but the mechanism of their formation is not fully understood. Several competing mechanisms exist that are difficult to distinguish empirically, including liquid-liquid phase separation, and the trapping of molecules by multiple binding sites. Here we propose a theoretical framework and outline observables to differentiate between these scenarios from single molecule tracking experiments. In the binding site model, we derive relations between the distribution of proteins, their diffusion properties, and their radial displacement. We predict that protein search times can be reduced for targets inside a liquid droplet, but not in an aggregate of slowly moving binding sites. These results are applicable to future experiments and suggest different biological roles for liquid droplet and binding site foci.

Yu Luo, Anton Granzhan, Daniela Verga, Jean-Louis Mergny (2021 Apr 1)
FRET-MC: A fluorescence melting competition assay for studying G4 structures

in vitro
Biopolymers : 112 : e23415 : DOI : 10.1002/bip.23415

Résumé

G-quadruplexes (G4) play crucial roles in biology, analytical chemistry and nanotechnology. The stability of G4 structures is impacted by the number of G-quartets, the length and positions of loops, flanking motifs, as well as additional structural elements such as bulges, capping base pairs, or triads. Algorithms such as G4Hunter or Quadparser may predict if a given sequence is G4-prone by calculating a quadruplex propensity score; however, experimental validation is still required. We previously demonstrated that this validation is not always straightforward, and that a combination of techniques is often required to unambiguously establish whether a sequence forms a G-quadruplex or not. In this article, we adapted the well-known FRET-melting assay to characterize G4 in batch, where the sequence to be tested is added, as an unlabeled competitor, to a system composed of a dual-labeled probe (F21T) and a specific quadruplex ligand. PhenDC3 was preferred over TMPyP4 because of its better selectivity for G-quadruplexes. In this so-called FRET-MC (melting competition) assay, G4-forming competitors lead to a marked decrease of the ligand-induced stabilization effect (ΔT_m), while non-specific competitors (e.g., single- or double-stranded sequences) have little effect. Sixty-five known sequences with different typical secondary structures were used to validate the assay, which was subsequently employed to assess eight novel sequences that were not previously characterized.



Romain-David Seban, Roman Rouzier, Aurelien Latouche, Nicolas Deleval, Jean-Marc

Guinebretiere, Irene Buvat, Francois-Clement Bidard, Laurence Champion (2021 Mar 28)
Total metabolic tumor volume and spleen metabolism on baseline [18F]-FDG PET/CT as independent prognostic biomarkers of recurrence in resected breast cancer.
European journal of nuclear medicine and molecular imaging : DOI : 10.1007/s00259-021-05322-2

Résumé

We evaluated whether biomarkers on baseline [F]-FDG PET/CT are associated with recurrence after surgery in patients with invasive breast cancer of no special type (NST).

Zackie Aktary, Alejandro Conde-Perez, Florian Rambow, Mathilde Di Marco, François Amblard, Ilse Hurbain, Graça Raposo, Cédric Delevoye, Sylvie Coscoy, Lionel Larue (2021 Mar 27)
A role for Dynlt3 in melanosome movement, distribution, acidity and transfer.
Communications biology : 423 : DOI : 10.1038/s42003-021-01917-5

Résumé

Skin pigmentation is dependent on cellular processes including melanosome biogenesis, transport, maturation and transfer to keratinocytes. However, how the cells finely control these processes in space and time to ensure proper pigmentation remains unclear. Here, we show that a component of the cytoplasmic dynein complex, Dynlt3, is required for efficient melanosome transport, acidity and transfer. In Mus musculus melanocytes with decreased levels of Dynlt3, pigmented melanosomes undergo a more directional motion, leading to their peripheral location in the cell. Stage IV melanosomes are more acidic, but still heavily pigmented, resulting in a less efficient melanosome transfer. Finally, the level of Dynlt3 is dependent on β-catenin activity, revealing a function of the Wnt/β-catenin signalling pathway during melanocyte and skin pigmentation, by coupling the transport, positioning and acidity of melanosomes required for their transfer.

Emeline Bonsergent, Eleonora Grisard, Julian Buchrieser, Olivier Schwartz, Clotilde Théry, Grégory Lavieu (2021 Mar 26)
Quantitative characterization of extracellular vesicle uptake and content delivery within mammalian cells.
Nature communications : 1864 : DOI : 10.1038/s41467-021-22126-y

Résumé

Extracellular vesicles (EVs), including exosomes, are thought to mediate intercellular communication through the transfer of cargoes from donor to acceptor cells. Occurrence of EV-content delivery within acceptor cells has not been unambiguously demonstrated, let alone quantified, and remains debated. Here, we developed a cell-based assay in which EVs

containing luciferase- or fluorescent-protein tagged cytosolic cargoes are loaded on unlabeled acceptor cells. Results from dose-responses, kinetics, and temperature-block experiments suggest that EV uptake is a low yield process (~1% spontaneous rate at 1 h). Further characterization of this limited EV uptake, through fractionation of membranes and cytosol, revealed cytosolic release (~30% of the uptaken EVs) in acceptor cells. This release is inhibited by bafilomycin A1 and overexpression of IFITM proteins, which prevent virus entry and fusion. Our results show that EV content release requires endosomal acidification and suggest the involvement of membrane fusion.

Daniel Jeffery, Alberto Gatto, Katrina Podsypanina, Charlène Renaud-Pageot, Rebeca Ponce Landete, Lorraine Bonneville, Marie Dumont, Daniele Fachinetti, Geneviève Almouzni (2021 Mar 26)

CENP-A overexpression promotes distinct fates in human cells, depending on p53 status

Communications Biology : 4 : 1-18 : DOI : 10.1038/s42003-021-01941-5

Résumé

Julien Robert-Paganin, Xiao-Ping Xu, Mark F Swift, Daniel Auguin, James P Robblee, Hailong Lu, Patricia M Fagnant, Elena B Krementsova, Kathleen M Trybus, Anne Houdusse, Niels Volkmann, Dorit Hanein (2021 Mar 26)

The actomyosin interface contains an evolutionary conserved core and an ancillary interface involved in specificity.

Nature communications : 1892 : DOI : 10.1038/s41467-021-22093-4

Résumé

Plasmodium falciparum, the causative agent of malaria, moves by an atypical process called gliding motility. Actomyosin interactions are central to gliding motility. However, the details of these interactions remained elusive until now. Here, we report an atomic structure of the divergent Plasmodium falciparum actomyosin system determined by electron cryomicroscopy at the end of the powerstroke (Rigor state). The structure provides insights into the detailed interactions that are required for the parasite to produce the force and motion required for infectivity. Remarkably, the footprint of the myosin motor on filamentous actin is conserved with respect to higher eukaryotes, despite important variability in the Plasmodium falciparum myosin and actin elements that make up the interface. Comparison with other actomyosin complexes reveals a conserved core interface common to all actomyosin complexes, with an ancillary interface involved in defining the spatial positioning of the motor on actin filaments.