Année de publication : 2019

Nicola de Franceschi, Maryam Alqabandi, Winfried Weissenhorn, Patricia Bassereau (2019 Jul 5)

Dynamic and Sequential Protein Reconstitution on Negatively Curved Membranes by Giant Vesicles Fusion.

Bio-Protocol : 9 : e3294 : DOI : 10.21769/BioProtoc.3294

Résumé

In vitro investigation of the interaction between proteins and positively curved membranes can be performed using a classic nanotube pulling method. However, characterizing protein interaction with negatively curved membranes still represents a formidable challenge. Here, we describe our recently developed approach based on laser-triggered Giant Unilamellar Vesicles (GUVs) fusion. Our protocol allows sequential addition of proteins to a negatively curved membrane, while at the same time controlling the buffer composition, lipid composition and membrane tension. Moreover, this method does not require a step of protein detachment, greatly simplifying the process of protein encapsulation over existing methods.

Andres Ernesto Zucchetti, Laurence Bataille, Jean-Marie Carpier, Stéphanie Dogniaux, Mabel San Roman-Jouve, Mathieu Maurin, Michael W Stuck, Rosa M Rios, Cosima T Baldari, Gregory J Pazour, Claire Hivroz (2019 Jun 30)

Tethering of vesicles to the Golgi by GMAP210 controls LAT delivery to the immune synapse.

Nature communications : 2864 : DOI : 10.1038/s41467-019-10891-w

Résumé

The T cell immune synapse is a site of intense vesicular trafficking. Here we show that the golgin GMAP210, known to capture vesicles and organize membrane traffic at the Golgi, is involved in the vesicular transport of LAT to the immune synapse. Upon activation, more GMAP210 interact with LAT-containing vesicles and go together with LAT to the immune synapse. Regulating LAT recruitment and LAT-dependent signaling, GMAP210 controls T cell activation. Using a rerouting and capture assay, we show that GMAP210 captures VAMP7-decorated vesicles. Overexpressing different domains of GMAP210, we also show that GMAP210 allows their specific delivery to the immune synapse by tethering LAT-vesicles to the Golgi. Finally, in a model of ectopic expression of LAT in ciliated cells, we show that GMAP210 tethering activity controls the delivery of LAT to the cilium. Hence, our results reveal a function for the golgin GMAP210 conveying specific vesicles to the immune synapse.

Anita Kumari, Judith Pineau, Pablo J Sáez, Mathieu Maurin, Danielle Lankar, Mabel San Roman, Katharina Hennig, Vanessa F Boura, Raphael Voituriez, Mikael C I Karlsson, Martial Balland, Ana-Maria Lennon Dumenil, Paolo Pierobon (2019 Jun 30)

Actomyosin-driven force patterning controls endocytosis at the immune synapse.
Nature communications : 2870 : DOI : 10.1038/s41467-019-10751-7

Résumé

An important channel of cell-to-cell communication is direct contact. The immune synapse is a paradigmatic example of such type of interaction: it forms upon engagement of antigen receptors in lymphocytes by antigen-presenting cells and allows the local exchange of molecules and information. Although mechanics has been shown to play an important role in this process, how forces organize and impact on synapse function is unknown. We find that mechanical forces are spatio-temporally patterned at the immune synapse: global pulsatile myosin II-driven tangential forces are observed at the synapse periphery while localised forces generated by invadosome-like F-actin protrusions are detected at its centre. Noticeably, we observe that these force-producing actin protrusions constitute the main site of antigen extraction and endocytosis and require myosin II contractility to form. The interplay between global and local forces dictated by the organization of the actomyosin cytoskeleton therefore controls endocytosis at the immune synapse.

Patrick Veit-Haibach, Irène Buvat, Ken Herrmann (2019 Jun 27)
EJNMMI supplement: bringing AI and radiomics to nuclear medicine.
European journal of nuclear medicine and molecular imaging : 2627-2629 : DOI : 10.1007/s00259-019-04395-4

Résumé

Année de publication : 2015

Bonsang-Kitzis H1, Sadacca B2, Hamy-Petit AS3, Moarii M4, Pinheiro A3, Laurent C3, Reyal F1. (2019 Jun 24)
Biological network-driven gene selection identifies a stromal immune module as a key determinant of triple-negative breast carcinoma prognosis.
Oncoimmunology : 5 : 1061176 : DOI : 10.1080/2162402X.2015.1061176

Résumé

Triple-negative breast cancer (TNBC) is a heterogeneous group of aggressive breast cancers for which no targeted treatment is available. Robust tools for TNBC classification are required, to improve the prediction of prognosis and to develop novel therapeutic interventions. We analyzed 3,247 primary human breast cancer samples from 21 publicly available datasets, using a five-step method: (1) selection of TNBC samples by bimodal filtering on ER-HER2 and PR, (2) normalization of the selected TNBC samples, (3) selection of the most variant genes, (4) identification of gene clusters and biological gene selection within gene clusters on the basis of String© database connections and gene-expression

correlations, (5) summarization of each gene cluster in a metagene. We then assessed the ability of these metagenes to predict prognosis, on an external public dataset (METABRIC). Our analysis of gene expression (GE) in 557 TNBCs from 21 public datasets identified a six-metagene signature (167 genes) in which the metagenes were enriched in different gene ontologies. The gene clusters were named as follows: Immunity1, Immunity2, Proliferation/DNA damage, AR-like, Matrix/Invasion1 and Matrix2 clusters respectively. This signature was particularly robust for the identification of TNBC subtypes across many datasets (n = 1,125 samples), despite technology differences (Affymetrix© A, Plus2 and Illumina©). Weak Immunity two metagene expression was associated with a poor prognosis (disease-specific survival; HR = 2.68 [1.59-4.52], p = 0.0002). The six-metagene signature (167 genes) was validated over 1,125 TNBC samples. The Immunity two metagene had strong prognostic value. These findings open up interesting possibilities for the development of new therapeutic interventions.

Année de publication : 2019

Merlotti A1,2, Malizia AL1, Michea P2, Bonte PE2, Goudot C2, Carregal MS1, Nuñez N2, Sedlik C2, Ceballos A1, Soumelis V2, Amigorena S2, Geffner J1, Piaggio E2, Sabatte J1. (2019 Jun 24)
Aberrant fucosylation enables breast cancer clusterin to interact with dendritic cell-specific ICAM-grabbing non-integrin (DC-SIGN).
Oncoimmunology : 8(9) : DOI : 10.1080/2162402X.2019.1629257

Résumé

Manuel Rodrigues, Lenha Mobuchon, Alexandre Houy, Samar Alsafadi, Sylvain Baulande, Odette Mariani, Benjamin Marande, Khadija Ait Rais, Monique K Van der Kooij, Ellen Kapiteijn, Sieta Gassama, Sophie Gardrat, Raymond L Barnhill, Vincent Servois, Rémi Dendale, Marc Putterman, Sarah Tick, Sophie Piperno-Neumann, Nathalie Cassoux, Gaëlle Pierron, Joshua J Waterfall, Sergio Roman-Roman, Pascale Mariani, Marc-Henri Stern (2019 Jun 23)
Evolutionary Routes in Metastatic Uveal Melanomas Depend on Alterations.
Clinical cancer research : an official journal of the American Association for Cancer Research : 5513-5524 : DOI : 10.1158/1078-0432.CCR-19-1215

Résumé

Uveal melanomas (UM) are genetically simple tumors carrying few copy number alterations (CNA) and a low mutation burden, except in rare -deficient, hypermutated cases. The genomics of uveal melanoma metastatic progression has not been described. We assessed the genetic heterogeneity of primary and metastatic -proficient and -deficient uveal melanomas. We prospectively collected 75 metastatic and 16 primary samples from 25 consecutive uveal melanoma patients, and performed whole-exome sequencing.

Andrea Frapporti, Caridad Miró Pina, Olivier Arnaiz, Daniel Holoch, Takayuki Kawaguchi, Adeline Humbert, Evangelia Eleftheriou, Bérangère Lombard, Damarys Loew, Linda Sperling, Karine Guitot, Raphaël Margueron, Sandra Duharcourt (2019 Jun 22)

The Polycomb protein Ezl1 mediates H3K9 and H3K27 methylation to repress transposable elements in Paramecium.

Nature communications : 2710 : DOI : 10.1038/s41467-019-10648-5

Résumé

In animals and plants, the H3K9me3 and H3K27me3 chromatin silencing marks are deposited by different protein machineries. H3K9me3 is catalyzed by the SET-domain SU(VAR)3-9 enzymes, while H3K27me3 is catalyzed by the SET-domain Enhancer-of-zeste enzymes, which are the catalytic subunits of Polycomb Repressive Complex 2 (PRC2). Here, we show that the Enhancer-of-zeste-like protein Ezl1 from the unicellular eukaryote Paramecium tetraurelia, which exhibits significant sequence and structural similarities with human EZH2, catalyzes methylation of histone H3 in vitro and in vivo with an apparent specificity toward K9 and K27. We find that H3K9me3 and H3K27me3 co-occur at multiple families of transposable elements in an Ezl1-dependent manner. We demonstrate that loss of these histone marks results in global transcriptional hyperactivation of transposable elements with modest effects on protein-coding gene expression. Our study suggests that although often considered functionally distinct, H3K9me3 and H3K27me3 may share a common evolutionary history as well as a common ancestral role in silencing transposable elements.

Federica Arbizzani, Sergio A Rincon, Anne Paoletti (2019 Jun 21)

Increasing ergosterol levels delays formin-dependent assembly of F-actin cables and disrupts division plane positioning.

Journal of cell science : DOI : jcs.227447

Résumé

In most eukaryotes, cytokinesis is mediated by the constriction of a contractile acto-myosin ring (CR) which promotes the ingression of the cleavage furrow. Many components of the CR interact with plasma membrane lipids suggesting that lipids may regulate CR assembly and function. Although there is clear evidence that phospho-inositides play an important role in cytokinesis, much less is known about the role of sterols in this process. Here we studied how sterols influence division plane positioning and CR assembly in fission yeast. We show that increasing ergosterol levels on the plasma membrane blocks the assembly of F-actin cables from cytokinetic precursor nodes, preventing their compaction into a ring. Abnormal F-actin cables form after a delay, leading to randomly placed septa. Since the formin Cdc12 was detected on cytokinetic precursors and the phenotype can be partially rescued by inhibiting the Arp2/3 complex, which competes with formins for F-actin nucleation, we propose that ergosterol may inhibit formin dependent assembly of F-actin cables from cytokinetic precursors.

Elena Beltrán-Heredia, Feng-Ching Tsai, Samuel Salinas-Almaguer, Francisco J. Cao*, Patricia Bassereau*, Francisco Monroy* (2019 Jun 20)

Membrane curvature induces cardiolipin sorting.

Communications Biology : 2 : 225 : DOI : 10.1038/s42003-019-0471-x

Résumé

Cardiolipin is a cone-shaped lipid predominantly localized in curved membrane sites of bacteria and in the mitochondrial cristae. This specific localization has been argued to be geometry-driven, since the CL's conical shape relaxes curvature frustration. Although previous evidence suggests a coupling between CL concentration and membrane shape in vivo, no precise experimental data are available for curvature-based CL sorting in vitro. Here, we test this hypothesis in experiments that isolate the effects of membrane curvature in lipid-bilayer nanotubes. CL sorting is observed with increasing tube curvature, reaching a maximum at optimal CL concentrations, a fact compatible with self-associative clustering. Observations are compatible with a model of membrane elasticity including van der Waals entropy, from which a negative intrinsic curvature of -1.1 nm^{-1} is predicted for CL. The results contribute to understanding the physicochemical interplay between membrane curvature and composition, providing key insights into mitochondrial and bacterial membrane organization and dynamics.

Anne-Ségolène Cottereau, Christophe Nioche, Anne-Sophie Dirand, Jérôme Clerc, Franck Morschhauser, Olivier Casasnovas, Michel Meignan, Irène Buvat (2019 Jun 16)

F-FDG PET Dissemination Features in Diffuse Large B-Cell Lymphoma Are Predictive of Outcome.

Journal of nuclear medicine : official publication, Society of Nuclear Medicine : 40-45 : DOI : 10.2967/jnumed.119.229450

Résumé

We assessed the predictive value of new radiomic features characterizing lesion dissemination in baseline F-FDG PET and tested whether combining them with baseline metabolic tumor volume (MTV) could improve prediction of progression-free survival (PFS) and overall survival (OS) in diffuse large B-cell lymphoma (DLBCL) patients. From the LNH073B trial (NCT00498043), patients with advanced-stage DLCBL and F-FDG PET/CT images available for review were selected. MTV and several radiomic features, including the distance between the 2 lesions that were farthest apart (Dmax), were calculated. Receiver-operating-characteristic analysis was used to determine the optimal cutoff for quantitative variables, and Kaplan-Meier survival analyses were performed. With a median age of 46 y, 95 patients were enrolled, half of them treated with R-CHOP biweekly (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) and the other half with R-ACVBP (rituximab, doxorubicin, cyclophosphamide, vindesine, bleomycin, and prednisone), with no significant impact on outcome. Median MTV and Dmax were 375 cm and 45 cm, respectively. The median follow-up was 44 mo. High MTV and Dmax were adverse factors for PFS (= 0.027 and = 0.0003, respectively) and for OS (= 0.0007 and = 0.0095, respectively). In

multivariate analysis, only Dmax was significantly associated with PFS (= 0.0014) whereas both factors remained significant for OS (= 0.037 and = 0.0029, respectively). Combining MTV (>384 cm) and Dmax (>58 cm) yielded 3 risk groups for PFS (= 0.0003) and OS (= 0.0011): high with 2 adverse factors (4-y PFS and OS of 50% and 53%, respectively, = 18), low with no adverse factor (94% and 97%, = 36), and an intermediate category with 1 adverse factor (73% and 88%, = 41). Combining MTV with a parameter reflecting the tumor burden dissemination further improves DLBCL patient risk stratification at staging.

Héloïse Muller, José Gil, Jr, Ines A Drinnenberg (2019 Jun 11)
The Impact of Centromeres on Spatial Genome Architecture
Trends in Genetics : 35 : 565-578 : DOI : 10.1016/j.tig.2019.05.003

Résumé

The development of new technologies and experimental techniques is enabling researchers to see what was once unable to be seen. For example, the centromere was first seen as the mediator between spindle fiber and chromosome during mitosis and meiosis. Although this continues to be its most prominent role, we now know that the centromere functions beyond cellular division with important roles in genome organization and chromatin regulation. Here we aim to share the structures and functions of centromeres in various organisms beginning with the diversity of their DNA sequence anatomies. We zoom out to describe their position in the nucleus and ultimately detail the different ways they contribute to genome organization and regulation at the spatial level.

Sylvain Auvity, Sébastien Goutal, Benoît Thézé, Catarina Chaves, Benoît Hosten, Bertrand Kuhnast, Wadad Saba, Raphaël Boisgard, Irène Buvat, Salvatore Cisternino, Nicolas Tournier (2019 Jun 10)
Corrigendum to « Evaluation of TSPO PET imaging, a marker of glial activation, to study the neuroimmune footprints of morphine exposure and withdrawal » [Drug Alcohol Depend. 170 (2017) 43-50].
Drug and alcohol dependence : 266-268 : DOI : S0376-8716(19)30162-0

Résumé

Emeline Bonsergent, Gregory Lavieu (2019 Jun 9)
Content release of extracellular vesicles in a cell-free extract.
FEBS letters : DOI : 10.1002/1873-3468.13472

Résumé

Extracellular Vesicles (EVs) transfer molecules from donor to acceptor cells. The EV-content delivery process within the acceptor cell is poorly characterized. We developed a new cell-

free assay to assess EV-content release in vitro. We found that EV-cytosolic cargoes are released from EVs when isolated vesicles are incubated with purified plasma membrane sheets at acidic pH, a characteristic of the endo/lysosomal environment. This process is protein dependent. Our results suggest that EV-content delivery occurs within the endo/lysosomes of acceptor cells and is triggered by acidification. This process resembles virus content delivery and may require membrane fusion. The assay presented here will facilitate investigations into the core machinery and mechanisms underlying EV content delivery. This article is protected by copyright. All rights reserved.

Tim Schneider, Annalisa Patriarca, Yolanda Prezado (2019 Jun 8)

Improving the dose distributions in minibeam radiation therapy: Helium ions vs protons.

Medical physics : 3640-3648 : DOI : 10.1002/mp.13646

Résumé

Charged particle minibeam radiation therapy is a novel therapeutic strategy aiming at reducing the normal tissue complication probability by combining the normal tissue sparing of submillimetric, spatially fractionated beams with the improved dose deposition of ions. This may allow a safe dose escalation in the tumor and other targets. In particular, proton minibeam radiation therapy has already proven a remarkable increase of the therapeutic index for high-grade gliomas in animal experiments. The reduced multiple Coulomb scattering and nuclear fragmentation of helium ions compared to protons and heavier ions, respectively, make them a good candidate for minibeam radiation therapy (MBRT). The purpose of the present work was to perform a comprehensive dosimetric comparison between proton and helium MBRT (pMBRT and HeMBRT).