Année de publication : 2020

Zablocki-Thomas L1, Menzies SA2, Lehner PJ2, Manel N1, Benaroch P1. (2020 Apr 4)
A genome-wide CRISPR screen identifies regulation factors of the TLR3 signalling pathway.
Innate immunology : DOI : 10.1177/1753425920915507

Résumé

Chabaud M1,2,3, Paillon N1, Gaus K2,3, Hivroz C1. (2020 Apr 2)
Mechanobiology of antigen-induced T cell arrest.
Biology of the Cell : DOI : 10.1111/boc.201900093

Résumé

Ménoret S1,2,3, Ouisse LH1,2,3, Tesson L1,2,3, Remy S1,2,3, Usal C1,2,3, Guiffes A1,2,3, Chenouard V1,2,3, Royer PJ4, Evanno G4, Vanhove B4, Piaggio E5, Anegon I1,2,3. (2020 Apr 1)
In Vivo Analysis of Human Immune Responses in Immunodeficient Rats.
Transplantation : 104(4) : 715-723 : DOI : 10.1097/TP.0000000000003047

Résumé

Brouiller F1, Ruffin N2, Benaroch P2. (2020 Apr 1)
A new population of blood precursors of dendritic cells endowed with specific properties regarding HIV-1
Medecine science : 36(4) : 316-319 : DOI : 10.1051/medsci/2020050

Résumé

Floris Bosveld, Yohanns Bellaïche (2020 Mar 26)
Tricellular junctions.
Current biology : CB : R249-R251 : DOI : S0960-9822(20)30029-4

Résumé

Bosveld and Bellaïche discuss the composition and assembly of tricellular junctions, as well as their roles in cell packing, tissue mechanics and signalling.

Caroline Louis-Brennetot, Olivier Delattre, Isabelle Janoueix-Lerosey (2020 Mar 23)

High CD44 expression is not a prognosis marker in patients with high-risk neuroblastoma.
EBioMedicine : 102702 : DOI : S2352-3964(20)30077-3

Résumé

Année de publication : 2019

Ruffin N1, Gea-Mallorquí E1, Brouiller F1, Jouve M2, Silvin A1,3, See P3, Dutertre CA3,4, Ginhoux F5, Benaroch P6. (2020 Mar 22)
Constitutive Siglec-1 expression confers susceptibility to HIV-1 infection of human dendritic cell precursors.
Proceedings of the National Academy of Sciences : 116 : Proc Natl Acad Sci U S A. 2019 Oct 22;116(43):21685-21693. doi: 10.1073/pnas.1911007116. Epub 2019 Oct 7. : 21685,21693 : DOI : 10.1073/pnas.1911007116

Résumé

The human dendritic cell (DC) lineage has recently been unraveled by high-dimensional mapping, revealing the existence of a discrete new population of blood circulating DC precursors (pre-DCs). Whether this new DC population possesses specific functional features as compared to the other blood DC subset upon pathogen encounter remained to be evaluated. A unique feature of pre-DCs among blood DCs is their constitutive expression of the viral adhesion receptor Siglec-1. Here, we show that pre-DCs, but not other blood DC subsets, are susceptible to infection by HIV-1 in a Siglec-1-dependent manner. Siglec-1 mediates pre-DC infection of CCR5- and CXCR4-tropic strains. Infection of pre-DCs is further enhanced in the presence of HIV-2/SIVmac Vpx, indicating that Siglec-1 does not counteract restriction factors such as SAMHD1. Instead, Siglec-1 promotes attachment and fusion of viral particles. HIV-1-infected pre-DCs produce new infectious viral particles that accumulate in intracellular compartments reminiscent of the virus-containing compartment of macrophages. Pre-DC activation by toll-like receptor (TLR) ligands induces an antiviral state that inhibits HIV-1 fusion and infection, but Siglec-1 remains functional and mediates replication-independent transfer of HIV-1 to activated primary T lymphocytes. Altogether, Siglec-1-mediated susceptibility to HIV-1 infection of pre-DCs constitutes a unique functional feature that might represent a preferential relationship of this emerging cell type with viruses.

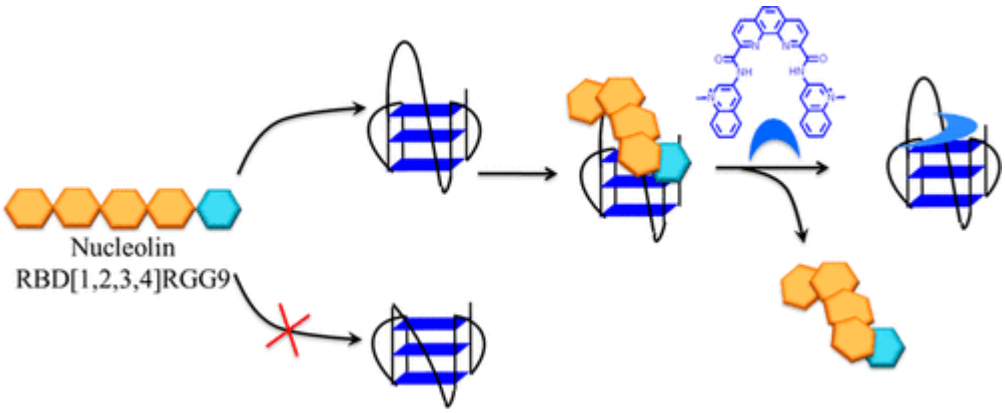
Année de publication : 2020

Abhijit Saha, Patricia Duchambon, Vanessa Masson, Damarys Loew, Sophie Bombard, Marie-Paule Teulade-Fichou (2020 Mar 20)
Nucleolin Discriminates Drastically between Long-Loop and Short-Loop

Quadruplexes.
Biochemistry : 59 : 1261-1272 : DOI : 10.1021/acs.biochem.9b01094

Résumé

We investigate herein the interaction between nucleolin (NCL) and a set of G4 sequences derived from the CEB25 human minisatellite that adopt a parallel topology while differing in the length of the central loop (from nine nucleotides to one nucleotide). It is revealed that NCL strongly binds to long-loop (five to nine nucleotides) G4 while interacting weakly with the shorter variants (loop with fewer than three nucleotides). Photo-cross-linking experiments using 5-bromo-2′-deoxyuridine (BrU)-modified sequences further confirmed the loop-length dependency, thereby indicating that the WT-CEB25-L191 (nine-nucleotide loop) is the best G4 substrate. Quantitative proteomic analysis (LC-MS/MS) of the product(s) obtained by photo-cross-linking NCL to this sequence enabled the identification of one contact site corresponding to a 15-amino acid fragment located in helix α2 of RNA binding domain 2 (RBD2), which sheds light on the role of this structural element in G4-loop recognition. Then, the ability of a panel of benchmark G4 ligands to prevent the NCL-G4 interaction was explored. It was found that only the most potent ligand PhenDC3 can inhibit NCL binding, thereby suggesting that the terminal guanine quartet is also a strong determinant of G4 recognition, putatively through interaction with the RGG domain. This study describes the molecular mechanism by which NCL recognizes G4-containing long loops and leads to the proposal of a model implying a concerted action of RBD2 and RGG domains to achieve specific G4 recognition via a dual loop-quartet interaction.



Moutel S1, Beugnet A1, Schneider A1, Lombard B2, Loew D2, Amigorena S3, Perez F1, Segura E4. (2020 Mar 16)
Surface LSP-1 Is a Phenotypic Marker Distinguishing Human Classical versus Monocyte-Derived Dendritic Cells.
iScience. : 23(4) : DOI : 10.1016/j.isci.2020.100987

Résumé

Martin F Orth, Tilman L B Hölting, Marlene Dallmayer, Fabienne S Wehweck, Tanja Paul, Julian Musa, Michaela C Baldauf, Didier Surdez, Olivier Delattre, Maximilian M L Knott, Laura Romero-Pérez, Merve Kasan, Florencia Cidre-Aranaz, Julia S Gerke, Shunya Ohmura, Jing Li, Aruna Marchetto, Anton G Henssen, Özlem Özen, Shintaro Sugita, Tadashi Hasegawa, Takayuki Kanaseki, Stefanie Bertram, Uta Dirksen, Wolfgang Hartmann, Thomas Kirchner, Thomas G P Grünewald (2020 Mar 14)

High Specificity of BCL11B and GLG1 for EWSR1-FLI1 and EWSR1-ERG Positive Ewing Sarcoma.

Cancers : DOI : E644

Résumé

Ewing sarcoma (EwS) is an aggressive cancer displaying an undifferentiated small-round-cell histomorphology that can be easily confused with a broad spectrum of differential diagnoses. Using comparative transcriptomics and immunohistochemistry (IHC), we previously identified BCL11B and GLG1 as potential specific auxiliary IHC markers for -positive EwS. Herein, we aimed at validating the specificity of both markers in a far larger and independent cohort of EwS (including -positive cases) and differential diagnoses. Furthermore, we evaluated their intra-tumoral expression heterogeneity. Thus, we stained tissue microarrays from 133 molecularly confirmed EwS cases and 320 samples from morphological mimics, as well as a series of patient-derived xenograft (PDX) models for BCL11B, GLG1, and CD99, and systematically assessed the immunoreactivity and optimal cut-offs for each marker. These analyses demonstrated that high BCL11B and/or GLG1 immunoreactivity in CD99-positive cases had a specificity of 97.5% and an accuracy of 87.4% for diagnosing EwS solely by IHC, and that the markers were expressed by -positive EwS. Only little intra-tumoral heterogeneity in immunoreactivity was observed for differential diagnoses. These results indicate that BCL11B and GLG1 may help as specific auxiliary IHC markers in diagnosing EwS in conjunction with CD99, especially if confirmatory molecular diagnostics are not available.

Samah Matmati, Sarah Lambert, Vincent Géli, Stéphane Coulon (2020 Mar 12)

Telomerase Repairs Collapsed Replication Forks at Telomeres.

Cell reports : 3312-3322.e3 : DOI : S2211-1247(20)30233-3

Résumé

Telomeres are difficult-to-replicate sites whereby replication itself may threaten telomere integrity. We investigate, in fission yeast, telomere replication dynamics in telomerase-negative cells to unmask problems associated with telomere replication. Two-dimensional gel analysis reveals that replication of telomeres is severely impaired and correlates with an accumulation of replication intermediates that arises from stalled and collapsed forks. In the absence of telomerase, Rad51, Mre11-Rad50-Nbs1 (MRN) complex, and its co-factor CtIP become critical to maintain telomeres, indicating that homologous recombination processes these intermediates to facilitate fork restart. We further show that a catalytically dead mutant of telomerase prevents Ku recruitment to telomeres, suggesting that telomerase and

Ku both compete for the binding of telomeric-free DNA ends that are likely to originate from a reversed fork. We infer that Ku removal at collapsed telomeric forks allows telomerase to repair broken telomeres, thereby shielding telomeres from homologous recombination.

Edwards-Jorquera SS, Bosveld F, Bellaïche YA, Lennon-Duménil AM, Glavic Á. (2020 Mar 2)
Trpml controls actomyosin contractility and couples migration to phagocytosis in fly macrophages.
Journal of cell biology : 2 : J Cell Biol. 2020 Mar 2;219(3). pii: e201905228. doi: 10.1083/jcb.201905228. : DOI : 10.1083/jcb.201905228

Résumé

Phagocytes use their actomyosin cytoskeleton to migrate as well as to probe their environment by phagocytosis or macropinocytosis. Although migration and extracellular material uptake have been shown to be coupled in some immune cells, the mechanisms involved in such coupling are largely unknown. By combining time-lapse imaging with genetics, we here identify the lysosomal Ca2+ channel Trpml as an essential player in the coupling of cell locomotion and phagocytosis in hemocytes, the Drosophila macrophage-like immune cells. Trpml is needed for both hemocyte migration and phagocytic processing at distinct subcellular localizations: Trpml regulates hemocyte migration by controlling actomyosin contractility at the cell rear, whereas its role in phagocytic processing lies near the phagocytic cup in a myosin-independent fashion. We further highlight that Vamp7 also regulates phagocytic processing and locomotion but uses pathways distinct from those of Trpml. Our results suggest that multiple mechanisms may have emerged during evolution to couple phagocytic processing to cell migration and facilitate space exploration by immune cells.

Lynn GM1,2, Sedlik C3,4, Baharom F5, Zhu Y6, Ramirez-Valdez RA5, Coble VL6, Tobin K5, Nichols SR6, Itzkowitz Y6, Zaidi N5, Gammon JM7, Blobel NJ5, Denizeau J3,4, de la Rochere P3,4, Francica BJ8,9, Decker B6, Maciejewski M6, Cheung J5, Yamane H5, Smelkinson MG10, Francica JR5, Laga R11, Bernstock JD6,12, Seymour LW13, Drake CG8,14, Jewell CM7, Lantz O3,4, Piaggio E3,4, Ishizuka AS5,6, Seder RA15. (2020 Mar 2)
Peptide-TLR-7/8a conjugate vaccines chemically programmed for nanoparticle self-assembly enhance CD8 T-cell immunity to tumor antigens.
Nature biotechnology : 38(3) : 320-332 : DOI : 10.1038/s41587-019-0390-x

Résumé

Paudel B.P., Moye A.L., Assi H.A., El-Khoury R., Cohen S.B., Birrento M.L., Samosorn S., Intharapichai K., Tomlinson C.G., Teulade-Fichou M.P., Gonz'alez C., Beck J.L., Damha M.J., van Oijen A.M., Bryan T.M. (2020 Feb 27)

A mechanism for the extension and unfolding of parallel telomeric G-quadruplexes by human telomerase at single-molecule resolution
bioRxiv : DOI : 10.1101/2020.02.26.965269

Résumé

Telomeric G-quadruplexes (G4) were long believed to form a protective structure at telomeres, preventing their extension by the ribonucleoprotein telomerase. Contrary to this belief, we have previously demonstrated that parallel-stranded conformations of telomeric G4 can be extended by human and ciliate telomerase. However, a mechanistic understanding of the interaction of telomerase with structured DNA remained elusive. Here, we use single-molecule fluorescence resonance energy transfer (smFRET) microscopy and bulk-phase enzymology to propose a mechanism for the resolution and extension of parallel G4 by telomerase. Binding is initiated by the RNA template of telomerase interacting with the G-quadruplex; nucleotide addition then proceeds to the end of the RNA template. It is only through the large conformational change of translocation following synthesis that the G-quadruplex structure is completely unfolded to a linear product. Surprisingly, parallel G4 stabilization with either small molecule ligands or by chemical modification does not always inhibit G4 unfolding and extension by telomerase. These data reveal that telomerase is a parallel G-quadruplex resolvase.

Carsten Janke, Maria M Magiera (2020 Feb 27)
The tubulin code and its role in controlling microtubule properties and functions.
Nature reviews. Molecular cell biology : DOI : 10.1038/s41580-020-0214-3

Résumé

Microtubules are core components of the eukaryotic cytoskeleton with essential roles in cell division, shaping, motility and intracellular transport. Despite their functional heterogeneity, microtubules have a highly conserved structure made from almost identical molecular building blocks: the tubulin proteins. Alternative tubulin isotypes and a variety of post-translational modifications control the properties and functions of the microtubule cytoskeleton, a concept known as the 'tubulin code'. Here we review the current understanding of the molecular components of the tubulin code and how they impact microtubule properties and functions. We discuss how tubulin isotypes and post-translational modifications control microtubule behaviour at the molecular level and how this translates into physiological functions at the cellular and organism levels. We then go on to show how fine-tuning of microtubule function by some tubulin modifications can affect homeostasis and how perturbation of this fine-tuning can lead to a range of dysfunctions, many of which are linked to human disease.