**Year of publication 2019**

Mijo Simunovic, Emma Evergren, Andrew Callan-Jones*, Patricia Bassereau* (2019 Oct 7)

**Curving Cells Inside and Out: Roles of BAR Domain Proteins in Membrane Shaping and Its Cellular Implications.**

*Annual Review of Cell and Developmental Biology* : 35 : DOI : 10.1146/annurev-cellbio-100617-060558

**Summary**

Many cellular processes rely on precise and timely deformation of the cell membrane. While many proteins participate in membrane reshaping and scission, usually in highly specialized ways, Bin/amphiphysin/Rvs (BAR) domain proteins play a pervasive role, as they not only participate in many aspects of cell trafficking but also are highly versatile membrane remodelers. Subtle changes in the shape and size of the BAR domain can greatly impact the way in which BAR domain proteins interact with the membrane. Furthermore, the activity of BAR domain proteins can be tuned by external physical parameters, and so they behave differently depending on protein surface density, membrane tension, or membrane shape. These proteins can form 3D structures that mold the membrane and alter its liquid properties, even promoting scission under various circumstances. As such, BAR domain proteins have numerous roles within the cell. Endocytosis is among the most highly studied processes in which BAR domain proteins take on important roles. Over the years, a more complete picture has emerged in which BAR domain proteins are tied to almost all intracellular compartments; examples include endosomal sorting and tubular networks in the endoplasmic reticulum and T-tubules. These proteins also have a role in autophagy, and their activity has been linked with cancer. Here, we briefly review the history of BAR domain protein discovery, discuss the mechanisms by which BAR domain proteins induce curvature, and attempt to settle important controversies in the field. Finally, we review BAR domain proteins in the context of a cell, highlighting their emerging roles in cell signaling and organelle shaping.

Anissia Ait-Saada, Olga Khorosjutina, Jiang Chen, Karol Kramarz, Vladimir Maksimov, J Peter Svensson, Sarah Lambert, Karl Ekwall (2019 Oct 1)

**Chromatin remodeler Fft3 plays a dual role at blocked DNA replication forks.**

*Life science alliance* : DOI : e201900433

**Summary**

Here, we investigate the function of fission yeast Fun30/Smarcad1 family of SNF2 ATPase-dependent chromatin remodeling enzymes in DNA damage repair. There are three Fun30 homologues in fission yeast, Fft1, Fft2, and Fft3. We find that only Fft3 has a function in DNA repair and it is needed for single-strand annealing of an induced double-strand break. Furthermore, we use an inducible replication fork barrier system to show that Fft3 has two distinct roles at blocked DNA replication forks. First, Fft3 is needed for the resection of nascent strands, and second, it is required to restart the blocked forks. The latter function is

independent of its ATPase activity.

Dubois R., Imbert A., Samacoïts A., Peter M., Bertrand E., Müller F., Walter T. (2019 Sep 24)
**A Deep Learning Approach To Identify MRNA Localization Patterns**
*IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019)IEEE 16th International Symposium on Biomedical Imaging (ISBI 2019)*

**Summary**

Attner MA*, Keil W*, Benavidez JM, Greenwald I (2019 Sep 23)
**HLH-2/E2A Expression Links Stochastic and Deterministic Elements of a Cell Fate Decision during C. elegans Gonadogenesis**
*Current Biology* : 29 : 1-7 : DOI : https://doi.org/10.1016/j.cub.2019.07.062

**Summary**

Franck Court, Elisa Le Boiteux, Anne Fogli, Mélanie Müller-Barthélémy, Catherine Vaurs-Barrière, Emmanuel Chautard, Bruno Pereira, Julian Biau, Jean-Louis Kemeny, Toufic Khalil, Lucie Karayan-Tapon, Pierre Verrelle, Philippe Arnaud (2019 Sep 20)
**Transcriptional alterations in glioma result primarily from DNA methylation-independent mechanisms.**
*Genome research* : Epub ahead of print : DOI : 10.1101/gr.249219.119

**Summary**

In cancer cells, aberrant DNA methylation is commonly associated with transcriptional alterations, including silencing of tumor suppressor genes. However, multiple epigenetic mechanisms, including polycomb repressive marks, contribute to gene deregulation in cancer. To dissect the relative contribution of DNA methylation-dependent and -independent mechanisms to transcriptional alterations at CpG island/promoter-associated genes in cancer, we studied 70 samples of adult glioma, a widespread type of brain tumor, classified according to their isocitrate dehydrogenase (*IDH1*) mutation status. We found that most transcriptional alterations in tumor samples were DNA methylation-independent. Instead, altered histone H3 trimethylation at lysine 27 (H3K27me3) was the predominant molecular defect at deregulated genes. Our results also suggest that the presence of a bivalent chromatin signature at CpG island promoters in stem cells predisposes not only to hypermethylation, as widely documented, but more generally to all types of transcriptional alterations in transformed cells. In addition, the gene expression strength in healthy brain cells influences the choice between DNA methylation- and H3K27me3-associated silencing in glioma. Highly expressed genes were more likely to be repressed by H3K27me3 than by DNA methylation. Our findings support a model in which altered H3K27me3 dynamics, more specifically defects in the interplay between polycomb protein complexes and the brain-

specific transcriptional machinery, is the main cause of transcriptional alteration in glioma cells. Our study provides the first comprehensive description of epigenetic changes in glioma and their relative contribution to transcriptional changes. It may be useful for the design of drugs targeting cancer-related epigenetic defects.

Héctor Climente-González, Chloé-Agathe Azencott, Samuel Kaski, Makoto Yamada (2019 Sep 13)

**Block HSIC Lasso: model-free biomarker detection for ultra-high dimensional data.**

*Bioinformatics (Oxford, England)* : i427-i435 : DOI : 10.1093/bioinformatics/btz333

**Summary**

Finding non-linear relationships between biomolecules and a biological outcome is computationally expensive and statistically challenging. Existing methods have important drawbacks, including among others lack of parsimony, non-convexity and computational overhead. Here we propose block HSIC Lasso, a non-linear feature selector that does not present the previous drawbacks.

Moitrier Sarah, Pricoupenko Nastassia, Kerjouan Adèle, Oddou Christiane, Destaing Olivier, Battistella Aude, Silberzan Pascal, Bonnet Isabelle (2019 Sep 3)

**Local light-activation of the Src oncoprotein in an epithelial monolayer promotes collective extrusion**

*Communications Physics* : 2 : 98 : DOI : 10.1038/s42005-019-0198-5

**Summary**

Transformed isolated cells are usually extruded from normal epithelia and subsequently eliminated. However, multicellular tumors outcompete healthy cells, highlighting the importance of collective effects. Here, we investigate this situation in vitro by controlling in space and time the activity of the Src oncoprotein within a normal Madin–Darby Canine Kidney (MDCK) epithelial cell monolayer. Using an optogenetics approach with cells expressing a synthetic light-sensitive version of Src (optoSrc), we reversibly trigger the oncogenic activity by exposing monolayers to well-defined light patterns. We show that small populations of activated optoSrc cells embedded in the non-transformed monolayer collectively extrude as a tridimensional aggregate and remain alive, while the surrounding normal cells migrate towards the exposed area. This phenomenon requires an interface between normal and transformed cells and is partially reversible. Traction forces show that Src- activated cells either actively extrude or are pushed out by the surrounding cells in a non- autonomous way.

Angrand G., Quillévéré A., Loaëc N., Daskalogianni C., Granzhan A., Teulade-Fichou M.P., Fahraeus R., Prado Martins R., Blondel M. (2019 Sep 1)

**Sneaking Out for Happy Hour: Yeast-Based Approaches to Explore and Modulate Immune Response and Immune Evasion**
*Genes* : 10 : 667-689 : DOI : 10.3390/genes10090667

**Summary**

Many pathogens (virus, bacteria, fungi, or parasites) have developed a wide variety of mechanisms to evade their host immune system. The budding yeast Saccharomyces cerevisiae has successfully been used to decipher some of these immune evasion strategies. This includes the cis-acting mechanism that limits the expression of the oncogenic Epstein–Barr virus (EBV)-encoded EBNA1 and thus of antigenic peptides derived from this essential but highly antigenic viral protein. Studies based on budding yeast have also revealed the molecular bases of epigenetic switching or recombination underlying the silencing of all except one members of extended families of genes that encode closely related and highly antigenic surface proteins. This mechanism is exploited by several parasites (that include pathogens such as Plasmodium, Trypanosoma, Candida, or Pneumocystis) to alternate their surface antigens, thereby evading the immune system. Yeast can itself be a pathogen, and pathogenic fungi such as Candida albicans, which is phylogenetically very close to S. cerevisiae, have developed stealthiness strategies that include changes in their cell wall composition, or epitope-masking, to control production or exposure of highly antigenic but essential polysaccharides in their cell wall. Finally, due to the high antigenicity of its cell wall, yeast has been opportunistically exploited to create adjuvants and vectors for vaccination.

François Legoux, Déborah Bellet, Celine Daviaud, Yara El Morr, Aurelie Darbois, Kristina Niort, Emanuele Procopio, Marion Salou, Jules Gilet, Bernhard Ryffel, Aurélie Balvay, Anne Foussier, Manal Sarkis, Ahmed El Marjou, Frederic Schmidt, Sylvie Rabot, Olivier Lantz (2019 Aug 31)
**Microbial metabolites control the thymic development of mucosal-associated invariant T cells.**
*Science (New York, N.Y.)* : DOI : eaaw2719

**Summary**

How the microbiota modulate immune functions remains poorly understood. Mucosal-associated invariant T (MAIT) cells are implicated in mucosal homeostasis and absent in germ-free mice. Here, we show that commensal bacteria govern murine MAIT intrathymic development, as MAIT cells did not recirculate to the thymus. MAIT development required expression in bacteria, indicating that production of the MAIT antigen 5-(2-oxopropylideneamino)-6-d-ribitylaminouracil (5-OP-RU) was necessary. 5-OP-RU rapidly traveled from mucosal surfaces to the thymus, where it was captured by the major histocompatibility complex class Ib molecule MR1. This led to increased numbers of the earliest MAIT precursors and the expansion of more mature receptor-related orphan receptor γt-positive MAIT cells. Thus, a microbiota-derived metabolite controls development of mucosally targeted T cells, in a process blurring the distinction between exogenous and self-antigens.

Ugo Szachnowski, Sara Andus, Dominika Foretek, Antonin Morillon, Maxime Wery (2019 Aug 30)
**Endogenous RNAi pathway evolutionarily shapes the destiny of the antisense lncRNAs transcriptome.**
*Life science alliance* : DOI : e201900407

**Summary**

Antisense long noncoding (aslnc)RNAs are extensively degraded by the nuclear exosome and the cytoplasmic exoribonuclease Xrn1 in the budding yeast , lacking RNAi. Whether the ribonuclease III Dicer affects aslncRNAs in close RNAi-capable relatives remains unknown. Using genome-wide RNA profiling, here we show that aslncRNAs are primarily targeted by the exosome and Xrn1 in the RNAi-capable budding yeast , Dicer only affecting Xrn1-sensitive aslncRNAs levels in Xrn1-deficient cells. The and mutants display synergic growth defects, indicating that Dicer becomes critical in the absence of Xrn1. Small RNA sequencing showed that Dicer processes aslncRNAs into small RNAs, with a preference for Xrn1-sensitive aslncRNAs. Consistently, Dicer localizes into the cytoplasm. Finally, we observed an expansion of the exosome-sensitive antisense transcriptome in compared with , suggesting that the presence of cytoplasmic RNAi has reinforced the nuclear RNA surveillance machinery to temper aslncRNAs expression. Our data provide fundamental insights into aslncRNAs metabolism and open perspectives into the possible evolutionary contribution of RNAi in shaping the aslncRNAs transcriptome.

Roberta Ragazzini, Raquel Pérez-Palacios, Irem H Baymaz, Seynabou Diop, Katia Ancelin, Dina Zielinski, Audrey Michaud, Maëlle Givelet, Mate Borsos, Setareh Aflaki, Patricia Legoix, Pascal W T C Jansen, Nicolas Servant, Maria-Elena Torres-Padilla, Deborah Bourc'his, Pierre Fouchet, Michiel Vermeulen, Raphaël Margueron (2019 Aug 28)
**EZHIP constrains Polycomb Repressive Complex 2 activity in germ cells.**
*Nature communications* : 3858 : DOI : 10.1038/s41467-019-11800-x

**Summary**

The Polycomb group of proteins is required for the proper orchestration of gene expression due to its role in maintaining transcriptional silencing. It is composed of several chromatin modifying complexes, including Polycomb Repressive Complex 2 (PRC2), which deposits H3K27me2/3. Here, we report the identification of a cofactor of PRC2, EZHIP (EZH1/2 Inhibitory Protein), expressed predominantly in the gonads. EZHIP limits the enzymatic activity of PRC2 and lessens the interaction between the core complex and its accessory subunits, but does not interfere with PRC2 recruitment to chromatin. Deletion of Ezhip in mice leads to a global increase in H3K27me2/3 deposition both during spermatogenesis and at late stages of oocyte maturation. This does not affect the initial number of follicles but is associated with a reduction of follicles in aging. Our results suggest that mature oocytes Ezhip-/- might not be fully functional and indicate that fertility is strongly impaired in Ezhip-/- females. Altogether, our study uncovers EZHIP as a regulator of chromatin landscape in gametes.

Markus Frederik Schliffka, Jean-Léon Maître (2019 Aug 25)
**Stay hydrated: basolateral fluids shaping tissues.**
*Current opinion in genetics & development* : 70-77 : DOI : S0959-437X(19)30021-8

**Summary**

During development, embryos perform a mesmerizing choreography, which is crucial for the correct shaping, positioning and function of all organs. The cellular properties powering animal morphogenesis have been the focus of much attention. In contrast, much less consideration has been given to the invisible engine constituted by the intercellular fluid. Cells are immersed in fluid, of which the composition and physical properties have a considerable impact on development. In this review, we revisit recent studies from the perspective of the fluid, focusing on basolateral fluid compartments and taking the early mouse and zebrafish embryos as models. These examples illustrate how the hydration levels of tissues are spatio-temporally controlled and influence embryonic development.

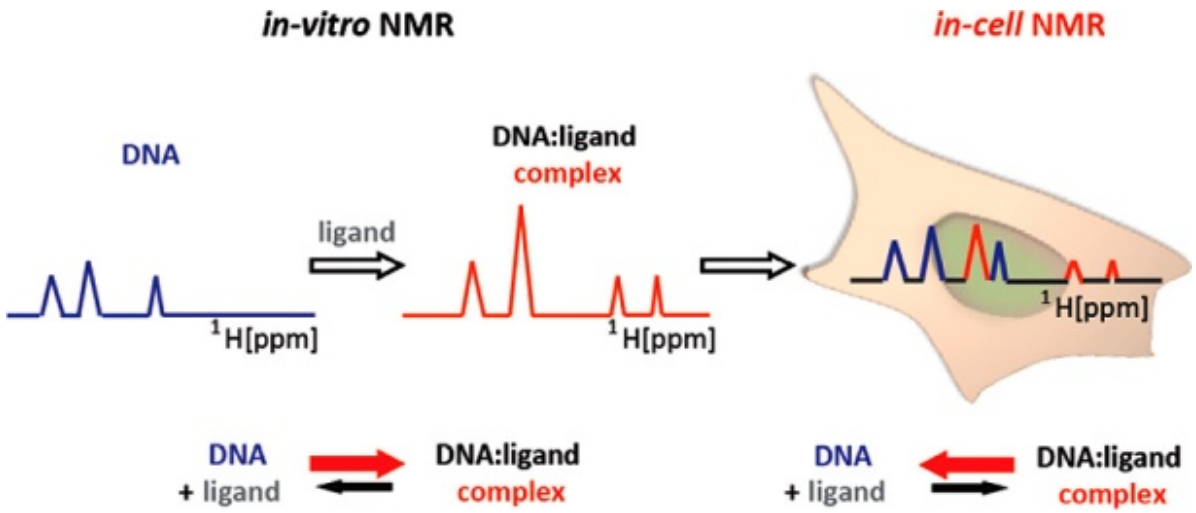
Abegão L.M.G., Fonseca R.D., Santos F.A., Rodrigues J.J., Kamada K., Mendonça C.R., Piguel S., De Boni L. (2019 Aug 23)
**First molecular electronic hyperpolarizability of series of π-conjugated oxazole dyes in solution: an experimental and theoretical study**
*RSC Adv.* : 9 : 26476-26482 : DOI : 10.1039/C9RA05246A

**Summary**

In this work, we report the experimental and theoretical first molecular electronic hyperpolarizability (βHRS) of eleven π-conjugated oxazoles compounds in toluene medium. The Hyper-Rayleigh Scattering (HRS) technique allowed the determination of the experimental dynamic βHRS values, by exciting the compounds with a picosecond pulse trains from a Q-switched and mode-locked Nd:YAG laser tuned at 1064 nm. Theoretical predictions based on time-dependent density functional theory level using the Gaussian 09 program package were performed with three different functionals (B3LYP, CAM-B3LYP, and M06-2X), to calculate both static and dynamic theoretical βHRS values. Good accordance was found between the experimental and theoretical values, in particular for the CAM-B3LYP and M06-2X functionals.

Michaela Krafcikova, Simon Dzatko, Coralie Caron, Anton Granzhan, Radovan Fiala, Tomas Loja, Marie-Paule Teulade-Fichou, Tomas Fessl, Robert Hänsel-Hertsch, Jean-Louis Mergny, Silvie Foldynova-Trantirkova, Lukas Trantirek (2019 Aug 9)
**Monitoring DNA–Ligand Interactions in Living Human Cells Using NMR Spectroscopy**
*Journal of the Americal Chemical Society* : 141 : 13281-13285 : DOI : 10.1021/jacs.9b03031

**Summary**



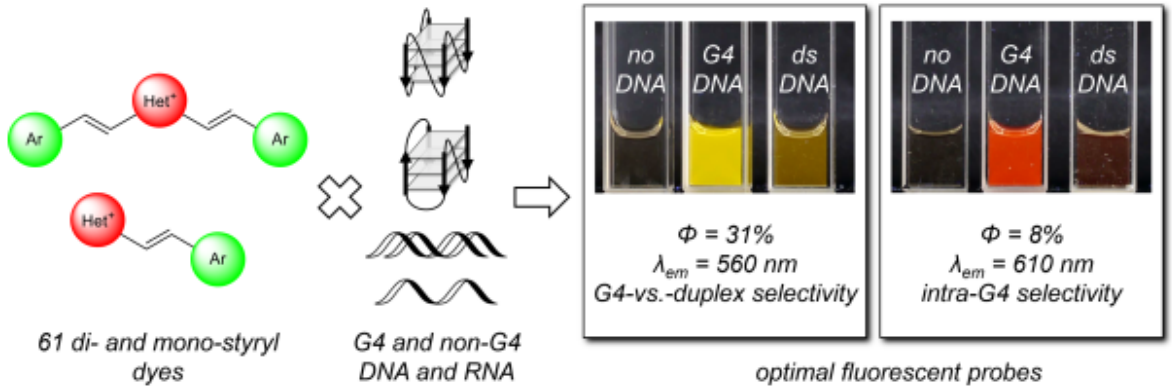

Studies on DNA–ligand interactions in the cellular environment are problematic due to the lack of suitable biophysical tools. To address this need, we developed an *in-cell* NMR-based approach for monitoring DNA–ligand interactions inside the nuclei of living human cells. Our method relies on the acquisition of NMR data from cells electroporated with preformed DNA–ligand complexes. The impact of the intracellular environment on the integrity of the complexes is assessed based on *in-cell* NMR signals from unbound and ligand-bound forms of a given DNA target. This technique was tested on complexes of two model DNA fragments and four ligands, namely, a representative DNA minor-groove binder (netropsin) and ligands binding DNA base-pairing defects (naphthalenophanes). In the latter case, we demonstrate that two of the three *in vitro*-validated ligands retain their ability to form stable interactions with their model target DNA *in cellulo*, whereas the third one loses this ability due to off-target interactions with genomic DNA and cellular metabolites. Collectively, our data suggest that direct evaluation of the behavior of drug-like molecules in the intracellular environment provides important insights into the development of DNA-binding ligands with desirable biological activity and minimal side effects resulting from off-target binding.

Xiao Xie, Michela Zuffo, Marie-Paule Teulade-Fichou, Anton Granzhan (2019 Aug 6)

**Identification of optimal fluorescent probes for G-quadruplex nucleic acids through systematic exploration of mono- and distyryl dye libraries**

*Beilstein Journal of Organic Chemistry* : 15 : 1872–1889 : DOI : 10.3762/bjoc.15.183

**Summary**




A library of 52 distyryl and 9 mono-styryl cationic dyes was synthesized and investigated with respect to their optical properties, propensity to aggregation in aqueous medium, and capacity to serve as fluorescence “light-up” probes for G-quadruplex (G4) DNA and RNA structures. Among the 61 compounds, 57 dyes showed preferential enhancement of fluorescence intensity in the presence of one or another G4-DNA or RNA structure, while no dye displayed preferential response to double-stranded DNA or single-stranded RNA analytes employed at equivalent nucleotide concentration. Thus, preferential fluorimetric response towards G4 structures appears to be a common feature of mono- and distyryl dyes, including long-known mono-styryl dyes used as mitochondrial probes or protein stains. However, the magnitude of the G4-induced “light-up” effect varies drastically, as a function of both the molecular structure of the dyes and the nature or topology of G4 analytes. Although our results do not allow to formulate comprehensive structure–properties relationships, we identified several structural motifs, such as indole- or pyrrole-substituted distyryl dyes, as well as simple mono-stryryl dyes such as **DASPMI** [2-(4-(dimethylamino)styryl)-1-methylpyridinium iodide] or its 4-isomer, as optimal fluorescent light-up probes characterized by high fluorimetric response (*I/I* of up to 550-fold), excellent selectivity with respect to double-stranded DNA or single-stranded RNA controls, high quantum yield in the presence of G4 analytes (up to 0.32), large Stokes shift (up to 150 nm) and, in certain cases, structural selectivity with respect to one or another G4 folding topology. These dyes can be considered as promising G4-responsive sensors for in vitro or imaging applications. As a possible application, we implemented a simple two-dye fluorimetric assay allowing rapid topological classification of G4-DNA structures.