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Marine Verhulsel, Anthony Simon, Moencopi Bernheim-Dennery, Venkata Ram Gannavarapu, Lauriane Gérémié, Davide Ferraro, Denis Krndija, Laurence Talini, Jean-Louis Viovy, Danijela Matic Vignjevic, Stéphanie Descroix (2020 Dec 11)

Developing an advanced gut on chip model enabling the study of epithelial cell/fibroblast interactions.

Lab on a chip : 365-377 : [DOI : 10.1039/d0lc00672f](https://doi.org/10.1039/d0lc00672f)

Résumé

Organoids are widely used as a model system to study gut pathophysiology; however, they fail to fully reproduce the complex, multi-component structure of the intestinal wall. We present here a new gut on chip model that allows the co-culture of primary epithelial and stromal cells. The device has the topography and dimensions of the mouse gut and is based on a 3D collagen I scaffold. The scaffold is coated with a thin layer of laminin to mimic the basement membrane. To maintain the scaffold structure while preserving its cytocompatibility, the collagen scaffold was rigidified by threose-based post-polymerization treatment. This treatment being cytocompatible enabled the incorporation of primary intestinal fibroblasts inside the scaffold, reproducing the gut stromal compartment. We observed that mouse organoids, when deposited into crypts, opened up and epithelialized the scaffold, generating a polarized epithelial monolayer. Proper segregation of dividing and differentiated cells along the crypt-villus axis was achieved under these conditions. Finally, we show that the application of fluid shear stress allows the long-term culture of this intestinal epithelium. Our device represents a new biomimetic tool that captures key features of the gut complexity and could be used to study gut pathophysiology.

Valentin Partula, Mélanie Deschasaux-Tanguy, Stanislas Mondot, Agnès Victor-Bala, Nadia Bouchemal, Lucie Lecuyer, Christine Bobin-Dubigeon, Marion J Torres, Emmanuelle Kesse-Guyot, Bruno Charbit, Etienne Patin, Karen E Assmann, Paule Latino-Martel, Chantal Julia, Pilar Galan, Serge Hercberg, Lluís Quintana-Murci, Matthew L Albert, Darragh Duffy, Olivier Lantz, Philippe Savarin, Mohamed Nawfal Triba, Mathilde Touvier, (2020 Dec 10)

Associations between untargeted plasma metabolomic signatures and gut microbiota composition in the population of healthy adults.

The British journal of nutrition : 1-29 : [DOI : 10.1017/S0007114520004870](https://doi.org/10.1017/S0007114520004870)

Résumé

Host-microbial co-metabolism products are being increasingly recognized to play important roles in physiological processes. However, studies undertaking a comprehensive approach to consider host-microbial metabolic relationships remain scarce. Metabolomic analysis yielding detailed information regarding metabolites found in a given biological compartment holds promise for such an approach. This work aimed to explore the associations between host plasma metabolomic signatures and gut microbiota composition in healthy adults of the

Milieu Intérieur study. For 846 subjects, gut microbiota composition was profiled through sequencing of the 16S rRNA gene in stools. Metabolomic signatures were generated through proton nuclear magnetic resonance analysis of plasma. The associations between metabolomic variables and α - and β -diversity indexes and relative taxa abundances were tested using multi-adjusted partial Spearman correlations, PERMANOVAs, and MaAsLins, respectively. A Multiple testing correction was applied (Benjamini-Hochberg, 10%-FDR). Microbial richness was negatively associated with lipid-related signals and positively associated with amino acids, choline, creatinine, glucose, and citrate ($-0.133 \leq \text{Spearman's } \rho \leq 0.126$). Specific associations between metabolomic signals and abundances of taxa were detected (25 at the genus level and 19 at the species level): notably, numerous associations were observed for creatinine (positively associated with 11 species, and negatively associated with *Faecalibacterium prausnitzii*). This large-scale population-based study highlights metabolites associated with gut microbial features and provides new insights into the understanding of complex host-gut microbiota metabolic relationships. In particular, our results support the implication of a « gut-kidney axis ». More studies providing a detailed exploration of these complex interactions, and their implications for host health are needed.

Wolfgang A Weber, Johannes Czernin, Carolyn J Anderson, Ramsey D Badawi, Henryk Barthel, Frank Bengel, Lisa Bodei, Irène Buvat, Marcelo DiCarli, Michael M Graham, Jan Grimm, Ken Herrmann, Lale Kostakoglu, Jason S Lewis, David A Mankoff, Todd E Peterson, Heinrich Schelbert, Heiko Schöder, Barry A Siegel, H William Strauss (2020 Dec 9)

The Future of Nuclear Medicine, Molecular Imaging, and Theranostics.

Journal of nuclear medicine : official publication, Society of Nuclear Medicine : 263S-272S : DOI : [10.2967/jnumed.120.254532](https://doi.org/10.2967/jnumed.120.254532)

Résumé

Antoine Vasseur, Nicolas Kiavue, François-Clément Bidard, Jean-Yves Pierga, Luc Cabel (2020 Dec 8)

Clinical utility of circulating tumor cells: an update.

Molecular oncology : DOI : [10.1002/1878-0261.12869](https://doi.org/10.1002/1878-0261.12869)

Résumé

The prognostic role of circulating tumor cells (CTCs) has been clearly demonstrated in many types of cancer. However, their roles in diagnostic and treatment strategies remain to be defined. In this review, we present an overview of the current clinical validity of CTCs in non-metastatic and metastatic cancer, and the main studies or concepts investigating the clinical utility of CTCs. In particular, we focus on breast-, lung-, colorectal- and prostate cancer. Two major topics concerning the clinical utility of CTC are discussed: treatment based on CTC count or CTC variations; and treatment based on the molecular characteristics of CTCs. Although some of these studies are inconclusive, many are still ongoing, and their results could help to define the role of CTCs in the management of cancers. A summary of published or ongoing phase II-III trials is also presented.

A-S Cottreau, M Meignan, C Nioche, N Capobianco, J Clerc, L Chartier, L Vercellino, O Casasnovas, C Thieblemont, I Buvat (2020 Dec 5)

Risk stratification in diffuse large B-cell lymphoma using lesion dissemination and metabolic tumor burden calculated from baseline PET/CT.

Annals of oncology : official journal of the European Society for Medical Oncology : 404-411 : [DOI : S0923-7534\(20\)43174-6](#)

Résumé

We analyzed the prognostic value of a new baseline positron emission tomography (PET) parameter reflecting the spread of the disease, the largest distance between two lesions (Dmax). We tested its complementarity to metabolic tumor volume (MTV) in a large cohort of diffuse large B-cell lymphoma (DLBCL) patients from the REMARC trial (NCT01122472).

Pierre-François Lenne, Edwin Munro, Idse Heemskerk, Aryeh Warmflash, Laura Bocanegra-Moreno, Kasumi Kishi, Anna Kicheva, Yuchen Long, Antoine Fruleux, Arezki Boudaoud, Timothy E Saunders, Paolo Caldarelli, Arthur Michaut, Jerome Gros, Yonit Maroudas-Sacks, Kinneret Keren, Edouard Hannezo, Zev J Gartner, Benjamin Stormo, Amy Gladfelter, Alan Rodrigues, Amy Shyer, Nicolas Minc, Jean-Léon Maître, Stefano Di Talia, Bassma Khamaisi, David Sprinzak, Sham Tlili (2020 Dec 4)

Roadmap for the multiscale coupling of biochemical and mechanical signals during development.

Physical biology : [DOI : 10.1088/1478-3975/abd0db](#)

Résumé

The way in which interactions between mechanics and biochemistry lead to the emergence of complex cell and tissue organization is an old question that has recently attracted renewed interest from biologists, physicists, mathematicians and computer scientists. Rapid advances in optical physics, microscopy and computational image analysis have greatly enhanced our ability to observe and quantify spatiotemporal patterns of signalling, force generation, deformation, and flow in living cells and tissues. Powerful new tools for genetic, biophysical and optogenetic manipulation are allowing us to perturb the underlying machinery that generates these patterns in increasingly sophisticated ways. Rapid advances in theory and computing have made it possible to construct predictive models that describe how cell and tissue organization and dynamics emerge from the local coupling of biochemistry and mechanics. Together, these advances have opened up a wealth of new opportunities to explore how mechanochemical patterning shapes organismal development. In this roadmap, we present a series of forward-looking case studies on mechanochemical patterning in development, written by scientists working at the interface between the physical and biological sciences, and covering a wide range of spatial and temporal scales, organisms, and modes of development. Together, these contributions highlight the many ways in which the dynamic coupling of mechanics and biochemistry shapes biological dynamics: from mechanoenzymes that sense force to tune their activity and motor output, to

collectives of cells in tissues that flow and redistribute biochemical signals during development.

Silvia Menegatti, Vincent Guillemot, Eleonora Latis, Hanane Yahia-Cherbal, Daniela Mittermüller, Vincent Rouilly, Elena Mascia, Nicolas Rosine, Surya Koturan, Gael A Millot, Claire Leloup, Darragh Duffy, Aude Gleizes, Salima Hacein-Bey-Abina, , Jérémie Sellam, Francis Berenbaum, Corinne Miceli, Maxime Dougados, Elisabetta Bianchi, Lars Rogge (2020 Dec 3)

Immune response profiling of patients with spondyloarthritis reveals signalling networks mediating TNF-blocker function in vivo.

Annals of the rheumatic diseases : [DOI : annrheumdis-2020-218304](https://doi.org/10.1093/rheumatism/kzab001)

Résumé

Antitumour necrosis factor (TNF) therapy has revolutionised treatment of several chronic inflammatory diseases, including spondyloarthritis (SpA). However, TNF inhibitors (TNFi) are not effective in all patients and the biological basis for treatment failure remains unknown. We have analysed induced immune responses to define the mechanism of action of TNF blockers in SpA and to identify immunological correlates of responsiveness to TNFi.

François Anna, Sophie Goyard, Ana Ines Lalanne, Fabien Nevo, Marion Gransagne, Philippe Souque, Delphine Louis, Véronique Gillon, Isabelle Turbiez, François-Clément Bidard, Aline Gobillion, Alexia Savignoni, Maude Guillot-Delost, François Dejardin, Evelyne Dufour, Stéphane Petres, Odile Richard-Le Goff, Zaineb Choucha, Olivier Helynck, Yves L Janin, Nicolas Escriou, Pierre Charneau, Franck Perez, Thierry Rose, Olivier Lantz (2020 Dec 1)

High seroprevalence but short-lived immune response to SARS-CoV-2 infection in Paris.

European journal of immunology : [DOI : 10.1002/eji.202049058](https://doi.org/10.1002/eji.202049058)

Résumé

Although the COVID-19 pandemic peaked in March/April 2020 in France, the prevalence of infection is barely known. Using high-throughput methods, we assessed herein the serological response against the SARS-CoV-2 virus of 1847 participants working in three sites of an institution in Paris conurbation. In May-July 2020, 11% (95% CI: 9.7-12.6) of serums were positive for IgG against the SARS-CoV-2 N and S proteins, and 9.5% (CI:8.2-11.0) were neutralizer in pseudo-typed virus assays. The prevalence of seroconversion was 11.6% (CI:10.2-13.2) when considering positivity in at least one assays. In 5% of RT-qPCR positive individuals, no systemic IgGs were detected. Among immune individuals, 21% had been asymptomatic. Anosmia (loss of smell) and ageusia (loss of taste) occurred in 52% of the IgG-positive individuals and in 3% of the negative ones. In contrast, 30% of the anosmia-ageusia cases were seronegative suggesting that the true prevalence of infection may have reached 16.6%. In sera obtained 4-8 weeks after the first sampling anti-N and anti-S IgG titers and neutralization activity in pseudo-virus assay declined by 31%, 17% and 53%,

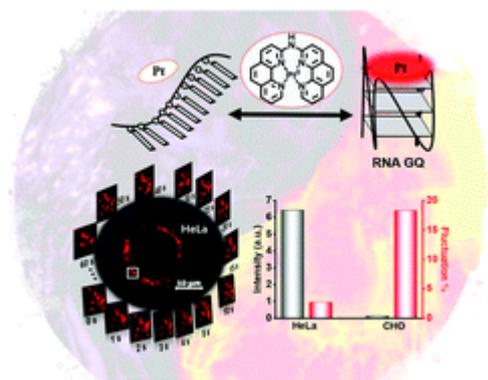
resulting thus in half-life of respectively 35, 87 and 28 days. The population studied is representative of active workers in Paris. The short lifespan of the serological systemic responses suggests an underestimation of the true prevalence of infection. This article is protected by copyright. All rights reserved.

Lei He, Zhenyu Meng, Qianqian Guo, Xiangyang Wu, Marie-Paule Teulade-Fichou, Edwin Kok Lee Yeow, Fangwei Shao (2020 Nov 28)

Fluorogenic Pt complexes distinguish the quantity and folding behavior of RNA G-quadruplexes between live cancerous and healthy cells.

Chemical communications (Cambridge, England) : 56 : 14459-14462 : [DOI : 10.1039/d0cc05622g](https://doi.org/10.1039/d0cc05622g)

Résumé



Two Pt complexes with high quantum yields and photostability, and low cytotoxicity, were developed to track RNA G-quadruplexes (GQs) in live cells. Higher number and intensity, and longer lifetime of fluorescent foci in cancer cells than those in healthy cells suggest that the quantity and folding dynamics of RNA GQs could not only correlate to their biological functions, but be two novel biomarkers to characterize cancerous cells.

Leduc A., Chaouni S., De marzi L., Pouzoulet F., Mégnin-Chanet F., Stephan D., Habrand J.L., Sichel F., Laurent C. (2020 Nov 24)

Biological Effects of Scattered Versus Scanned Proton Beams on Normal Tissues in Total Body Irradiated Mice: Survival, Genotoxicity, Oxidative Stress and Inflammation

Antioxidants : 9 : 1170 : [DOI : 10.3390/antiox9121170](https://doi.org/10.3390/antiox9121170)

Résumé

Side effects of proton therapy are poorly studied. Moreover, the differences in the method of dose delivery on normal tissues are not taken into account when proton beams are scanned instead of being scattered. We proposed here to study the effects of both modalities of

proton beam delivery on blood; skin; lung and heart in a murine model. In that purpose; C57BL/6 mice were total body irradiated by 190.6 MeV proton beams either by Double Scattering (DS) or by Pencil Beam Scanning (PBS) in the plateau phase before the Bragg Peak. Mouse survival was evaluated. Blood and organs were removed three months after irradiation. Biomarkers of genotoxicity; oxidative stress and inflammation were measured. Proton irradiation was shown to increase lymphocyte micronucleus frequency; lung superoxide dismutase activity; erythrocyte and skin glutathione peroxidase activity; erythrocyte catalase activity; lung; heart and skin oxidized glutathione level; erythrocyte and lung lipid peroxidation and erythrocyte protein carbonylation even 3 months post-irradiation. When comparing both methods of proton beam delivery; mouse survival was not different. However, PBS significantly increased lymphocyte micronucleus frequency; erythrocyte glutathione peroxidase activity and heart oxidized glutathione level compared to DS. These results point out the necessity to take into account the way of delivering dose in PT as it could influence late side effects.

Carol Haddoub, Mohamad Rima, Sandrine Heurtebise, Myriam Lawand, Dania Jundi, Riyad Sadek, Sebastian Amigorena, Ziad Fajloun, Marc C Karam (2020 Nov 16)

Cytotoxic effect of venom on cancer cell lines: in vitro and in vivo studies.

PeerJ : e9909 : [DOI : 10.7717/peerj.9909](https://doi.org/10.7717/peerj.9909)

Résumé

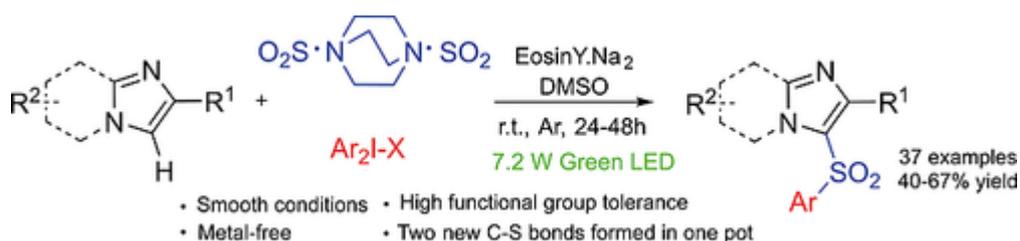
's venom has shown immunomodulation of cytokines release in mice and selective cytotoxicity on cancer cells in a dose-dependent manner, highlighting an anticancer potential. Here, we extend these findings by elucidating the sensitivity of murine B16 skin melanoma and 3-MCA-induced murine fibrosarcoma cell lines to 's venom and its effect on tumor growth in vivo.

Breton-Patient C., Naud-Martin D., Mahuteau-Betzer F., Piguel S. (2020 Nov 15)

Three-component C-H bond sulfonylation of imidazoheterocycles via visible-light organophotoredox catalysis.

European Journal of Organic Chemistry : 2020 : 6653-6660 : [DOI : 10.1002/ejoc.202001219](https://doi.org/10.1002/ejoc.202001219)

Résumé



The first entirely visible-light photoredox catalyzed sulfonylation of imidazoheterocycles has

been developed. This transformation demonstrates an efficient C-H functionalization for the straightforward synthesis of novel C-3 sulfonylated imidazoheterocycles from various imidazopyridines and diaryliodonium salts with different electronic and steric properties and easy handled DABCO- bis (sulfur dioxide). The reaction proceeds in moderate to good yields under mild conditions at room temperature using the inexpensive organophotocatalyst EosinY.Na 2 and shows a high functional group tolerance (37 examples).

Marie-Judith Saint Martin, Fanny Orlhac, Pia Akl, Fahad Khalid, Christophe Nioche, Irène Buvat, Caroline Malhaire, Frédérique Frouin (2020 Nov 12)

A radiomics pipeline dedicated to Breast MRI: validation on a multi-scanner phantom study.

Magma (New York, N.Y.) : [DOI : 10.1007/s10334-020-00892-y](https://doi.org/10.1007/s10334-020-00892-y)

Résumé

Quantitative analysis in MRI is challenging due to variabilities in intensity distributions across patients, acquisitions and scanners and suffers from bias field inhomogeneity. Radiomic studies are impacted by these effects that affect radiomic feature values. This paper describes a dedicated pipeline to increase reproducibility in breast MRI radiomic studies.

Abou-Ghali M, Kusters R, Körber S, Manzi J, Faix J, Sykes C, Plastino J (2020 Nov 6)

Capping protein is dispensable for polarized actin network growth and actin-based motility

Journal of Biological Chemistry : [DOI : 10.1074/jbc.RA120.015009](https://doi.org/10.1074/jbc.RA120.015009)

Résumé

François-Clément Bidard, William Jacot, Nicolas Kiavue, Sylvain Dureau, Amir Kadi, Etienne Brain, Thomas Bachelot, Hugues Bourgeois, Anthony Gonçalves, Sylvain Ladoire, Hervé Naman, Florence Dalenc, Joseph Gligorov, Marc Espié, George Emile, Jean-Marc Ferrero, Delphine Loirat, Sophie Frank, Luc Cabel, Véronique Diéras, Laure Cayrefourcq, Cécile Simondi, Frédérique Berger, Catherine Alix-Panabières, Jean-Yves Pierga (2020 Nov 5)

Efficacy of Circulating Tumor Cell Count-Driven vs Clinician-Driven First-line Therapy Choice in Hormone Receptor-Positive, ERBB2-Negative Metastatic Breast Cancer: The STIC CTC Randomized Clinical Trial.

JAMA oncology : [DOI : 10.1001/jamaoncol.2020.5660](https://doi.org/10.1001/jamaoncol.2020.5660)

Résumé

The choice between chemotherapy and endocrine therapy as first-line treatment for hormone receptor-positive, ERBB2 (also known as HER2)-negative metastatic breast cancer



Publications de l'unité UMR3348 - Intégrité du génome, ARN et cancer

is usually based on the presence of clinical features associated with a poor prognosis. In this setting, a high circulating tumor cell (CTC) count (≥ 5 CTCs/7.5 mL) is a strong adverse prognostic factor for overall survival and progression-free survival (PFS).