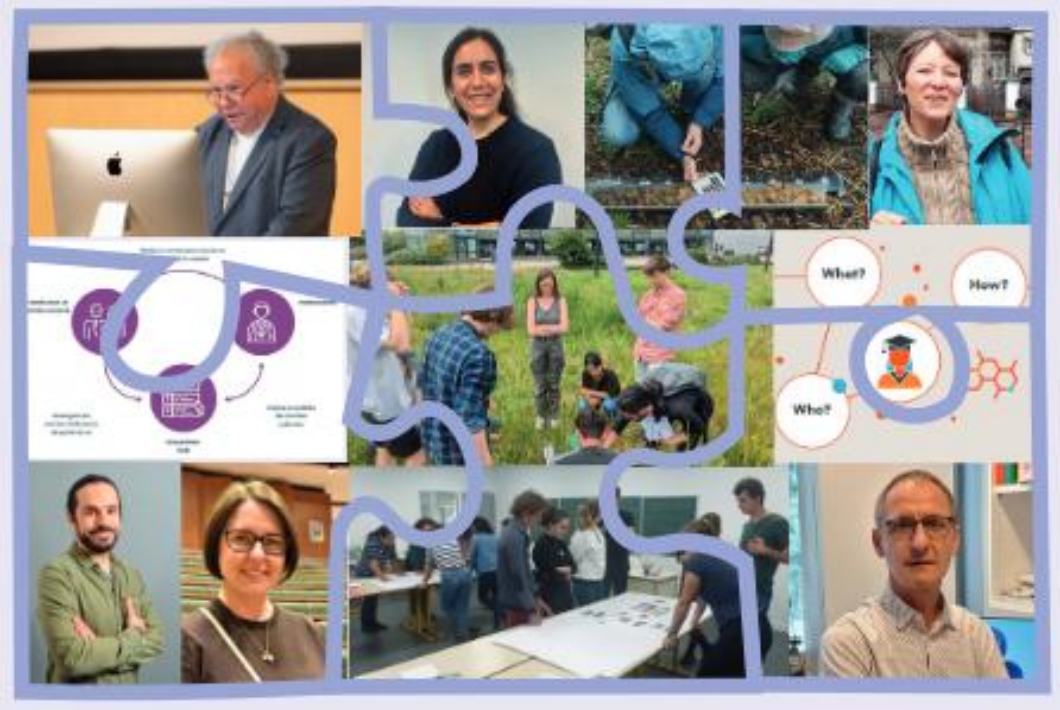
JCI 2026

Journées du Campus Illkirch

May 21st-22nd

Pôle API - Illkirch



Abstract Book

co-organised by labs and schools

BSC | CamBap | CBST | iCube | IGBMC | IUT Robert Schuman | LBP | LIT | PCBIS

under the supervision of

Université de Strasbourg | cnrs | Inserm

sponsored by

Advion Interchim scientific | BRAND | cloup | cytiva | INTEGRA | Metrohm France sas | ThermoFisher SCIENTIFIC | VACUUBRAND | MN MACHEREY-NAGEL

JCI 2026 - Illkirch Campus Days Pole API

	Thursday 21 May 2026		Friday 22 May 2026
08:45	Introduction by Pr. Claire GAVERIAUX	**08:45**	Welcome
09:00	Invited Young researcher **Dr. Guilhem Chaubet**, CBST	**09:00**	Invited Young researcher **Dr. Julie Karpenko**, LIT
09:30	Talk 1 Victorine ARTOT IGBMC Talk 2 Yelyzaveta DENYSIEVA LBP Talk3 Christos PASCHALIDIS BSC	**09:30**	Talk 8 Yamina BOUKENADEL LBP Talk 9 Sophie WALTER CBST Talk 10 Laura YEDIAGARYAN IGBMC
10:15	Metrohm, Cytiva, Opus	**10:15**	Pôle Appui 5 min
10:30	Coffee break	**10:20**	Coffee break
11:00	Talk 4 Yu QIU CBST Talk 5 Léa DENECHERE LBP Talk 6 Valeria BOIDE LBP Talk 7 Baptiste DUPOUY LIT	**10:50**	Talk 11 Maeva MARTIN LBP Talk 12 Mubarak OLAOLUWA Icube Talk 13 Shayan AHMED LBP Talk 14 Anthony AUGER LIT
12:00	Poster flash talks	**11:50**	Poster session Even
12:15	Lunch		
13:00	Poster session Odd	**12:50**	**Cocktail Tartes flambées** *Awards ceremony*
14:00	**Plenary Session-debate** ***"Science Together"*** ***Photo of all the participants*** **Pr. Jean-Louis Mandel** **& Dr. Maria-Victoria Hinckelmann,** IGBMC - Illkirch **Dr.Sandrine Glatron** MISHA-Strasbourg **Pr. Pascal Marchand**, IICiMed - Nantes	**14:15**	Ateliers HAL, Bases de données biblio
17:00 **19:00**	**Get-together Cocktail**		

ORAL COMMUNICATIONS

Talk 1 Dyrk1a dosage in Cortical Interneuron Migration: insights for DYRK1A and Down Syndromes

Victorine Artot, IGBMC

Talk 2 Long Fluorescence Lifetime Molecular Rotors Based on the 4,4-dicyanoBODIPY core

Yelyzaveta Denysieva, LBP, Faculté de Pharmacie

Talk 3 A story of a frog, a fungus and some bacteria: Siderophore mediated colonisation resistance against chytridiomycosis

Christos Paschalidis, Métaux et microorganismes, UMR7242, BSC, ESBS

Talk 4 Correlating the Viscosity, Polarity and Porosity of Polymer Nanoparticles Matrix with Drug Release Efficiency by Fluorescence

Yu Qiu, CBST, Faculté de Pharmacie

Talk 5 Aptamer-mediated selective and modulable siRNA delivery

Léa Denechere, LBP, Faculté de Pharmacie

Talk 6 Functionalized fluorescent lipid nanoemulsions for active cell targeting

Valeria Boide, LBP, Faculté de Pharmacie

Talk 7 Nitrogen-Assisted Decarbonylative Fukuyama Coupling for Amine Synthesis

Baptiste Dupouy, LIT, Faculté de Pharmacie

Talk 8 Mechanisms of invadopodia assembly and positioning in melanoma

Yamina Boukenadel, LBP, Faculté de Pharmacie

Talk 9 pH-sensitive membrane probes for ratiometric imaging and monitoring of intracellular vesicle acidification

Sophie Walter, CBST, Faculté de Pharmacie

Talk 10 Nuclear state alterations in centronuclear myopathy

Laura Yedigaryan, IGBMC

Talk 11 Innovative therapeutic approach based on nucleic acid aptamers for the treatment of sepsis-induced disseminated intravascular coagulation

Maeva Martin, LBP, Faculté de Pharmacie

Talk 12 GeoHSAF: Geometric Hippocampus Shape Analysis Framework for Longitudinal Alzheimer's Disease Classification

Mubarak Olaoluwa, iCube

Talk 13 Optimizing siRNA delivery for liver cancer therapy: an interdisciplinary approach using lipid nanoparticles decorated with nucleic acid

Shayan Ahmed, LBP, Faculté de Pharmacie

Talk 14 AI-Generated Fluorescent Antimicrobial Peptides: From De Novo Design to Mode-of-Action Elucidation

Anthony Augé, LIT, Faculté de Pharmacie

Dyrk1a dosage in Cortical Interneuron Migration : insights for DYRK1A and Down Syndromes

Victorine Artot*[1], Maria-Victoria Hinckelmann , Véronique Brault[1], and Yann Herault[1]

[1]Institut de Génétique et de Biologie Moléculaire et Cellulaire – université de Strasbourg – France

Résumé

Proper development of excitatory and inhibitory neural systems is essential for normal brain function. Disruptions in the balance between these systems are a hallmark of various neurodevelopmental disorders, including Down syndrome (DS) and DYRK1A-haploinsufficiency syndrome (DHS). In DS, the excitatory/inhibitory imbalance is commonly attributed to gene dosage effects, particularly involving *DYRK1A*, a gene located on chromosome 21. While *DYRK1A* overexpression has been implicated in altered neurogenesis and intellectual disability, its role in GABAergic interneuron development remains underexplored. Conversely, DHS is caused by gene mutations and is associated with epilepsy, intellectual disability, and autism spectrum disorder, suggesting that both increased and decreased dosage of *Dyrk1a* can impair GABAergic circuit formation.
In this study, we investigated how *Dyrk1a* dosage affects the migration of GABAergic interneurons originating from the medial and caudal ganglionic eminences. Using mouse models combined with time-lapse imaging, we analyzed key migratory parameters, including speed, pausing behavior and nucleokinesis dynamics. In parallel, we assessed morphological changes of migrating interneurons, such as leading process extension and branching.

We found that *Dyrk1a* critically control GABAergic interneuron migration and alterations in its dosage lead to convergent migratory phenotypes. Both overexpression and haploinsufficiency result in reduced migratory efficiency, characterized by decreased speed, increased pausing and impaired nucleokinesis. These shared defects are accompanied by common morphological alterations, including unstable leading processes. In addition, increased branching leads to a more complex morphology of migrating interneurons, which likely interferes with directional persistence and efficient nucleokinesis.

Mechanistically, we identify that these migratory defects are linked to the dysregulation of *Dyrk1a* downstream targets controlling actomyosin dynamics. In the DHS model, altered phosphorylation of key cytoskeletal regulators leads to impaired actomyosin contractility, thereby disrupting nucleokinesis. These findings uncover a molecular pathway through which *Dyrk1a* dosage controls the cytoskeletal machinery required for efficient interneuron migration.
Together, our findings highlight a critical requirement for precise *Dyrk1a* dosage in regulating interneuron migration by controlling actomyosin-dependent cytoskeletal dynamics, with important implications for neurodevelopmental disorders.

Mots-Clés: Neurodevelopment, DYRK1A, Interneuron, Cortex, Down syndrome

*Intervenant

Long Fluorescence Lifetime Molecular Rotors Based on the 4,4-dicyanoBODIPY core

Yelyzaveta Denysieva*[1], Ludovic Richert[1], Yves Mély[1], Julie Karpenko[2,3], and Dmytro Dziuba[1]

[1]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

[2]Laboratoire d'Innovation Thérapeutique – université de Strasbourg, Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique – France

[3]Institut Universitaire de France – Institut universitaire de France, Institut universitaire de France – France

Résumé

Environmentally sensitive fluorescent probes with long emission lifetimes are essential for fluorescence lifetime imaging microscopy (FLIM) in living cells. Here, we report that substituting fluorine atoms in the BODIPY-based molecular rotors with cyano groups produced viscosity-sensitive probes with significantly increased fluorescence lifetimes.
The synthesized 4,4-dicyano-BODIPY derivatives exhibited physicochemical and spectroscopic properties comparable to 4,4-difluoro-BODIPY analogues. Importantly, time-resolved measurements revealed prolonged fluorescence lifetimes across a wide viscosity range, with increases of up to 1.6 ns, reaching 5.18 ns in some cases.

A membrane-targeting cyano-BODIPY probe was successfully applied to live *Staphylococcus epidermidis* cells, where it localized to the plasma membrane and enabled quantitative FLIM-based viscosity measurements.
Our result demonstrate that CN-BODIPY molecular rotors are promising viscosity-sensitive fluorophores for biological applications.

Mots-Clés: Live cell imaging, Fluorescent probes, FLIM

*Intervenant

A story of a frog, a fungus and some bacteria: Siderophore mediated colonisation resistance against chytridiomycosis

Christos Paschalidis*[1], Elliot Murphy[2], Emily Read[3], Fritz Ka-Ho Ho[2], Marc-Emmanuel Dumas[2], Kieran Bates[3], and Olivier Cunrath[4]

[1]Métaux et microorganismes, UMR7242, BSC, ESBS – Université de Strasbourg, CNRS, UMR 7242 – France

[2]Division of Systems Medicine, Department of Metabolism, Digestion and Reproduction, Imperial College London, London, W12 0NN – Royaume-Uni

[3]Queen Mary University of London – Royaume-Uni

[4]Université de Strasbourg, CNRS, UMR7242, ESBS – CNRS : UMR7242 – France

Résumé

Batrachochytrium dendrobatidis (*Bd*) is a fungal pathogen that has led to catastrophic declines in amphibian populations worldwide. *Bd* zoospores infect amphibian skin, disrupting its function and ultimately leading to death. Iron competition is a well-defined battleground in host-pathogen interactions across diverse systems, ranging from the human gut to aquatic vertebrates. However, its role in amphibian skin defense remains unexplored. In parallel, we know that commensal bacteria can produce iron-chelating molecules, called siderophores. We hypothesized that the skin microbiome may drive this iron competition, through siderophores, acting in synchrony with the host to restrict metal availability to *Bd*. We used a combination of culture-dependent assays and LC-MS to screen and identify siderophores produced by skin bacterial isolates from *Alytes obstetricans*. To evaluate the anti-fungal potential, we challenged *Bd* with these siderophores in *in vitro* growth assays. Our research suggests that siderophore production is prevalent within *A.obstetricans* skin microbiome. These secondary metabolites displayed potent anti-fungal activity against *Bd*, in an iron-dependent manner. Consequently, we are currently designing siderophore producing synthetic communities (SynComs) of native skin bacteria to screen *in vivo* as probiotics. Our findings suggest that microbiome-derived siderophores may provide a critical layer of colonization resistance against *Bd* though iron limitation.

Mots-Clés: Batrachochytrium dendrobatidis, siderophores, skin microbiome, colonisation resistance

*Intervenant

Correlating the Viscosity, Polarity and Porosity of Polymer Nanoparticles Matrix with Drug Release Efficiency by Fluorescence

Yu Qiu*[1], Mayeul Collot[2], and Nicolas Anton[3]

[1]UMR 7199 CNRS, Chemo-Biologie Synthetique Therapeutique, Faculté de Pharmacie, UNISTRA – CNRS, Université de Strasbourg – France
[2]UMR7199 CBST – Faculté de Pharmacie, UNISTRA – France
[3]Inserm 1260 CRBS – Faculté de Pharmacie, UNISTRA – France

Résumé

Polymeric nanoparticles (NPs) continue to be a promising nanovector for nanomedicine and imaging agents.1 Among them, biocompatible polyester block copolymers (BCPs) exhibit appealing features as their physicochemical properties can be readily modified by the composition of their blocks, which in turn affects the cargo release behaviours.2 However, the effects of nanoscopic properties of polymeric NPs are rarely studied. In this work, we assumed that tuning the monomer and chain length could impact the nanoscopic properties of the nanoparticles, which further helps in controlling their cargo encapsulation and release. To achieve this, clickable PEG-PCL/PLA block copolymers with different monomers and chain lengths were synthesized. Owing to their covalent fluorescent labelling using strain-promoted azide-alkyne cycloaddition, several parameters like the colloidal stability, the core viscosity, the core polarity, the core porosity and stealth of the NPs have been studied. Beyond simple fluorescent tagging, these new tools represent a major innovation as nanosensors of the internal properties of polymeric nanoparticles, enabling a finer understanding of their composition, inference of their morphology, and evaluation of how nanoprecipitation parameters shape nanoparticle structure and performance. Taking advantage of the fluorescence labelling of the NPs' core, their ability to encapsulate and release a fluorescent cargo (Sulfo-Cyanine3) was assessed by Forster resonance energy transfer (FRET). The study proved that the covalent fluorescent labelling of the BCPs is an efficient tool, offering various methods to characterize and assess the effects of the polymers' modifications on the NP's properties.

Mots-Clés: block copolymers, fluorescence labelling, nanoscopic properties, encapsulation, drug delivery, FRET

*Intervenant

Aptamer-mediated selective and modulable siRNA delivery

Léa Denechere*[1], Charlène D'ancona[1,2], Béni Twendimbadi[1], Sandrine Pelet[1], Sylvie Friant[2], Séverine Bär[2], Mayeul Collot[3], Pierre Fechter[4], and Laurence Choulier[1]

[1]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

[2]Laboratoire de Génétique Médicale – université de Strasbourg, Institut National de la Santé et de la Recherche Médicale – France

[3]Chémo-Biologie Synthétique et Thérapeutique – université de Strasbourg, Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique – France

[4]Biotechnologie et Signalisation Cellulaire – CNRS : UMR7242, CNRS – France

Résumé

Small interfering RNAs (siRNAs) are specific and effective molecules for gene silencing. However, their use is limited by poor cell penetration due to their negative charge, size and hydrophilicity. Active targeting delivery, the conjugation of siRNAs to ligands targeting cell-surface receptors, is a promising approach to overcome these barriers. Aptamers appear to be interesting candidates since they are single-stranded DNA or RNA with high affinity and selectivity for a specific target, such as cell-surface receptors. Thus, we aim to develop selective and modulable vehicles associating an siRNA with one or more aptamers called mono- or multivalent aptamer-siRNA chimeras (AsiCs). As a proof of concept, we are using an siRNA PGL3 anti-luciferase, combined with the E07 RNA aptamer anti-human epidermal growth factor receptor (EGFR) identified by Li *et al.* (2011).

First, to investigate the possibility of combining RNA and DNA aptamers in one vehicle, we created AsiCs formed thanks to an RNA-RNA or RNA-DNA sticky bridge. In the RNA-RNA AsiC, the sense strand of siRNA and the aptamer are elongated with RNA complementary sequences to form the sticky bridge. In the RNA-DNA AsiC, the nature of aptamer sticky bridge is change to DNA to mimic the addition of DNA aptamer. Our preliminary results show a similar assembly. Furthermore, a functional assay was performed with an RNA-RNA AsiC on two glioblastoma cell lines, modified to express luciferase: U87 EGFR LUC (EGFR-positive cell line) and LN319 LUC (EGFR-negative cell line). Luciferase expression was significantly decreased using the RNA-RNA AsiC on U87 EGFR LUC compared to non-treated cells. Second, we have designed an innovative homomultivalent AsiC, which combines one siRNA with two E07 aptamers (E07). The various elements contain hybridization sequences which enable controlled self-assembly. So far, we have predicted their secondary structure thanks to prediction software (RNAfold and predict1), and checked the vehicle assembly.

Our preliminary results of RNA-RNA and RNA-DNA AsiCs are encouraging and confirm the feasibility to combine DNA and RNA aptamers in a multivalent AsiC, a new siRNA active delivery tool with great potential. Thanks to their versatile nature, the number, position, and type of aptamers (DNA or RNA, homo- or heteromultivalent) could be easily

*Intervenant

changed. As perspectives, we wish to (1) deepen the characterization of AsiCs (stability and affinity), (2) perform functional assays with RNA-DNA AsiC and multivalent vehicles, and (3) study their intracellular trafficking by bioimaging. We will use either a pH-ratiometric probe developed by our collaborator or a FRET-based approach to track the AsiC during endocytosis.

Mots-Clés: siRNA, aptamer, active targeting delivery, innovative delivery tool, multivalent conjugate, cell surface receptor

Functionalized fluorescent lipid nanoemulsions for active cell targeting

Valeria Boide*[1] and Andrey S. Klymchenko

[1]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

Résumé

Fluorescent lipid nanoemulsions (LNEs), owing to their biocompatibility, good in vivo stability, and
low toxicity, have found applications in biomedical imaging (1). However, their targeting to specific
cells remains challenging because of difficulties in functionalizing them (2). Here, we have developed
an approach to functionalize LNEs with antibodies by inserting an azide linker (NH2-PEG-N3) via
in situ reaction with a cholesterol derivative inside LNEs. Azide-LNEs were further decorated with
antibodies bearing "clickable" DBCO group and tested in cancer cells. Fluorescence microscopy
showed selective accumulation of Cy5.5-loaded LNEs in HER2-positive cells. Our approach offers a
plug-and-play fluorescent nano-platform for cellular targeting in cancer and cardiovascular diseases.

Mots-Clés: Lipid nanoemulsion, bioimaging, Nanoparticles fuctionalization, cell targeting.

*Intervenant

Nitrogen-Assisted Decarbonylative Fukuyama Coupling for Amine Synthesis

Baptiste Dupouy*[1]

[1]Laboratoire d'Innovation Thérapeutique – université de Strasbourg, Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique – France

Résumé

The Fukuyama coupling is a well-established method for the synthesis of ketones from thioesters and organozinc reagents. However, its application to the direct synthesis of amines remains limited. In 2019, Bihel and co-workers introduced POxAP as an efficient palladium precatalyst for Fukuyama cross-coupling, enabling mild and practical conditions.
Herein, we report a nitrogen-assisted decarbonylative variant that provides direct access to substituted amines from amino-thioesters. The transformation proceeds via a palladium intermediate in which the proximal nitrogen functionality promotes decarbonylation, diverting the classical pathway from ketone formation toward C–C bond formation at the amine center.

The method operates under mild conditions and exhibits broad scope, tolerating secondary, tertiary and quaternary carbon centers. More than 25 examples were obtained with moderate to excellent yields. In addition, the use of flow conditions for the preparation of organozinc reagents improves scalability and reproducibility.
This work expands the reactivity of Fukuyama-type couplings and provides a practical approach to structurally diverse amines.

Mots-Clés: Fukuyama Coupling, Decarbonylation, Flow Chemistry

*Intervenant

Mechanisms of invadopodia assembly and positioning in melanoma

Yamina Boukenadel*[1], Gabrielle Boisson , Rana Abdallah[1], Marlène Legrand , Hélène Justiniano[1], Marie Zinsius , Nadir Maar , Imane Djene , Grégory Adam[1], Philippe Carl[1], Denis Dujardin[1], and Philippe Rondé[1]

[1]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

Résumé

Cell invasion is an extremely complex process that requires polarized cell migration and directional degradation of the extracellular matrix. In melanoma cells, as in many highly invasive cancer types, these processes are governed by the controlled assembly of adhesive structures and invasive protrusions known as invadopodia. However, how migration and matrix degradation are coordinated to produce efficient cell invasion remains poorly described and a clear understanding of the mechanisms of invadopodia positioning and formation is still lacking. In this study, we examined the mechanisms of invadopodia assembly in melanoma using high-end imaging techniques. We show that melanoma are polarized cells thereby enabling directional migration. Our results indicate that melanoma cell polarity impacts invadopodia positioning as nascent invadopodia assemble in the vicinity of the Golgi apparatus/centrosome ahead of the nucleus and stabilize upon Tks5 arrival. Finally, we found that cytoplasmic dynein controls the localisation of the Golgi/centrosome and the formation of polarized invadopodia in melanoma cells.

Mots-Clés: Melanoma, Cancer, Invadopodia, Cell migration, Invasion, Cell polarity

*Intervenant

pH-sensitive membrane probes for ratiometric imaging and monitoring of intracellular vesicle acidification

Sophie Walter*[1], Erwan Grandgirard[2], Marc Nothisen[1], and Mayeul Collot[1]

[1]Chémo-Biologie Synthétique et Thérapeutique – université de Strasbourg, Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique – France

[2]Institut de Génétique et de Biologie Moléculaire et Cellulaire – université de Strasbourg, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Institut National de la Santé et de la Recherche Médicale : U964, Centre National de la Recherche Scientifique : UMR7104, université de Strasbourg : UMR7104, Institut National de la Santé et de la Recherche Médicale : U1258 – France

Résumé

Tracking pH variations within intracellular vesicles along the endocytic pathway is essential for a deeper understanding of cellular trafficking and metabolism. Although small-molecule fluorescent pH probes are valuable tools in bioimaging, they are typically not specifically targeted to intracellular vesicles or are directed primarily toward acidic lysosomes, thereby limiting the dynamic observation of vesicular acidification.
Here, we report the design of a novel ratiometric FRET-based pH probe that initially targets the plasma membrane (PM) and subsequently accumulates within intracellular vesicles via endocytosis. This probe combines two dyes: a spiroamide rhodamine acting as the FRET acceptor and a green BODIPY dye serving as the FRET donor. Spiroamide rhodamines featuring an intramolecular nucleophilic moiety are particularly well-suited due to their dynamic equilibrium between an emissive open form and a non-emissive spirocyclic form.

Upon exposure to the vesicular lumen, the probe enables real-time monitoring of vesicle acidification throughout the endocytic pathway. Importantly, this approach allows for statistical analysis of intracellular vesicle acidification under various biological conditions. Moreover, this ratiometric FRET probe provides the capability to track pH changes over time within individual vesicles, including highly dynamic and mobile populations.
Michelis et al. *Anal. Chem.* 2022, 94, 15, 5996–6003

Mots-Clés: pH, FRET, ratiometric, intracellular vesicle acidification

*Intervenant

Nuclear state alterations in centronuclear myopathy

Laura Yedigaryan*[1], Alix Simon[1], Christine Kretz[1], Horia Boursas[1], Minchul Kim[1], and Jocelyn Laporte[1]

[1]Institut de G´en´etique et de Biologie Mol´eculaire et Cellulaire (IGBMC), INSERM U1258, CNRS UMR7104, Strasbourg University, 1 rue Laurent Fries, 67400 Illkirch, France – IGBMC – France

Résumé

Centronuclear myopathies (CNMs) are severe muscle disorders characterized by the abnormal accumulation of myonuclei in central or internal positions, rather than at the fiber periphery. Although this nuclear mispositioning is a defining feature of the disease, the mechanisms connecting altered nuclear organization to muscle dysfunction remain poorly understood.

Using the myotubularin 1 (*Mtm1*) knockout mouse model of X-linked myotubular myopathy, this work examines how centrally positioned myonuclei differ from normally positioned peripheral nuclei. Transcriptomic analyses reveal disease-associated nuclear populations and candidate molecular regulators, including the long non-coding RNA *Lincmd1*. These molecular changes are accompanied by pronounced nuclear remodeling, with imaging and ultrastructural analyses showing altered nuclear morphology and changes in chromatin organization.

The linker of nucleoskeleton and cytoskeleton (LINC) complex, which connects the cytoskeleton to the nuclear envelope, represents a potential interface between cytoskeletal forces, nuclear positioning, nuclear architecture, and gene regulation. Analysis of LINC-complex and nuclear-envelope components, both *in vivo* and in an *Mtm1* knockdown C2C12 model, supports the possibility that disrupted nucleo-cytoskeletal coupling contributes to disease-associated nuclear phenotypes.

Together, these findings suggest that nuclear mispositioning in centronuclear myopathy is not only a structural hallmark but is also associated with broader changes in nuclear identity, chromatin state, and nuclear envelope organization. This work highlights LINC-associated nuclear remodeling as a potential contributor to CNM pathogenesis.

Mots-Clés: Centronuclear myopathy, MTM1, myonuclear positioning, LINC complex, nuclear envelope, Lamin A/C, Nesprin1, chromatin remodelling.

Innovative therapeutic approach based on nucleic acid aptamers for the treatment of sepsis-induced disseminated intravascular coagulation

Maeva Martin*[1,2], Julie Helms[1], and Laurence Choulier[2]

[1]Centre de Recherche en Biomédecine de Strasbourg – université de Strasbourg, Institut National de la Santé et de la Recherche Médicale – France

[2]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

Résumé

Context & Hypothesis: Septic shock is complicated in 30% of cases by disseminated intravascular coagulation (DIC), linked to excessive activation of the coagulation cascade and fibrinolytic insufficiency. We hypothesize that targeted treatment aimed at simultaneously modulating the procoagulant response and restoring fibrinolytic balance in patients with septic DIC could reduce disseminated microthrombi, thus contributing to limiting organ dysfunction and reducing the associated mortality.
Objective. My thesis work aims to develop an innovative strategy based on the use of aptamers to vectorize microvesicles at the level of disseminated microthrombi. Aptamers are short sequences of oligonucleotides with high affinity and specificity for their targets, with many advantages over antibodies, such as their chemical synthesis with high reproducibility, and their less restrictive storage conditions. The proposed strategy consists of: (i) fibrinolytic molecules-enriched microvesicles derived from mesenchymal stem cells, aimed at restoring local fibrinolytic activity; (ii) an anticoagulant aptamer conjugated to a lipophilic molecule capable of anchoring in the membrane of fibrinolytic microvesicles, allowing the vectorization of microvesicles to microthrombi.

Method: The stability of the aptamer was evaluated on polyacrylamide gel after 72h incubation in plasma from septic patients. The coagulation parameters (thrombin, activated partial thromboplastin and prothrombin times) were measured by a haemostasis analyzer within 4 hours of blood sampling. The anchoring of aptamers to cells and microvesicles was confirmed respectively by flow cytometry and by the anticoagulant activity of the aptamer once anchored, particularly by inhibiting thrombin generation. Microvesicle characterization was performed with Zetasizer® to determine the Zeta potential, the diameter and microvesicle concentration was obtained by nanoparticle tracking analysis, and the amount of surface protein was determined at 280 nm with Nanodrop®. The microvesicle fibrinolytic activity was evaluated by monitoring plasmin generation by its chromogenic substrate.

Results: We first characterized the anticoagulant aptamer. Its half-life is 24 hours (n=3) in plasma from septic patients. The anticoagulant aptamer extends thrombin and activated partial thromboplastin times to 0.098 ± 0.020 s/nM and 0.086 ± 0.013 s/nM (n=3), respectively, and inhibit up to 90% thrombin generation (n=3). The tested aptamer concentration

*Intervenant

range (0.05–10 μM) enabled anchoring of the aptamer to 100% of living cells. Half-saturation of cells is 1μM aptamer per 500,000 cells (n=3). By comparing cell and microvesicle surfaces, this concentration allowed to determine the quantity of aptamer to be used for conjugation to microvesicles. After demonstrating the anchoring of aptamer in microvesicles by the ability of aptamer to inhibit thrombin generation (n=4), we showed the dual *in vitro* effect of aptamer-enriched microvesicles: anticoagulant and profibrinolytic activities without impacting the diameter of the microvesicles (n=3). The efficacy and tolerance of the *in vivo* strategy are ongoing to be evaluated in a murine model of septic DIC.
Conclusion: The innovative dual strategy based on the use of aptamers anchored to microvesicles appears to be a promising targeted therapeutic in septic DIC.

Mots-Clés: Sepsis, Disseminated intravascular coagulation, Aptamers, Coagulation, Fibrinolysis

GeoHSAF: Geometric Hippocampus Shape Analysis Framework for Longitudinal Alzheimer's Disease Classification

Mubarak Olaoluwa*[1], Heni Loukil[2], Arafet Sbei[3], and Hassen Drira[1]

[1]Images, Modélisation, Apprentissage, Géométrie et Statistique – Laboratoire des sciences de l'ingénieur, de l'informatique et de l'imagerie – France
[2]National Institute of Applied Science and Technology (INSAT), Tunis 1080 – Tunisie
[3]MData One, Les Berges du Lac, Tunis 1053 – Tunisie

Résumé

Alzheimer's disease (AD) is the most common form of dementia and a progressive, irreversible brain disorder that affects millions worldwide. The majority of existing research on AD classification relies on cross-sectional brain magnetic resonance imaging studies, which consider information from a single time point and fail to account for the progressive nature of AD. Longitudinal analysis, however, is crucial for capturing AD evolution and enabling more accurate diagnosis. To address this gap, we propose GeoHSAF, a novel hippocampus-based geometric learning framework for longitudinal AD classification. To the best of our knowledge, GeoHSAF is the first hippocampus-based geometric learning framework for AD classification in longitudinal datasets.

The proposed GeoHSAF includes various components, one of which is a shape interpolation module that addresses the problem of missing or inconsistent hippocampal shapes across subjects by predicting intermediate shapes to ensure temporal continuity. We evaluate the effectiveness of GeoHSAF on three public longitudinal AD database: The Alzheimer's Disease Neuroimaging Initiative (ADNI), the Open Access Series of Imaging Studies (OASIS), and The Australian Imaging, Biomarker and Lifestyle (AIBL), and benchmark its performance against existing approaches. GeoHSAF achieves new state-of-the-art results on binary classification tasks (AD versus Normal controls (NC)), while also demonstrating strong performance on more challenging triple-class classification tasks (AD versus NC versus Mild Cognitive Impairments (MCI)).

Furthermore, we demonstrate the contribution of other components of the proposed GeoHSAF (shape space modeling, tangent space configuration, and dimensionality reduction) through ablation studies and assess the interpolation module both quantitatively and qualitatively to validate its fidelity. Our proposed method is fully reproducible, and all codes are publicly released at: https://github.com/ayodejimb/GeoHSAF

Mots-Clés: Longitudinal Alzheimer's Disease, Hippocampus, Shape Analysis, Shape Interpolation, Deep Learning

*Intervenant

Optimizing siRNA delivery for liver cancer therapy: an interdisciplinary approach using lipid nanoparticles decorated with nucleic acid aptamers, including photochemical internalization

Shayan Ahmed*[1], Julia Richert[1], Sandrine Pelet[1], Ines Barahona[2], Celia Sequera[2], Flavio Maina[2], Halina Anton[1], Maria Vittoria Spanedda[3], and Laurence Choulier[1]

[1]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

[2]Centre de Recherche en Cancérologie de Marseille – Aix Marseille Université, Institut Paoli-Calmettes, Institut National de la Santé et de la Recherche Médicale, Centre National de la Recherche Scientifique, Centre National de la Recherche Scientifique : UMR7258, Institut National de la Santé et de la Recherche Médicale : U1068, Institut Paoli-Calmettes : UMR7258, Aix Marseille Université : UM105 – France

[3]Laboratoire d'Innovation Thérapeutique – université de Strasbourg, Institut de Chimie - CNRS Chimie, Centre National de la Recherche Scientifique – France

Résumé

The tumor microenvironment significantly influences cancer development, progression, and therapeutic resistance. We are interested in targeting a secreted protein found highly overexpressed in hepatocellular carcinoma (HCC). Our project aims to inhibit its expression, using small interfering RNAs (siRNAs). They are a powerful molecule for gene silencing, but their clinical application is limited by challenges such as instability in biological fluids and poor cellular uptake. To overcome these barriers, this study focuses on developing a targeted delivery strategy using aptamers. Aptamers are short, single-stranded DNA or RNA molecules that can fold into defined three-dimensional structures to bind specific targets with high affinity. Aptamers targeting cell-surface receptors can be internalized, making them promising carriers for the delivery of therapeutic molecules like siRNAs. Our objective is to evaluate the potential of siRNA encapsulated in lipid nanoparticles (LNP) and decorated with nucleic acid aptamers to target HCC.
Lipid nanoparticles (LNPs) decorated with aptamers were formulated using a lipid composition of DLin-MC3-DMA (50%), cholesterol (_˜38.5%), DSPC (10%), PEG-2000-C-DMG (0.75%), and PEG-2000-N3 (0.75%). These LNPs exhibited an average size of approximately 100 nm, a zeta potential near neutrality, and low cytotoxicity, as confirmed by MTT assays. High encapsulation efficiency (> 90%) for siRNA and conjugation efficiency (> 86%) for aptamers were achieved. The siRNA demonstrated effective gene silencing in HCC13 and HUH1 cell lines.

To further enhance cytosolic internalization, photochemical internalization (PCI) was employed. Two photosensitizers, PS1 (A1PcS2a)1 and PS2 (BODIPY), were tested to trigger

*Intervenant

light-induced endosomal disruption. Incubation with PS1 and PS2 led to a two-fold improvement in gene silencing efficiency, as quantified by RT-qPCR.

Overall, LNPs emerge as a promising delivery platform to enhance targeted internalization and bioavailability of aptamer-guided siRNA toward HCC cell-surface receptors. Furthermore, PCI facilitates endosomal escape, thereby improving cytosolic siRNA release and therapeutic efficacy. We next plan to encapsulate the photosensitizers (PS) within LNPs. In parallel, a pharmacological approach will be employed to evaluate siRNA cytosolic delivery using drug-based strategies. Additionally, confocal microscopy and flow cytometry experiments are scheduled to assess intracellular localization and binding efficiency of our formulation. Based on the outcomes of these experiments, we will design and initiate *in vivo* studies.

References

1. Figliola C, Anton H, Sutter C, Chériaux C, Sutter A, Mazan V, et al. Lysosomes Targeting pH Activable Imaging-Guided Photodynamic Agents. ChemBioChem. 2023;24(12):e202300139. doi:10.1002/cbic.202300139

Mots-Clés: Hepatocellular carcinoma, Aptamer, siRNA, LNP, Photochemical Internalization and Photosensitizer.

AI-Generated Fluorescent Antimicrobial Peptides: From De Novo Design to Mode-of-Action Elucidation

Anthony Augé*[1], Evgeniia Milova[2], Alexey Orlov[2], Alexandre Varnek[2], Dmytro Dziuba[3], Dragos Horvath[2], and Julie Karpenko[1]

[1]Laboratoire d'Innovation Thérapeutique – CNRS : UMR7200 – France
[2]Laboratoire de Chémoinformatique – Chimie de la matière complexe – France
[3]Laboratoire de Bioimagerie et Pathologies – université de Strasbourg, Centre National de la Recherche Scientifique – France

Résumé

Fluorescent probes for detecting pathogenic bacteria have emerged as promising tools for the clinical diagnosis of infectious diseases. Their design is typically based on bacteria-targeting antibiotics or antimicrobial peptides (AMPs). To date, however, most of these probes have relied on a limited repertoire of naturally occurring AMPs, while the vast sequence space of linear peptides of comparable length ($> 10^1$) remains largely unexplored. In this context, artificial intelligence (AI) approaches offer a powerful alternative to traditional screening methods by enabling the rational design of molecular structures with tailored properties (1). In this study, we investigate the feasibility of leveraging explainable AI models to design bacteria-targeting fluorescent probes, thereby expanding the toolkit for infectious disease diagnostics. Ten selected peptides were synthesized, evaluated for their activity against a panel of model bacteria, and their mode of action was investigated using a combination of biophysical and chemical approaches. The lead peptide exhibited a low-micromolar MIC against Gram-positive bacteria, including *Staphylococcus aureus*. Finally, the peptides were labelled with a red fluorophore to generate bright fluorescent probes, which will be further optimized as tools for the clinical detection of bacteria.

Références :
K. Pikalyova, et al. *J. Chem. Inf. Model.* **2026**, *66*, 744

Mots-Clés: Fluorescent probes, Antimicrobial peptides, Artificial intelligence

*Intervenant