



Journée de rentrée de l'école doctorale BioSE

21 novembre 2023

Amphithéâtre LEPOIS – Campus Santé Brabois

10h00 **Accueil des doctorantes et doctorants en 1^{ère} année 2023-2024**

- Présentation de l'ED BioSE – Sophie Rahuel-Clermont, directrice ED BioSE
- Intervention des représentants des doctorant(e)s
- La vie doctorante à l'UL – Sanae El Karkri, Doctorante
- Les formations transverses – Marc Dalaut, Sous-Direction des Etudes Doctorales (SDED)
- L'Offre de Services et d'orientation professionnelle pour les doctorants – Magali Brunel, Service d'Orientation et d'Insertion Professionnelle

12h30 **Buffet**

13h40 **Accueil de tous les doctorant-e-s de l'ED**

13h45 **Le concours Ma Thèse en 180' – Catherine FLAUDER**

Présentations Flash

UNITE DE RECHERCHE	NOM	PRENOM	TITRE ABSTRACT	HORAIRE
APEMAC	AUGUSTIN	Camille	Ethics of medico-social workers involved in the pathways of accompanied children in Haute-Marne	14h00
CITHEFOR	LAHOUARI	Sephora	Dynamics of molecular interactions between Concanavalin A and gold nanoparticles.	14h05
CRAN	SCHNELLER	Perrine	Radiolabeled Chitosan Hydrogel for Internal Radiation Therapy of Glioblastoma	14h10
IMOPA	BROUARD	Jordan	Development of anti-CD123 CAR-iNKT for the treatment of acute myeloid leukemia: production and comparison to CAR-T	14h15
DCAC	ABD AL RAHIM	Sara	Characterization of Hypercoagulability in Pulmonary Hypertensive Patients	14h20
DEVAH	HANEN	Nicolas	Biomechanical analysis of sumo and conventional style deadlifts	14h25
IADI	BOURSIER	Caroline	Clinical implementation of dosimetry protocol in radionuclide therapy	14h30
IMOPA	SARDINI	Lucas	Study of the biogenesis of the Signal Recognition Particle (SRP)	14h35
NGERE	NOMINE-CRIQUI	Claire	Setting up a large cohort of obese patients undergoing bariatric surgery to identify factors linked to weight change	14h40



14h45 Intervention de l'association de doctorants ADUL'TEAM

14H50 Informations ED BioSE, actualités, formations ...

Présentations Flash

UNITE DE RECHERCHE	NOM	PRENOM	TITRE ABSTRACT	HORAIRE
APEMAC	LIENARD	Julie	Enhancing Risk information in pediatric surgery: A study of Disclosure by the surgeon and Interpretation by the patient and parents (ARCADIE)	15h00
IMOPA	NASRALLAH	Rim	Identification and characterization of new bio-sourced molecules affecting the functions of the LSR receptor	15h05
DCAC	RASTOGI	Tripti	Identification of clinical phenotypes in patients with acute heart failure using unsupervised machine learning techniques	15h10
DEVAH	JACQUOT	Raphaël	Biomechanical modelling of shooting performance in biathlon	15h15
IMOPA	TIRADO	Magali	Advancing polyketide synthases engineering	15h20
NGERE	PIUCCO	Romain	Epigenetic and proteomic characterization of Richter syndrome	15h25
LCPME	CENRAUD	Emilie	Developing the next generation of anti-staphylococci bacteriophage-based biomaterials	15h30
IMOPA	WISNIEWSKI	Nathan	Harvesting extracellular matrix of wharton's jelly by extraction or or cellularization process: a promising material for cardiovascular tissue engineering	15h35
APEMAC	TODOROVIC	Anja	Resilience and perceived health of University students in the Lorraine region (France) during the COVID-19 pandemic: longitudinal analysis and psychometric approach	15h40

15h45 Pause « café » organisée par ADUL'TEAM

16h15 Les dispositifs d'aide à la mobilité internationale – Claire Bacheter, SDED - Maison Du Doctorat (MDD)

16h30 Les clubs Orion, interventions de Magali TIRADO - club « What health », Emilien SCHALL – club « Mat et Met » et Théo WEBER club « HumanInteract ».

Présentations Flash

UNITE DE RECHERCHE	NOM	PRENOM	TITRE ABSTRACT	HORAIRE
CRAN	BETZ	Margaux	Genomic signatures found in DNA from FFPE samples of advanced or metastatic breast cancer patients treated with endocrine therapy : first results of the CICLADES-CE study	17h05
APEMAC	REGAD	Marie	Evaluation of automated surveillance for surgical site infections	17h10
DCAC	SCHALL	Emilien	A study of the multiphysical properties of human skin to assess the burn degree.	17h15
IMOPA	WENZEL	Jade	Molecular mechanisms of enteric virus inactivation under oxidative conditions	17h20
NGERE	ALIX	Tom	Tatton-Brown-Rahman syndrome: Consequences of DNMT3A loss-of-function variations on DNA methylation and gene expression profiles	17h25
APEMAC	HASNAOUI	Sabrina	Physical activity intervention for cancer patients, taking into account the socio-economic context	17h30
IMOPA	PIGNOT	Théa	Obtention of pro-inflammatory mesenchymal stromal cells from umbilical cords	17h35
NGERE	POURIE	Elise	Consequence of impaired one-carbon metabolism in the pathophysiology of Huntington's disease	17h40

Merci par avance de votre participation active aux questions.

Quatre prix seront décernés pour les meilleures présentations, l'un sélectionné par vos représentants élus au conseil de l'école doctorale et le deuxième par les autres membres du conseil.

Tou(te)s les chercheur(e)s et enseignant(e)s chercheur(e)s sont invité(e)s à assister aux présentations des doctorant(e)s, particulièrement les directeurs.trices et encadrant(e)s de doctorants.

18h00 – Fin de la journée

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

AUGUSTIN, Camille + IVANAJ, Vera + LIGIER, Fabienne

APEMAC UR 4360, 9 avenue de la Foret de Haye 54550 Vandœuvre-lès-Nancy

Ethics of medico-social workers involved in the pathways of accompanied children in Haute-Marne

Abstract

Outpatient care for children with disabilities and/or mental health problems is set to expand. Moreover, building care pathways requires the mobilization of a whole actors' network from different professional backgrounds, who need to be coordinated, while taking into account the needs and expression of users. This coordination can prove difficult, given the different professions, professional identities and institutional logics involved.

In what way, why and how does the care ethic of medico-social players involved in supporting children impact the care's quality of paths? This problematic is declined in three purposes: identify the ethics' components of medico-social actors that can have an impact on the care's quality of pathways, identify the ethics' processes and mechanisms on the care's quality of pathways and eventually, propose a model to explain ethics and the care's quality of pathways in the medico-social sector.

I mobilize an abductive method as inference method via participative approach in a collaborative research-action project named COOPER-ACTION. It's an inductive method which let to formalize explicatives hypothesis from interviews of users, professionals, and partners, and observatives participations.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Sephora Lahouari, Jérémie Gouyon, Grégory Francius, Fabien Picaud, Roberta Albino dos Reis, Amedea B. Seabra, Igor Clarot, Ariane Boudier

CITHEFOR EA 3452
Campus Brabois Santé
Bâtiment AB, 1er étage
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54505 Vandoeuvre-lès-Nancy Cedex

Dynamics of molecular interactions between Concanavalin A and gold nanoparticles.

Abstract

Bacterial culture is the gold standard for diagnosis but is very time-consuming. We propose a rapid test made of gold nanoparticles stabilized by Concanavalin A (AuNP-ConA). This work describes the binding mechanism of ConA and AuNP.

Citrate-stabilized AuNP were synthesized, characterized (3.3 ± 0.8 and 6.5 ± 0.4 nm for core and hydrodynamic diameters, respectively), directly incubated with ConA and the created entity was further characterized. Fluorescence spectrophotometry was used to investigate the binding mechanism and confronted to data obtained by molecular dynamics.

AuNP-ConA showed a surface plasmon resonance peak value at 517 ± 1 nm versus 513 ± 1 nm for AuNP, confirming a change in their electronic environment. Thermodynamic parameters were determined, confirming a spontaneous binding and the presence of low energy bonds between AuNP and ConA. The contribution of dynamic and static mechanisms was analyzed, and results were in accordance with the molecular modeling study.

In conclusion, AuNP-ConA were synthesized and characterized to decipher their binding mechanism. In the future, AuNP-ConA interaction with LPS in biological samples (plasma and cerebrospinal fluid) will be studied.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Authors (name, surname of PhD student + collaborators + supervisor(s))

Perrine SCHNELLER, Muriel BARBERI-HEYOB, Joël DAOUK, Arthur DURAND, Olivier TILLEMENT et Augustin TILLEMENT

UL Laboratory address of the PhD student

CRAN UMR 7039, 9 Avenue de la Forêt de Haye, 54505 VANDOEUVRE-Lès-NANCY

Title

Radiolabeled Chitosan Hydrogel for Internal Radiation Therapy of Glioblastoma

Abstract

Glioblastoma (GBM) is the most aggressive tumor of the central nervous system without a cure. Poor local control and infiltrative tumor cells into healthy brain parenchyma result in recurrence. Standard treatment involves tumor resection followed by radiochemotherapy. Nowadays, internal radiotherapy, is suggested as an additional procedure. IRHydroBRAIN project consists in the implantation during surgery, of a hydrogel labeled with a radionuclide, Yttrium-90 (^{90}Y). The goal is to provide proof of concept for improved local control and reduced post-operative recurrence. The multi-scale experimental approach is currently characterized by 4 axes. *In silico*, a map of ^{90}Y dose deposition into brain tissue was obtained *via* Monte Carlo simulations. Preliminary radiochemistry experiments demonstrated a 95% yield for cation chelation in hydrogel DOTAGA cages. Invasive properties of F98 GBM cells were confirmed using a relevant 3D *ex vivo* model. *In vivo*, F98 cells growth was assessed for an orthotopic GBM syngeneic model in rats, with an estimated mean survival of 24 days without any treatment. Outcomes of IRHydroBRAIN project have the potential to lead to a phase 1 clinical trial.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Jordan Brouard¹, Maude Gaffet^{1,2}, Cécile Pochon^{1,2}, Elodie Bole-Richard³, Maxime Fredon³, David Moulin¹, Francine Garnache-Ottou³, and Marie-Thérèse Rubio^{1,2}

1. Université de Lorraine – CNRS, UMR 7365 IMoPA
2. Université de Lorraine, CHRU Nancy Brabois Département d'Hématologie
3. Université Bourgogne Franche-Comté, INSERM, EFS BFC, UMR1098, RIGHT

IMoPA CNRS-UL UMR7365, 9 avenue de la forêt de haye, 54500 Vandoeuvre-lès-nancy

Development of anti-CD123 CAR-iNKT for the treatment of acute myeloid leukemia: production and comparison to CAR-T

Abstract

Genetically engineered CAR-T lymphocytes have demonstrated efficacy in B lymphoid malignancies but are underdeveloped in acute myeloid leukemia (AML). Invariant NKT lymphocytes (iNKT) possess innate cytotoxicity against CD1d-expressing tumors and mediate antitumor responses. Using iNKT cells as a foundation for CAR expression, instead of T cells, could be a way to enhance the effectiveness of CAR therapy. Our team had optimized a protocol to create CD123-targeting 3rd generation CAR-iNKT cells, yielding high transduction efficiency (close to 95%) and cell quantities comparable to CAR-T production. After achieving stable and efficient transduction, we compare the functional characteristics and properties of human CAR-iNKTs *versus* CAR-T cells. In this objective, we analyse the phenotype, cytokine production, cytotoxic receptor, metabolism, and specific lysis of leukemic myeloid cell lines *in-vitro*. It appeared that CAR-iNKT were as effective as CAR-T *in-vitro*, although there are differences in metabolism and cytokine expression.

We are investigating methods to assess the interaction of iNKT and T cells with the tumor microenvironment, both in humanized mouse models and *in-vitro* systems replicating the leukemic niche.

Abd Al Rahim Sara¹, Valentin Simon², Jeremy Lagrange¹, Huguette Louis¹, Muhammad Usman Ahmed¹, Véronique Regnault¹, Patrick Lacolley¹, Julien Perrin¹, Chaouat Ari²

¹ Université de Lorraine, Inserm, DCAC, Nancy, France

² Department of Pneumology, CHRU Nancy, Vandœuvre-lès-Nancy, France

Characterization of Hypercoagulability in Pulmonary Hypertensive Patients

Background:

Hemostatic abnormalities and dysregulation of the coagulation cascade has long been recognized in the context of pulmonary arterial hypertension (PAH). Anatomopathological data suggest an *in situ* intra pulmonary thrombosis, however, mechanisms are little known.

Objective:

To compare coagulation profile in whole blood and plasma samples, obtained from Jugular veins and Pulmonary arteries of patients having PAH.

Methods and Results:

Blood samples were collected directly from the patients' jugular vein and pulmonary artery during the initial right-heart catheterization performed at CHRU Nancy. *In vitro* clot formation was observed by total Thrombus-formation Analyser System (T-TAS) by perfusing whole blood through a Chip coated with collagen and tissue factor at high shear rate. We observed a different pattern of clot formation in patients treated with anticoagulants (prolonged occlusion time, lower thrombus formation). There was no difference in occlusion time, and thrombus formation between samples obtained from pulmonary artery and jugular vein. In addition, T-TAS parameters were similar in PAH patients and healthy volunteers.

We also measured the thrombin generation in plasma using thrombography. Thrombin generation profile was different in patients treated with anticoagulants. In addition, endogenous thrombin potential, and the maximum amount of thrombin formed were higher in plasma of pulmonary artery compared to jugular vein (1497±71.8 nM.min vs 1222±172 nM.min). The Results were coherent when comparing plasma rich and plasma poor in platelets.

Conclusion:

These preliminary results suggest that there is difference in clotting potential in patients having PAH. Our results also suggest a more favorable environment for thrombosis in the pulmonary arteries than in the jugular veins.

Abstract journée de rentrée de l'école doctorale BioSE
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Hanen Nicolas, Gauchard Gérome, Ben Mansour Khaireddine

EA 3450 DevAH, 9 avenue de la Forêt de Haye 54505 VANDOEUVRE LÈS NANCY

Biomechanical analysis of sumo and conventional style deadlifts

Abstract

Different deadlift techniques are widely used in strength training and rehabilitation. The aims of this study were i) to quantify kinematic and kinetic parameters analysis and ii) to compare muscle activity during sumo and conventional style deadlifts.

Fourteen optoelectronic cameras collected kinematic data, two force plates assessed ground reaction force and electromyography data were recorded by thirteen EMG sensors from two lifters who performed sumo and conventional deadlifts.

From lift off to knee passing, the knees extended approximately 5° more for the conventional group, hips position were similar, whereas the sumo group had 8° greater vertical trunk. EMG activity in the erector spinae muscles was consistent between groups. Conventional lifters exhibited higher trunk and hip moments, while the sumo group had higher knee moments.

Biomechanical differences between sumo and conventional deadlifts result from technique variations between those exercises, with a more horizontal spine position increasing the moment arm on the lumbar spine, potentially elevating shearing forces in spine. Thus, whole-body modeling will validate this hypothesis, enhancing our understanding of injury risks, especially in the lower back.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**Authors (name, surname of PhD student + collaborators + supervisor(s))**

Caroline Boursier, Timothée Zaragori, Marie Bros, Manon Bordonné, Saifeddine Melki, Laetitia Imbert, Antoine Verger.

IADI - Inserm U1254 - CHRU de Nancy Brabois, Bâtiment Recherche, 5 Rue du Morvan, 54500 Vandœuvre-lès-Nancy

Clinical implementation of dosimetry protocol in radionuclide therapy**Abstract**

Radionuclide therapy uses radioactivity to treat patient's cancer. My aim is finding a method can be used in clinical routine to determine radioactivity dose in tumors for each patient with post-radionuclide therapy scintigraphy performed in new generation of gamma camera with better performances. This method would secondarily make it possible to adapt the doses injected to each patient to increase effectiveness of treatment during therapy. This project need to three steps : i) define tumor segmentation; ii) quantify volumetric activities and iii) determine the doses absorbed. First results concerns meningioma radionuclide therapy to propose semi-automated segmentation methods to determine metabolic tumor volume with pretherapeutic ^{68}Ga -DOTATOC PET. The ground truth PET (VolGT-PET) were computed from manual segmentations by five experienced nuclear physicians. Several semi-automated segmentation methods were tested and the PET volumes providing the best Dice index with VolGT-PET was the optimized volume (Volopt). Volopt was obtained from 1.7-fold meninges SUVpeak (Dice index 0.85 ± 0.07). Tumor-absorbed doses were defined with Volopt. Accurate definition of pretherapeutic PET volumes is justified since SUVmean-derived values provide the best tumor-absorbed dose predictions in refractory meningioma patients.



**Abstract journée de rentrée de l'école doctorale BioSE
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SARDINI Lucas (PhD student) and MASSENET Séverine (supervisor)

**IMoPA Laboratory
Biopôle, Université de Lorraine
Campus Brabois-Santé
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54505 Vandoeuvre-lès-Nancy**

Study of the biogenesis of the Signal Recognition Particle (SRP)

Abstract

Signal Recognition Particle (SRP) is a ribonucleoprotein complex which is composed of 6 proteins and one non-coding RNA. The SRP is necessary for the co-translational targeting to the endoplasmic reticulum of secretory and membrane-bound proteins. Mutations within SRP proteins are linked to diseases such as hematological disorders. Despite the importance of SRP, how the particle is assembled in cells and how this mechanism is regulated is still mostly unknown. My thesis research aims to better understand SRP's biogenesis by: 1) identifying all the different complexes formed successively during SRP assembly, and 2) identifying and studying the assembly factors involved. In order to accumulate potentially SRP assembly intermediate complexes, I constructed stable cell lines expressing mutated GFP-SRP72 fusion proteins. I revealed that some GFP-SRP72 mutants have defective associations with the other SRP proteins and are mislocalized in cells. I am currently further defining the assembly defects due to the mutations. Proteomics studies will allow to characterize these complexes in the future, and potentially reveal assembly factors present in the stalled intermediates.

Abstract journée de rentrée de l'école doctorale BioSE Mardi 21 novembre 2023

Authors : Claire Nominé-Criqui (PhDstudent) ; **Collaborators** : Dr Emeline Renard(MCU-PH), Dr Florence Bihain ; **Supervisors** : Pr David Meyre, Pr Laurent Brunaud

UL Laboratory : NGERE laboratory-1256 INSERM ; Faculté de Médecine de Nancy-9avenue de la forêt de Haye 54500 VANDOEURE LES NANCY

Title : Setting up a large cohort of obese patients undergoing bariatric surgery to identify factors linked to weight change

Background

Excess body weight has recently become a global 'tsunami', with 1.9 billion adults. Treatments for obesity include lifestyle, behavioral and cognitive modifications, drug therapy, and bariatric surgery. The aim of this work is to understand in a very exhaustive way obesity in order to set up a prospective cohort of obese patients.

Methods

Currently we conducted a large review of the previous protocol of bariatric surgery focusing on different factors influencing weight variation. This review was conducted with another specialist of obesity. We extracted all factors previously studied.

Secondly, we identified the 1000 most cited articles about "obesity"; the aim of this work is to analyse them to gain a broad overview of the areas of research linked to obesity.

At last, we are using an existing cohort (OBESEPI-ALDEPI) to assess the association of a polygenic score of 941 polymorphisms linked to BMI in the general population.

Conclusion

These different reviews and the work about polygenic score will give us a very large knowledge of obesity in order to set up a prospective large cohort of obese patients treated at the Nancy University Hospital.

The long-term aim is to create an algorithm to select the patients who can benefit most from surgery and those who cannot.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Authors (name, surname of PhD student + collaborators + supervisor(s))

PhD student: Lienard Julie

Collaborators: Garcia Vivien, Guyon Gaele

Supervisors: Claudot Frédérique, Lemelle Jean Louis

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Enhancing Risk information in pediatriC surgery: A study of Disclosure by the surgeon and Interpretation by thE patient and parents (ARCADIE)

Abstract

Background: To obtain consent, surgeons must inform patients. Decision to accept or refuse surgery must be deliberated with the patient. This process may be biased by a misunderstood, non-existent, or incomplete information.

In pediatric surgery, disclosing is a challenge because patient's and parents' conceptions, concerns and questions vary, particularly regarding surgical risks, and must coexist within the same " timespace ".

Little is known about the 4-steps health literacy process in the pediatric context. We suspect that many factors influence patients' and parents' understanding of the disclosed information, and that the risk numeracy affects its interpretation and comprehension.

Objective: We aim to analyze the understanding of risk information by child-patients and parents studying how they interpret it and how pediatric surgeons disclose it.

Methods: We conduct a 3-population study based on 3-stages methods:

- A literature synthesis phase: 3 systematic literature reviews (practices, understanding factors, risk) and 1 systematic review of interventions
- A video-auto-ethnography phase
- A video-ethnographic phase with self-confrontation interviews.

Results: We expect to obtain a better understanding of risk communication components (information disclosure and interpretation).

Keywords: Disclosure, informed consent, understanding, pediatrics, risks

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Rim NASRALLAH - Pr. Sandrine BOSCHI-MULLER et Pr. Catherine CORBIER

Molecular and Structural Enzymology Group

IMoPA UMR 7365 CNRS-UL – Biopôle de l'Université de Lorraine – Campus Brabois-Santé
9, avenue de la Forêt de Haye

**Identification and characterization of new bio-sourced molecules affecting the
functions of the LSR receptor**

Abstract

Abnormal lipid levels in the circulation, otherwise known as dyslipidemias, are a result of perturbations of lipid homeostasis and risk factors for a number of diseases associated with inflammation, including cardiovascular, metabolic as well as neurodegenerative diseases, in particular, Alzheimer's disease. The lipolysis stimulated lipoprotein receptor, LSR, plays a key role in the removal of lipoproteins from the circulation, thus regulating plasma lipid levels, and represents a novel target for the treatment of dyslipidemias in the liver and in the brain.

In this context, the principal aim of my project is to identify bio-sourced molecules that can affect the activity or expression of this receptor. To achieve this, and by virtue of LSR's novelty, it is necessary first to characterize LSR/apolipoproteins E interactions and LSR expression regulation using a reporter system. During my first year, I developed protocols for the production and purification of recombinant soluble LSR domain and ApoE isoforms, and I begin the *in vitro* characterizations using SPR technologies. The next step will be to develop cell-based screening assays as well as binding experiments with the whole LSR.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Tripti Rastogi, Emmanuel Bresso, Kevin Duarte, Patrick Rossignol, Nicolas Girerd

Défaillance Cardiovasculaire Aigüe et Chronique (DCAC), BioSE

Identification of clinical phenotypes in patients with acute heart failure using unsupervised machine learning techniques

Abstract

Congestion is the main cause of hospitalization and symptoms in heart failure (HF). Data-driven clustering techniques may improve categorization of HF patients which may have prognostic and therapeutic implications. We aimed to identify clinical phenotypes of HF depending on the clinical and hemodynamic congestion profiles using unsupervised cluster analysis.

We used data of 741 patients enrolled in Nancy-HF cohort who were admitted for worsening HF. A total of 20 clinical, laboratory and echocardiographic congestion variables were used to identify congestion phenotypes. We identified 5 phenotypes which are: 1) younger patients with highest BNP levels, high filling pressure; 2) minimal congestion symptoms; 3) pulmonary and tissue congestion; 4) poor renal function, tissue, pulmonary and systemic intravascular congestion, and right ventricular dysfunction; 5) intravascular congestion and relatively normal RV function. Compared to patients with minimal congestion, the risk of cardiovascular outcome was higher in patients designated to cluster 3 and 4 [adjusted Hazards Ratio: 1.83 (1.12 - 2.99) and 2.78 (1.69 - 4.60), respectively].

In patients with worsening HF, unsupervised clustering techniques identified congestion profiles with different long-term clinical risk.



**Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**

Raphaël Jacquot, Gerôme Gauchard, Jean-Philippe Jehl

Developpement, Adaptation et Handicap (DevAH) – Université de Lorraine

Biomechanical modelling of shooting performance in biathlon

Abstract

All determinants of shooting performance in biathlon, such as postural control and rifle stability, have never been evaluated in a same study reproducing competition conditions. The aim of this study is to evaluate the effect of these factors on performance and their interactions between them. Ten young national and right-handed biathletes performed five minutes of roller skiing at 95% of their maximal heart rate before shooting. The acceleration of upper limbs and rifle in all axes was measured using inertial measurements units and postural sway was measured with a force plate, from 0.6 second before firing. Partial descriptive results show that successful prone shooting is linked to decreased rifle movements in all axis, and to movements of right arm, left forearm, and right hand, and successful standing shooting was linked to a decrease of rifle muzzle, left arm and forearm movements. No interactions between the factors was observed. Further, this protocol will be carried out in laboratory to evaluate more parameters such as kinematics with three-dimensional modelling, and the force ratio between the front leg and the rear leg.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Tirado, M., Weissman, K.J., Aigle, B., Jacob, C.

Ingénierie Moléculaire et Physiopathologie Articulaire (IMoPA)
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Advancing polyketide synthases engineering

Abstract

Polyketides are specialized metabolites amongst the most used in medicine. They are produced by mega-enzymes called polyketide synthases (PKSs) found in all living organisms. PKSs are multi-modular enzymes, each module contains catalytic domains adding acyl units to the elongating polyketide. Modules may be found distributed among subunits, connected by docking domains (DDs).

A promising way to improve polyketides used in therapy is synthetic biology of PKSs. Production of smaller compounds has been achieved, but at lower yields. Splitting PKSs into smaller subunits may increase yields of polyketide production, which is the first axe of this PhD project. Two PKSs will be split by introducing natural DDs or synthetic domains. Once the construction of genetic materials and the genome edition of *Streptomyces* spp. done, the impact on yields will be measured *in vivo*.

The second axe of this project is the understanding of PKSs macro-organization in bacterial cells. The coelimycin producer *S. coelicolor* is the model organism. PKSs subunits will be tagged *in vivo* with fluorescent proteins and observed by confocal microscopy. Genetic materials for *S. coelicolor* engineering are under construction.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Romain PIUCCO
(Supervisors: **Julien BROSEUS & Sébastien HERGALANT**)

INSERM U1256 – NGERE
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Epigenetic and proteomic characterization of Richter syndrome

Abstract

Chronic Lymphocytic Leukemia (CLL) refers to the abnormal proliferation of small, mature, circulating B cells. While CLL is often manageable, it may transform into an aggressive and large B-cell lymphoma called Richter syndrome (RS). RS patients usually die within 12 months. We face two vital challenges to improve RS clinical management: predicting transformation potential at the CLL stage, and distinguishing RS from other large B-cell lymphomas without information about the existence of prior CLL.

Micro-RNAs are small modifiers interfering with the translation process of many transcripts, including those involved in epigenetic regulation. Here we analyze RS and other lymphomas by micro-RNA sequencing and integrate the obtained data with other omics of the same samples: transcriptomes (RNAs), proteomes (proteins), DNA methylation and exomes (DNA variants).

We designed a micro-RNA-sequencing pipeline including many steps from quality control to data exploration, from single to multi-omics linking this molecular layer to the others.

For now, our pipeline was trained using publicly available CLL datasets. We will now analyze our newly sequenced data and begin to map micro-RNA dysregulations in RS.



**Abstract journée de rentrée de l'école doctorale BioSE
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Authors (name, surname of PhD student + collaborators + supervisor(s))

PhD student: Emilie CENRAUD

Collaborators: Vétophage, Biomaterials & Bioengineering UMR_S 1121 INSERM

Supervisors: Xavier BELLANGER, Grégory FRANCIUS

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Vandœuvre-lès-Nancy Cedex - FR

Developing the next generation of anti-staphylococci bacteriophage-based biomaterials

Abstract – 180 mots max

The increasing of therapeutic failures due to antibiotic resistance is of global concern. In this context, new alternative treatments such as the therapeutic use of bacterial viruses, also named bacteriophages or phages, are considered. Although phage therapy seems to be a promising solution, there still are numerous gaps in knowledge about fundamental and practical aspects to fill. Through this project, we aim to propose a prophylactic approach, focused on human and animal skin infections caused by *Staphylococcus aureus* and *Staphylococcus pseudintermedius*, by developing biocompatible hydrogels-based coatings/biomaterials with an intrinsic antimicrobial activity, that will be loaded with phages for a synergistic bactericidal effect.

In this work, we present the first results obtained by using 7 model *S. aureus* phages from different families. We notably loaded phages by co-incubating them with hydrogels. These phages seem to get into the hydrogel by passive diffusion but also to be concentrated/collected within the hydrogels. The phage charge and their size/geometry appear to be factors driving their behaviors in hydrogels. Replicates are needed but these results are promising for the development of efficient phages loaded biomaterials.



Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

Nathan Wisniewski, Reine El Omar, Déborah Helle, Caroline Gaucher

IMoPA UMR 7365 UL-CNRS, 9 avenue de la Forêt de Haye, 54500 Vandœuvre-lès-Nancy

**HARVESTING EXTRACELLULAR MATRIX OF WHARTON'S JELLY BY EXTRACTION OR
DECELLULARIZATION PROCESS: A PROMISING MATERIAL FOR CARDIOVASCULAR TISSUE ENGINEERING**

Abstract

Extracellular matrix (ECM) providing a support for cell growth *in vivo* and a complex mixture of components such as collagens, glycosaminoglycans and growth factors, shows potential applications in the field of tissue engineering. We focused on the umbilical cord as a neonatal tissue with low immunogenic potential. Especially, we studied the composition of ECM of the Wharton's Jelly, a conjunctive tissue surrounding umbilical vessels, using either an extraction or a decellularization process.

Our results indicate that the extraction process is much more efficient to collect different ECM components than decellularization processes. Moreover, the addition of an ultrasound step to the extraction protocol allows for greater yield of collagens and proteins, increase the variety of angiogenesis factors retrieved and lower the residual quantity of DNA, compared to the decellularization process. Thus, this material could be of great interest for cardiovascular applications such as coating a small diameter vascular graft to attain better performance and permeability.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**Authors (name, surname of PhD student + collaborators + supervisor(s))**

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**Resilience and perceived health of University students in the Lorraine
region (France) during the COVID-19 pandemic: longitudinal analysis and
psychometric approach****Abstract**

The COVID-19 pandemic and the measures taken to slow its spread have impacted the mental health of the general population, and students in Lorraine have been particularly affected. The objective of this thesis is to better understand how students' perceived health status and resilience level evolved during the COVID-19 pandemic and to characterize profiles of students at risk. Individual and environmental factors may have contributed to aggravating or protecting the health of certain groups of the student population that we intend to characterize. A psychometric approach is used to ensure the validity and invariance of measurement scales in this study. At the issue of the first lockdown, a cross-sectional study showed that 37.3% of students in Lorraine reported low resilience levels. Factors associated with low resilience included female gender, low social support, negative thoughts, lower quality of relationships, and studying arts, humanities, or languages. The perspectives of this thesis include a first longitudinal image of resilience and perceived health during the COVID-19 pandemic, identifying student profiles at risk, and shedding light on causal relationships between resilience and perceived health parameters.

Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

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Genomic signatures found in DNA from FFPE samples of advanced or metastatic breast cancer patients treated with endocrine therapy : first results of the CICLADES-CE study

Abstract

Hormonal breast cancers (BC) can be treated with endocrine therapy (ET), however treatments often lead to resistance. The genes *ESR1*, *PIK3CA* and *AKT1* have been identified in several ET resistance mechanisms. The CICLADES-CE study aims to analyze signatures and resistance mechanisms found in DNA extracted from FFPE samples of advanced or metastatic BC patients treated with ET.

DNA from nineteen samples were sequenced by hybridization capture with a 516 gene panel. Nucleotide variants and copy number variations were identified. Bioinformatic analysis was performed to extract mutational signatures matching those described by Alexandrov *et al.*, 2013. A custom gene panel was designed for the analysis of circulating tumor DNA (ctDNA) extracted from 36 months follow-up plasma samples.

Several genes in the PI3-kinase pathway were mutated, no mutations of interest were found in *ESR1* or *AKT1*. Three signatures associated with deficiency in DNA damage repair were identified. ctDNA analysis of the first patient showed varying frequency of three pathogenic mutations over 36 months follow-up. This data correlates with standard BC signatures and indicates promising results from ctDNA follow-up analysis.



**Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**

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APEMAC

Title: Evaluation of automated surveillance for surgical site infections

Abstract

Max 180 words, English, simple interline, police times 12

Abstract (15 lines):

The fight against surgical site infections (SSI) remains at the heart of the strategic priorities. Among prevention measures, the surveillance has already proven its ability to reduce these infections level by the simple fact of its implementation and the induced quality process Surveillance SSI represents a challenge, linked to the complex calculation of incidence and the difficulty of its implementation (missing data, validation based on the voluntary participation of surgeons). The hospital information systems provide an exhaustive database of medico-administrative data, enabling surveillance to be enriched and automated. The main objective is to measure the impact on SSI of a new surveillance system. First, we carried out a review in order to scope the current electronic SSIs surveillance systems worldwide and we started to develop our algorithm. Then, we will validate this algorithm (reliability, robustness, reproducibility) and set up monthly SSI surveillance based on this algorithm. To assess the impact of this new routine, we will carry out a before-and-after epidemiological study. We will assess changes in the incidence rate of SSIs, as well as surgeons' professional practices and satisfaction.

**Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**

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A study of the multiphysical properties of human skin to assess the burn degree.

Abstract

The human skin, the body's largest organ, serves as a protective barrier against external threats while maintaining homeostasis. It is divided into three main layers: the epidermis, which is the uppermost layer, the dermis which is where the vascularization of the skin is assured and the hypodermis, the deepest layer.

When a burn occurs, these layers are affected or even destroyed. The first degree harms the epidermis, but it can heal all by itself. The third degree is the destruction of all three layers. The second degree is the most difficult one to diagnose due to the existing hardly distinguishable types: superficial second-degree burns involve the upper dermis, causing blisters and redness; and deep second-degree burns that is in the dermis depth, manifesting as discolored, with less painful wounds.

Therefore, there is a need to characterize multiphysical properties of the skin. Assessing these properties can offer a more precise diagnosis, guiding therapeutic decisions for burn patients. Understanding the skin's inherent properties facilitates patient care improvement, reduces scarring, and supports recovery, making it an essential tool to develop a medical device.



**Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023**

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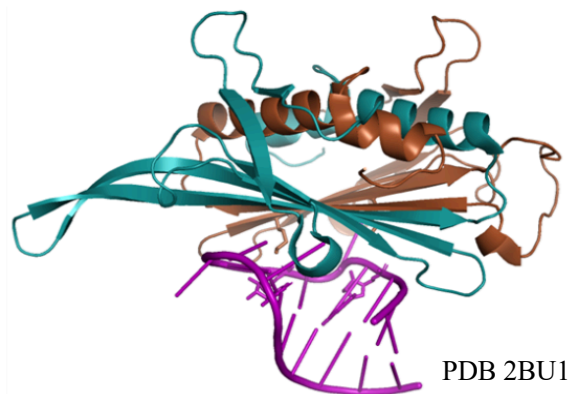
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Molecular mechanisms of enteric virus inactivation under oxidative conditions

ABSTRACT

Human noroviruses and hepatitis E viruses are pathogenic enteric viruses that lead to millions of gastroenteritis and hepatitis cases worldwide. The economic burden of these outbreaks is huge in terms of health and societal costs. Although, these viruses are known to be inactivated under oxidative conditions, the way by which this inactivation occurs remains unexplained. Recent data obtained on MS2 and Q β bacteriophages, currently used as surrogates to describe enteric virus behavior, suggest that oxidative conditions promote the formation of cross-links between the capsid proteins (CPs) and the genomic RNA that could abrogate virus infectivity (Bastin et al., 2020). Using a multidisciplinary approach combining protein biochemistry, RNA molecular biology and mass spectrometry, this project aims at identifying the molecular basis responsible for the formation of such oxidative modifications.

Simplified *in vitro* models were developed and preliminary data confirmed that cross-links can indeed be formed between mutated CP dimers and a 5'-fluorescently labelled cognate RNA upon oxidation. Optimized protocols for mapping of RNA-protein cross-links are developed and these studies will be extended to multiscale phage-derived *in vitro* models including Virus-Like particles.



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Tatton-Brown-Rahman syndrome:
Consequences of *DNMT3A* loss-of-function variations on DNA methylation and gene expression profiles

Abstract

Tatton-Brown-Rahman syndrome (TBRS) is characterized by overgrowth, obesity, behavioral disorders, hypotonia and intellectual disability, associated with facial dysmorphism. It is an autosomal dominant genetic disease, generally caused by *de novo* loss-of-function variations in *DNMT3A* which codes for a DNA methyltransferase involved in epigenetic regulation.

The main objective is to determine specific DNA methylation and gene expression profiles in these patients. Secondary objectives are to identify dysregulated genes in TBRS, and to target them for the development of a functional diagnostic test that would facilitate molecular diagnosis in particular for patients with a variant of uncertain significance.

Firstly, methylomic (Infinium MethylationEPIC BeadChip) and transcriptomic (Illumina TruSeq Stranded Total RNA) profiling will be established in 28 patients. Secondly, targeted functional analysis of the consequences of *DNMT3A* variations on critical genes will be performed.

During this year, we formed a cohort of 28 patients carrying constitutive mutations in the *DNMT3A* gene recruited at the national level. We have described their clinical phenotype (publication in preparation). At the same time, we responded to four calls for grants to finance future functional analyses.

178 words.

Abstract journée de rentrée de l'école doctorale BioSE
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| École de Santé Publique | 9, avenue de la Forêt de Haye | 54505 Vandœuvre-lès-Nancy**PHYSICAL ACTIVITY INTERVENTION FOR CANCER PATIENTS, TAKING INTO ACCOUNT THE SOCIO-ECONOMIC CONTEXT****Abstract**

Despite the proven benefits of physical activity (PA) in oncology, physical inactivity is a major concern among cancer patients, with poor adherence to exercise programs. The aim of INTERACSE project is to develop a PA intervention considering disease progression (pre-diagnosis, during treatment, post-treatment) and socio-economic context. Several studies have been planned: (1) an evaluative study of the implementation of an adapted fencing program (RIPOSTE); (2) an observational study of PA levels of 300 patients over one year, measuring the PA practice and its socio-economic and psychological determinants; (3) a qualitative study comparing 36 patient's experiences in an observational and interventional studies, using the theoretical domains framework; (4) the co-construction of an intervention with patients and healthcare professionals. Data from studies 1 to 3 have been collected. Study 1 demonstrated good reach of RIPOSTE among young and dynamic patients and positive trends in terms of effectiveness, identifying cooperation, exchanges and cohesion within the group as key factors. Studies (2) and (3) will build on these data to prepare the conception of the intervention, through an innovative and system approach.



Abstract journée de rentrée de l'école doctorale BioSE
Mardi 21 novembre 2023

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Title: Obtention of pro-inflammatory mesenchymal stromal cells from umbilical cords

Abstract

Objective: Mesenchymal stromal cells (MSC) are promising in cell therapy to treat inflammatory diseases. If the anti-inflammatory MSC2 phenotype is well described, there is less information on the pro-inflammatory MSC1 phenotype while they could be interesting on immunoparalysis context. The aim in this study is to evaluate the priming MSC strategy towards a MSC1 phenotype to improve their therapeutic action on immunoparalysis.

Methods: Wharton's Jelly Mesenchymal stromal cells which come from umbilical cords have been primed with different stimulations to obtain MSC1 and MSC2. Their immunomodulatory capacities have been studied by the analysis of specific markers in flow cytometry and by cocultures with T cells.

Results: MSC2 showed immunosuppressive capacity to inhibit T cell proliferation while MSC1 appeared to have no impact compared to unprimed MSC. No difference was observed on phenotype markers between MSC1 and MSC.

Conclusion: We confirmed that MSC2 showed immunosuppressive capacities on T cells proliferation and will be interesting to control inflammation state. However, MSC1 priming used did not permit to obtain MSC1 phenotype on parameters tested. So we need to test other primings to better characterise MSC1.

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Consequence of impaired one-carbon metabolism in the pathophysiology of Huntington's disease

Abstract

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disorder triggered by expansion of abnormal CAG repeats in the Huntingtin (HTT) gene encoding the HTT protein resulting in aggregation and impairment of its function leading to neurodegeneration. Several studies demonstrated that HD patients are hyperhomocysteinemic. This could be related to an altered one carbon metabolism (OCM). Hyperhomocysteinemia induces an irreversible fixation of homocysteine (N-homocysteinylation) on some proteins leading to their loss of function.

We demonstrated the N-homocysteinylation of the huntingtine and we hypothesized that it could be an aggravating risk factor in HD in terms of early and severe symptoms.

This work gave rise to the HO-HD protocol (CPP 1-21-018 ID 11541) and the establishment of a cohort of HD patients who will be followed longitudinally in terms of neurology and biochemistry (OCM). Fibroblast cell lines are established from a skin biopsy to investigate the N-homocysteinylation of the HTT by proximity ligation assay (Duolink®).

68% of HO-HD patients presented alterations of the OMC and 59% are hyperhomocysteinemic. Our first duolink results showed higher HTT's N-homocysteinylation and an increased course of the disease in these patients.