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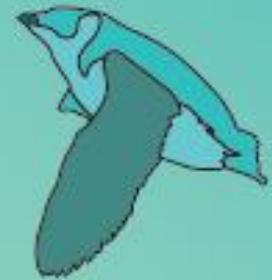
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Table des matières

Communications orales – Session 1 : 9h30-11h10

Sport et Santé

Role of muscle Fibronectin type III domain-containing 5 / Irisin on cerebral Brain-derived neurotrophic factor levels: impact of exercise intensity

Clémence Leger [1], **Aurore Quirié** [1], **Stéphanie Lemaire** [1], **Alexandre Méloux** [1], **Philippe Garnier** [1,2], **Anne Prigent-Tessier** [1]

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Physical exercise (EX) is crucial for brain health, as it increases the production of Brain-derived neurotrophic factor (BDNF), a neurotrophin that supports cognitive functions and neuronal plasticity. How EX elevates BDNF levels is not fully known, but the release of myokines produced by skeletal muscle contraction was involved. Recent studies have identified irisin, a peptide derived from Fibronectin type III domain-containing protein 5 (FNDC5) and secreted into the bloodstream, as a positive regulator of cerebral BDNF production. While the influence of EX intensity and modality on cerebral BDNF levels was characterized, the impact on muscular FNDC5/Irisin expression and circulating irisin levels remains to be explored.

The study was performed on adult male Wistar rats divided into four groups: sedentary (SED), low-intensity EX at speeds of 12m/min (EX12, 40% of maximal aerobic speed, MAS) and 14m/min (EX14, 50% of MAS), and high-intensity EX at the speed of 18m/min (EX18, 70% of MAS). The rats underwent a daily 30-minute run on a treadmill during seven consecutive days. Blood and tissues (hippocampus, soleus (SOL) and gastrocnemius (GAS) muscles) were collected after the last EX session and 24h later, respectively.

The study analyzed the expression of FNDC5 in oxidative (SOL) *versus* glycolytic (GAS) muscles and BDNF in hippocampus by Western blotting. Localization of FNDC5/Irisin was studied by immunofluorescence and serum irisin levels were determined by ELISA.

Our findings revealed that 1) upregulation of FNDC5 protein levels was limited to the GAS and only from an EX at 50% of MAS compared to SED rats, 2) FNDC5/Irisin immunostaining was limited to the fast-type fibers mostly found in the GAS, 3) serum irisin levels increased after an EX at 50% and 70% of MAS, and 4) a positive correlation was obtained between serum irisin and hippocampal BDNF levels when SED and EX rats were studied simultaneously.

Keywords: FNDC5/Irisin, BDNF, intensity, physical exercise, muscle fibers, hippocampus.

Effect of muscle lengthening speed on electrically-induced torque development

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Introduction: It has been previously reported that superimposing a muscle lengthening (LEN) at 180°/s during tibial nerve neuromuscular electrical stimulation (NMES) allowed increasing the evoked torque in comparison to the sole application of NMES or the combination with a lower LEN speed (60°/s). The present study examined the effect of increasing muscle LEN speed on torque production during the combined application of tibial nerve NMES and muscle LEN.

Methods: Fifteen participants volunteered to participate in a unique experimental session consisting of 15-s stimulation trains delivered over the tibial nerve at 100 Hz (1 ms, intensity set to initially evoke 5 – 10% of maximal voluntary contraction). NMES was either applied alone or in combination with a muscle LEN at 180 (NMES+LEN180) or 300°/s (NMES+LEN300). For all stimulation trains, the theoretical and the real values of the torque-time integral (TTIth and TTIr, respectively) were calculated, and the TTIr/TTIth ratio was determined to quantify the presence of extra-torque (ET).

Results: Results on TTIr showed that NMES combined with high-speed LEN (300°/s) induced a significantly higher TTIr than in the NMES condition (P<0.05). Results on TTIr/TTIth ratios showed higher ET levels when LEN was applied during NMES for both NMES+LEN180 and NMES+LEN300 conditions compared to NMES alone.

Discussion: These results indicate that NMES combined with high-speed LEN (300°/s) further increases torque production and ET phenomenon compared to muscle LEN at 180°/s. A possible explanation is that combining high-speed LEN with high-frequency NMES induced a higher afferents' solicitation, increasing the torque production and ET phenomenon.

Keywords: Ia afferents, Triceps surae, Extra-force

Physical activity as an effective strategy to prevent cardiac disorders in rheumatoid arthritis: a study in rat pristane-induced arthritis

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Rheumatoid arthritis, the most common chronic inflammatory rheumatic disease, is characterized by an increased risk of cardiovascular diseases, including heart failure and silent ischemia. While physical activity demonstrated cardiovascular benefits in the general population, these effects are not clearly defined in RA patients. The aim of this study was therefore 1) to determine if the pristane-induced arthritis model (PIA), a model of chronic arthritis, is suitable for reproducing the structural and functional cardiac changes of RA, 2) to determine whether physical activity can have positive effects on this model.

Chronic PIA was induced in male Dark-Agouti rats by intradermal injection of pristane. Controls rats received saline. A group of PIA rats (PIA-EX) was subjected to an individualized treadmill running protocol during the remission phase. At acute and chronic phases of PIA, cardiac structure and fibrosis were analyzed by histology. Cardiac function, in particular left ventricular developped pressure (LVDP), cardiac compliance and susceptibility to ischemia after ischemia/reperfusion, were explored in isolated hearts, Cardiac VCAM-1 mRNA expression and plasma irisin levels were measured by qRT-PCR and ELISA, respectively.

Cardiac hypertrophy and fibrosis as well as VCAM-1 mRNA overexpression were observed at both the acute and chronic inflammatory phases of PIA. As compared to controls, PIA rats exhibited a reduced LVDP and cardiac compliance at chronic phase, while PIA-EX did not show any difference. Moreover, exercise reduced infarct size, fibrosis, VCAM-1 mRNA expression and arthritis severity but enhanced irisin blood levels. VCAM-1 expression was positively correlated with cardiac fibrosis, while irisin was negatively correlated with VCAM-1 and cardiac fibrosis.

The PIA model is a relevant model to mimic the cardiac disorders of RA. A daily treadmill running program during remission attenuated cardiac fibrosis, inflammation, and reduced infarct size. These results support the implementation of physical activity in the management of RA patients.

Keywords: arthritis, physical activity, heart diseases, rat model

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Coronary angiographic findings in sport-related acute myocardial infarction: association between intraluminal thrombus and sport intensity

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Introduction

Coronary artery disease (CAD) characteristics and severity in sport-related acute myocardial infarction (SR-AMI) remain only poorly investigated. We aimed to study coronary angiographic findings of patients with SR-AMI according to sport intensities.

Method

From the IMACS database, a prospective ongoing monocenter acute MI survey, all consecutive patients hospitalized in a University Hospital from 2010 to 2021 who underwent coronary

angiography for SR-MI were included. SR-AMI was defined as MI occurring during sport practice or within the first hour of recovery. Angiographical data were retrospectively analyzed. Sport intensity, expressed in Metabolic Equivalent (MET), was adapted from Ainsworth classification, with 6 METs as intensity cut-off.

Results

One hundred seventy-three patients were included, median age was 60 years old, most were male (90%), and had ST segment elevation MI (STEMI). The SR-AMI often occurred while cycling (41%), jogging (23%), hiking (9%) or playing soccer (9%). Patients commonly underwent Out of Hospital Cardiac Arrest (OHCA) (17%). The rate of cardiovascular (CV) risk factors was high, including current smoking and history of CAD. Most (91%) had significant lesions (>50% stenosis). When compared with lower intensity sport (<6 METs), patients in the $\geq$ 6 METs group had similar age, and similar CAD severity, as assessed by SYNTAX score. Higher intensity group also had a higher rate of STEMI (p = 0.05), of intraluminal thrombus (p = 0.024), and showed a trend toward a lower rate of calcified lesions (p=0.103).

Conclusion

Our retrospective study suggests for the first time that SR-AMI occurring during a $\geq$ 6 METs intensity exercise was characterized by a more frequent thrombotic burden. If confirmed by larger prospective and coronary plaque imaging studies, these preliminary findings could help to understand the underlying mechanisms of these dramatic events.

Keywords: sport-related acute myocardial infarction, intraluminal thrombus, sport intensity

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Effects of a supervised exercise program on insomnia in patients with non-metastatic breast cancer undergoing chemotherapy

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Background: In women with breast cancer (BC), insomnia is frequent. Although physical activity has been consistently associated with reduced side effects, very few studies have investigated its effects for insomnia in BC.

Objective: To examine, in non-metastatic early BC patients the effects of a 3-month intermittent aerobic exercise program on insomnia.

Methods: 14 women (age: 47 $\pm$ 9 yrs), undergoing chemotherapy, were randomized to either a control group (CG) or a trained group (TG). Before initiating chemotherapy, a clinical interview (DSM-5) were carried out and Insomnia Severity Index (ISI), Pittsburgh Sleep Quality Index (PSQI) questionnaires were completed. After the first period of chemotherapy and 3 months

after, without or with the exercise program, sleep was evaluated by polysomnography and the same questionnaires were completed. A maximal graded exercise test was performed.

Results: Insomnia did not improve after 3 months in both groups whereas submaximal/maximal power and VO2 increased significantly in TG.

Variables before (T0) and after three months (T3) for control and training groups

		CG		TG	
		T0	T3	T0	T3
ISI		13.6 ± 5.7	13.6 ± 5.7	13.6 ± 5.7	13.6 ± 5.7
PSQI		9 ± 2.6	9 ± 2.6	9 ± 2.6	9 ± 2.6
Ventilatory threshold 1	**Power (W)**	58 ± 11	58 ± 11	58 ± 11	58 ± 11
	VO₂ (mL/kg/min)	13.1 ± 2.4	13.1 ± 2.4	13.1 ± 2.4	13.1 ± 2.4
Ventilatory threshold 2	**Power**	82.7 ± 13	82.7 ± 13	82.7 ± 13	82.7 ± 13
	VO₂	16.8 ± 3.6	16.8 ± 3.6	16.8 ± 3.6	16.8 ± 3.6
Maximal	**Power**	94.4 ± 14.6	94.4 ± 14.6	94.4 ± 14.6	94.4 ± 14.6
	VO₂	21.5 ± 4.4	21.5 ± 4.4	21.5 ± 4.4	21.5 ± 4.4

Conclusion: Insomnia did not decrease after training but exercise parameters improved in TG, with better tissue oxygenation.

Keywords: Breast cancer; Insomnia; Exercise

Cancérologie 1

Discovery of circulating tumor DNA methylation biomarkers for colorectal cancer using public databases and clinical validation

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Introduction: Colorectal cancer is a public health issue and is the third cause of cancer-related death worldwide in 2020. An early diagnosis can improve the prognostic giving to screening a central place in the management of colorectal cancer. Stool-based screening for colorectal cancer has a low compliance and a blood-based screening test have a better compliance. Blood-based colorectal cancer screening is possible using liquid biopsy, which is the exploration of the cell-free circulating tumor DNA. This study is a proof of concept to identify DNA methylation patterns on public databases that can be used in liquid biopsy.

Material and method: A bioinformatics analysis with R established a DNA methylation profile on the GEO databases and then confirmed with the TCGA database. The profile was then validated on local tissues and blood samples using methylation specific digital PCR.

Results: The bioinformatics analysis found a six CpG methylation profile that had a 98.5% sensitivity and 98.8% specificity of colorectal cancer compared to non-tumor colorectal tissues. The experiment on local samples confirmed the differential DNA methylation profile on three of the biomarkers ($p < 10^{-5}$). The DNA methylation profile was also found in the blood samples ($p = 0.019$), with one biomarker displaying a sensitivity of 71% and a specificity of 100%.

Discussion: A bioinformatics analysis of public database is able to predict clinically applicable blood-based DNA methylation biomarkers; the clinical performances of the biomarkers will have to be established by a prospective study. However, the bioinformatics analysis can be reproduced on other cancer types to expand the possibilities of cancer screening.

Keywords: epigenetic, DNA methylation, liquid biopsy, circulating tumor DNA, biomarker, colorectal cancer.

Investigating new partner proteins of EZH2 and KDM6B during Epithelial to Mesenchymal Transition

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Epithelial to mesenchymal transition (EMT) is a progressive and reversible mechanism that allows cells with an epithelial phenotype to lose it in favor of a mesenchymal one. During EMT, epithelial cells forming a cohesive tissue through cell-cell and cell-matrix junctions progressively dissociate from it and gain migratory properties. This mechanism has been linked to the formation of metastases in cancer. This switch in phenotype is made possible by a wide reprogramming of gene expression leading to the downregulation of pro-epithelial genes (e.g. CDH1, ZO-1) and upregulation of pro-mesenchymal genes (e.g. CDH2, Vimentin), both of which are tightly controlled by epigenetics. In particular, the methylation level of H3K27 (Lysine 27 oh the Histone H3) has been shown to vary significatively on the promoters of key genes during EMT. The methylation of H3K27 is regulated by the methyltransferase EZH2 (Enhancer of Zest Homolog 2) and the lysine-demethylase KDM6B (Lysine Demethylase 6 B). In spite of having opposite catalytic activities, both EZH2 and KDM6B induce EMT when overexpressed in cancerous cells. This could be due to the recruitment by partner proteins of these enzymes towards different sets of genes involved in EMT. To investigate this, we used RIME (Rapid Immunoprecipitation Mass spectroscopy of Endogenous proteins) to identify proteins interacting with EZH2 or with KDM6B and associated with chromatin while using a TGFβ/TNFα treatment to induce EMT. We identified, in A549 cells (non-small cell lung carcinoma), a set of partners pocessing DNA-binding capabilities and could be responsible for EZH2 and KDM6B targeting during EMT. Investigating these proteins and the importance of their interaction with EZH2 and KDM6B during EMT could help better understand the role of EZH2 and KDM6B during EMT as well as unravel new targets for cancer therapies.

Keywords: Epigenetics, Cancer, EZH2, KDM6B

Role of an autophagic protein in stress granule formation

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Many environmental factors can lead to induce stress inside eukaryotic cells e.g., osmotic, hypoxia or oxidative stress. Any stress in the cell will induce the activation of a specific kinase depending on the stress and it will phosphorylate a key factor of the translation mechanism leading to it inhibition. This inhibition has the impact of accumulate non-translated mRNA that will aggregate, and form structures called stress granules. They are non-membranous structures composed of mRNA and ribonucleoproteins. They allow the cell to reprogram some mechanism to survive to a specific stress.

Our laboratory has discovered by the past a protein called GABARAPL1 described has a part of the autophagic pathway. This mechanism is important for the cell because it allows to recycle a lot of specific structures e.g., stress granules by a specific mechanism called selective autophagy.

Our aim is to determine if GABARAPL1 could have an impact on selective autophagy of stress granules or if it could have possibly another impact during the stress granule formation.

Keywords: stress granule, GABARAPL1, translation inhibition, autophagy

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Peri-operative Immunotherapy for resectable non-small cell lung cancer, a living mapping of research and a living systematic review

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The Cochrane Collaboration is an independent, not-for-profit organization that offers a recognized methodology in the establishment of systematic reviews and meta-analyses.

The collaboration is increasingly interested in providing summaries of data from trials of different power and level of proof. Either by comparing the data from observational studies with those from randomized trials or by supplementing the information with a rigorous analysis of the literature and answering a question complementary to that of the randomized controlled trials.

In addition, the Cochrane Collaboration develops methodology in indirect comparison using the network meta-analyses.

The synthesis of data, by systematic review or meta-analysis, can be regularly updated and form the concept of living systematic review. The living systematic reviews are also developed the support of computer software.

There are several perioperative treatment regimens in terms of immunotherapy product, association with other immunotherapy, with chemotherapy and in terms of administration chronology (neoadjuvant, adjuvant). Similarly, the strategies being tested are also different. Therefore, uncertainty remains as to the best option for operable patients with early-stage NSCLC.

This project aims to pursue development both in the synthesis of data and apply the Cochrane Collaboration methodology in the development and knowledge of perioperative strategies for non-small cell lung cancer (NSCLC).

In the era of precision medicine, combining data from different trials is essential for the development of therapeutic strategies.

The project will be the implementation of a networks living systematic review for the evaluation of immunotherapy treatment strategies for patients operated on for NSCLC. For this study, we are going to develop and work out statistical methods allowing a synthesis of the data resulting from trials treating this question, and to develop interfaces by data processing, making it possible to actualize and present the results.

Keywords: Network Meta Analysis, Non Small Cell Lung Cancer, Immunotherapy, Living Systematic Review

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Combined incentive actions focusing on primary care professionals to improve cervical cancer screening in women living in socioeconomically disadvantaged geographical areas: a study protocol of a hybrid cluster randomised effectiveness and implementation trial

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Cervical cancer (CC) causes thousands of deaths each year. Nearly all cases are caused by oncogenic strains of human papillomavirus (HPV). In most developed countries, CC screening (CCS) is based on the detection of high-risk HPV infections. Studies showed a significant correlation between social deprivation and CC. Our aim is to demonstrate that use of incentives could improve the rate of screening, based on HPV-self sampling (HPVss), among underserved women by at least 10% compared to the control group.

Our cluster randomised controlled trial included 10 446 women aged 30-65 years eligible for CCS living in deprived areas in four French departments and not up to date of their CCS. HPVss-kits were mailed to them. The study employs a factorial analysis design with four arms, based on how the kits are returned: direct postal return or through a health care professional (HP). Each modality may or may not be associated with a financial incentive.

The main outcome is the proportion of women returning the HPVss or performing a phycisian-based HPV or pap-smear test within the year after receiving the kit.

In the three departments in which inclusions are completed and one-year data available, 15.6% of women met the primary endpoint among which 51% used the HPVss and 49% had a physician-based HPV test.

Even though use of incentives did not meet the expected CCS rates, first follow-up data shows that our intervention significantly increases screening uptake compared to the eligible but not included women (16% vs 5%, respectively).

Our study proves that a tailored approach is essential to reach underserved women and that offering the possibility to meet a HP might not be the best option for those who used the HPV kit since returns were much lower compared to simple postal return groups (6% vs 10% respectively).

<u>Keywords:</u> cervical cancer, HPV, self-sampling, social deprivation, public health

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Botanique 1

Development of a knowledge graph framework to ease and empower translational approaches in plant research: a use-case study on grain legumes

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Legumes, and especially pulses, are an important source of protein for food and feed, and are appreciated for their positive impact on the "one health". However, their unstable yields and their susceptibility to biotic and abiotic stresses highlight the need for varietal improvement in order to increase the cultivated areas and productivity. With the advent of sequencing technologies, a large pool of genetic and -omics resources, heterogeneous at the inter- and intra-species scale, is emerging. Thus, it is important to capitalize on these scattered heterogeneous data to develop translational research to boost breeding projects and crop diversification. To meet this need, we undertook the development of the Orthology-driven knowledge base framework for translational research (Ortho_KB). For a set of species of interest, it infers orthologous relationships between genes, proposes associated syntenic blocks between chromosomes and creates a graph database linking genetic and RNA-seq data. To explore the possibilities of this framework, we populated Ortho_KB to obtain OrthoLegKB, an instance dedicated to legumes. This database includes four cultivated crops, namely *Pisum sativum*, *Vicia faba*, *Lens culinaris* and *Vigna radiata*, and the model legume *Medicago truncatula*. Available information on quantitative trait loci (QTL) for multiple traits are being integrated as well as expression data. The proposed database model was evaluated by studying the conservation of a flowering-promoting gene.

<u>Keywords:</u> graph database, orthology, ontology, quantitative genetics, gene expression, comparative omics, legumes

Identification and functional characterization of proteins S-nitrosated during salt stress in *Klebsormidium nitens*

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The small gaseous molecule nitric oxide (NO) is well established as a major ubiquitous component of cell signalling. A key signalling mechanism mediating NO effects is S-nitrosation, a post-translational modification by which NO can impact the target protein activities, subcellular localizations, and capacities to form protein complexes. The identification of proteins targeted by NO is of major interest in order to elucidate NO functions. Interestingly, land plants lack NO synthase (NOS), which is the main enzyme for NO synthesis in metazoans, while a few algal species possess it, thus raising many interrogations. Therefore, we focused on the identification of S-nitrosated proteins during salt stress in *Klebsormidium nitens*, a freshwater algal species possessing a NOS and established as a model to study plants adaptation to land. We applied the Biotin Switch method followed by mass spectrometry analysis. This method allows the purification of S-nitrosated proteins. We found 43 proteins with significantly higher S-nitrosation levels in salt response condition. Orthology analysis were performed against the model plant *Arabidopsis thaliana*, in order to determine the potential function of these proteins. Among them, we selected an interesting protein called INOSITOL POLYPHOSPHATE MULTIKINASE 2 (IPK2), potentially involved in cell signaling and stress response. We produced it successfully in *Escherichia coli* and measured its activity in collaboration with the Leibniz-Forschungsinstitut für Molekulare Pharmakologie. The S-nitrosation of IPK2 was proved to occur on Cys125. We generated 2 mutants, IPK2(C125A) and IPK2(C125S), and will observe the conservation of their activity before proceeding to the measurement after S-nitrosation of the wild type and mutated proteins. Structure analysis were also caried *in silico* with alphafold, giving insights of potential NO effects. The identification and functional analysis of S-nitrosated proteins in *K. nitens*, this project will provide a better understanding of the functions of NO in unicellular green algae with NOS.

Keywords: algae, nitric oxide, S-nitrosation, mass spectrometry, biotin switch, abiotic stress

Study of beta-glucosidases activity of *Lactiplantibacillus plantarum* strains from fermented vegetables

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Beta-glucosidases are the enzymes hydrolysing the *O*-glycosidic bonds of glycosides family to release *β*-D-glucosides and aglycones. These enzymes are present in living organisms including human and other animals, plants, and microorganisms. The beta-glucosidase activities can vary within microorganisms due to reasons such as regulations, genes, enzyme kinetics and the structure of substrates. They are poorly characterized among Lactic acid bacteria (LAB). *Lactiplantibacillus plantarum* is a LAB, popularly present in fermented products (for instance, sausage, sourdough, kimchi, sauerkraut, and other fermented vegetables). In vegetables, many aglycones realeased by the beta glucosidase activities are volatile compounds which contributes to the flavours of foods. It is very interesting to study the beta-glucosidase activities present in *L. plantarum* strains in order to understand their contribution during the fermentation of vegetables. The aim of this study is to evaluate beta-glucosidase activities of different *L. plantarum* strains by using several substrates. *L. plantarum* strains were isolated from various types of fermented vegetables in Cambodia. They were differentiated by analysing the profiles using four different primers amplified by Random Amplified Polymorphic DNA-Polymerase Chain Reaction (RAPD-PCR). Beta-glucosidase activities of *L. plantarum* strains were evaluated. Three substrates were used separately in the assay reaction including, *p*-nitrophenyl-*β*-D-glucopyranoside, *m*-nitrophenyl-*β*-D-glucopyranoside, and *o*-nitrophenyl-*β*-D-glucopyranoside. The reaction was prepared by mixing the cell pellet of *L. plantarum* with the substrate, and incubated for 120 minutes, and then terminated by adding a sodium carbonate (Na_2CO_3) solution. The result shows that beta-glucosidase activities of *L. plantarum* strains are varied.

Keywords: Beta-glucosidase Activity; Lactic Acid Bacteria; *Lactiplantibacillus plantarum*; Fermented Food

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Molecular characterization and symbiotic efficiency of nitrogen-fixing *Bradyrhizobium* strains of *Lupinus luteus* in Morocco

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Lupinus luteus is a fodder legume cultivated in rotation with cereals for its high economic and ecological values in Morocco's semi-arid and sub-humid climates. It improves soil structure and reduces fertilization costs by fixing atmospheric nitrogen in symbiosis with rhizobia.

We are interested to analyze rhizobium microsymbionts nodulating *L. luteus* grown in the Agricultural soils of Morocco. Out of 83 isolated rhizobia, 18 strains were chosen based on

their rep-PCR fingerprint. The Multilocus sequence analysis using five gene sequences (*16s rRNA*, *glnII, gyrB*, *recA*, and *rpoB*) revealed that all isolated strains are members of Bradyrhizobium genus close to *B. canariense BTA1*[T], *B. cytisi CTAW11*[T], *B. hipponense aSej3*[T], *B. lupini USDA 3051*[T], and *B. rifense CTAW71*[T].

The analysis of the plant growth-promoting activities showed that all strains are able to produce auxin, solubilize rock phosphate, and produce siderophores. All strains used in the inoculation experiments improved significantly the growth of *L. luteus* under nitrogen-free conditions.

Keywords: Rhizobium-Legume symbiosis, *Bradyrhizobium*, *Lupinus luteus*, Symbiotic effectiveness, Plant growth promoting rhizobacteria (PGPR), Multilocus sequence analysis (MLSA)

Exploring Architectural Traits and Ecophysiological Responses in Soybean under Heat and Water Stress: Implications for Climate Change Adaptation

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In the context of climate change, characterized by increasingly frequent droughts and heat waves, it is anticipated that the global soybean yields, the most extensively grown legume, will experience a significant decline in the foreseeable future. There is thus an urgent need to improve its ability to maintain growth and productivity under such conditions. The objective of this study was to explore which plant traits make soybeans more resilient to heat and/or water stress, with a focus on plant architecture. For this purpose, two soybean genotypes, already shown to have contrasted root architecture (Maslard et *al*., 2021) were grown under controlled conditions in the high-throughput phenotyping platform 4PMI where either optimal conditions, heat waves, water stress or both heat waves and water stresses were applied during the vegetative stage. New root detection algorithms and tools were generated to quickly and accurately analyze many architectural traits (e.g. length, width, projected root area, plant height over time).

Under stress conditions the two genotypes displayed contrasted architectural features such as root width, root angle branching or plant height. By correlating architectural to functional traits, related to water and carbon allocation, we were able to explain the stress susceptibility level of the two genotypes. This cross analysis of plant ecophysiology and architectural traits under different stresses provides new information on soybean adaptation to climate change.

Keywords: Glycine max, climate change, deep learning, root architecture, ecophysiology

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Communications orales – Session 2 : 11h30-12h50

Agroécologie

Cropping system redesign enables pesticide use reduction in a diversity of French commercial farms: a diachronic approach.

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Pesticide use in agriculture has been increasing since the second half of the 20th century, with consequences on human and ecosystem health as well as pest resistance. Reducing pesticide use appears necessary for transitioning to sustainable cropping systems, allowing for sufficient food production with minimal environmental costs and satisfactory farmers income, in a context of climate change also impacting agriculture.

Non-chemical technics efficient to reduce pest pressure are individually well documented and available for farmers to decrease reliance on pesticides while reaching satisfying pest control and avoiding crop yield losses due to invertebrate pests, diseases and weeds. Cropping system diversification, thoughtful tillage, mechanical weeding and moderate fertilization have been shown to reduce pest pressure and therefore pesticide use in specific situations. However, proof on their generalized applicability by farmers remains scarce, and evidence of their efficiency in a large-scale commercial farm context is needed. Here we use data from 913 farms to identify evolutions in cropping systems and crop management associated with reduction or increase in pesticide use, in a diversity of agricultural contexts.

We demonstrated that pesticide use reduction is possible in a majority of contexts, and we quantified the proportion of the evolution in pesticide use related to cropping system re-design and to the optimization of decision making in pesticide application. We found the highest reduction rates in cropping system with the highest initial levels of pesticide use. Cropping system diversification and nitrogen fertilization reduction were most often associated with pesticide use reduction. Although pesticide use decreased in all French regions, climate characteristics related to temperature and humidity explained substantial parts of pesticide use evolution. Our study highlights the value of real farm network in sustainable agriculture research. The enlargement of studied farms' pathway at a national scale would result in substantial progress made towards the fifty percent pesticide use reduction goal set by the French EcoPhyto Plan.

Keywords: Cropping system, pesticide use, management practices, real farm network, transition to sustainable agriculture

Side effect of heavy metal on insect: Copper-based fungicide reduces the performance of non-targeted pest

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Global use of pesticides is rising worldwide, especially face with exacerbated insect pest pressures stimulated by rapid climate changes. Unfortunately, pesticides not only affect targeted pests but can also impact all other organisms within agroecosystems, sometime resulting in secondary pest outbreaks. However, little is yet known about the way pesticides affect non-targeted pests. The purpose of this study was to determine the extent to which copper-based fungicide impacts the performance of the European grapevine moth (EGVM) *Lobesia botrana* (Lepidoptera: Tortricidae), attacking vineyards in Europe, the Middle East, and North and South America. This major pest is not targeted by cooper-based fungicides but is chronically exposed to chemicals used during the vegetative growth of vines. Based on laboratory experiments, we explored the effects of copper consumed by larvae during their development on reproductive traits and behaviors. We found overall adverse effects of copper on the EGVM performance, both developmentally and reproductively, due to the exposure of larvae to increasing concentrations of copper in their diet. Copper negatively impacted almost all physiological traits (larvae survival, development time to emergence, fertility, fecundity, spermatophore volume, and number of eupyrene sperm) but did not affect reproductive behaviors (mating success, pre-mating latency and mating duration). Despite an apparent advantage of copper treatments in limiting EGVM populations highlighted in this study, the negative impact of copper could, however, affect other protagonists (predators, parasitoids, pollinators), generating adverse effects for integrated crop management.

Keywords: Copper, European grapevine moth, Pest, Fungicide, Viticulture, Performance

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Heavy metals used as fungicide may positively affect *Trichogramma* species used as biocontrol agents in Integrated Pest Management programs

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The use of biological control agents in Integrated Pest Management programs has increased in the last decades, but may be affected by the concurrent use of some pesticides and other

chemicals. The objective of this study was to evaluate the performance of *Trichogramma cordubensis* (Hymenoptera: Trichogrammatidae), a candidate agent to control grapevine moths, when these beneficial insects are exposed to copper treatments through trophic accumulation. A generation of the host *Lobesia botrana* (Lepidoptera: Tortricidae) was reared on a diet enriched with different concentrations of copper from Bordeaux mixture. The host eggs laid by these females having consumed copper during their larval development were then exposed to female parasitoids. Our results showed that copper consumed by the host parental generation had no effect on the parasitism rate but had positive effects on the emergence rate and size of emerging parasitoids at the highest copper concentration. These effects of copper on parasitoids may be due to stress effects of copper on the host parental generation, linked with a trade-off between development and defenses leading to a reduced immunity in their host eggs. Another hypothesis may be that copper has been transferred into the host eggs at potentially beneficial concentrations for parasitoids due to detoxification mechanisms of the hosts' mothers facing a chemical stress. These positive effects of copper pesticides on parasitoids have been observed at the highest copper concentration, consistent with real exposure conditions in the field. This study thus highlights potential synergetic effects between pesticides and natural enemies.

Keywords: Trichogramma, pesticides, non-target organisms, copper, biocontrol

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Abrupt late 1980s surface climate warming effects on drought risk over main french crop production basins

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The abrupt warming observed in the late 1980s over France has modified the hydrological cycle, evapotranspiration being identified as one of the main drivers of these changes. Along with this rapid warming, stagnation of crop yields is observed since the 1990s over France, especially for bread wheat. In this context, two major concerns need to be assessed: what are the patterns of water balance responses to abrupt changes in temperature? How did this abrupt warming impact drought risk over winter bread wheat main production basins?

Safran-Isba-Modcou dataset of reanalyzed surface meteorological observations offers the opportunity to address the complexity of processes leading to changes in local water cycle. Daily liquid precipitation and potential evapotranspiration on an 8km spatial resolution from 1959 to 2021 are used to quantify the evolution of climate hazard linked to water cycle. A simplified two reservoirs water balance model is used to compute daily water balance using agronomic parameters of winter bread wheat. The evolution of frequency and intensity of drought risk is analyzed using Tweedie distributions.

Our results suggest that the abrupt warming in air temperature in 1987/1988 had strong influence on water balance evolution. The latter displays various changes depending on the crop and the production basin studied. The exceeding of water stress threshold is more frequent or more pronounced, leading to modifications of intensity and/or duration of drought events. Risk structure evolves depending on the production basin studied.

Evolving climate hazard linked to water cycle impacts agro-climatic risks, identified as one of the main factors affecting the evolution of crop yields. Both mean conditions change and modifications of the spatio-temporal variability of water balance affect the probability to overcome risk threshold. This is of major concern for the agricultural sector, especially insurance companies, and may lead to adaptation process from managers.

Keywords: climate, abrupt warming, hazard, water balance, wheat, agro-climatic risk.

White wines oxidative stability: a 2-vintage study of Chardonnay champagne base wines aged on lees in barrels

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Ultra-premium champagne wines are characterized by a long aging on laths. The goal of the winemaker is to use all possible oenological techniques to keep the aromatic freshness of the future products. To that purpose, some champagne base wines can be aged first on lees in oak barrels. However, if it is now acknowledged that such ageing practices contribute to the oxidative stability of dry white wines, no study has been done on Chardonnay champagne base wines designed for a long ageing on laths (Romanet et al., 2023). The antioxidant capacity of Chardonnay champagne base wines was measured by DPPH assay during barrel ageing for two successive vintages, 2020 and 2021. Regardless of the vintage, ageing in new oak barrels significantly improves the Chardonnay champagne base wines oxidative stability. Oak wood ellagitannins followed a linear extraction profile during barrel ageing on champagne base wines similar to that already reported for dry Chardonnay wines (Nikolantonaki et al., 2019). Moreover, Chardonnay champagne base wines aged in new barrels preserved at the end of ageing an important number of S-N containing compounds, which in addition to the known ellagitannins contributed wines better antioxidant stability (Romanet et al., 2020). A metabolomic approach based on an untargeted ultra-high-performance liquid chromatography quadrupole time-of-flight mass spectrometry (UHPLC-Q-ToF-MS/MS) analysis allowed a clear discrimination of champagne base wines according to the ageing period on lees in new oak barrels regardless of the vintage.

Nikolantonaki, M., Daoud, S., Noret, L., Coelho, C., Badet-Murat, M.-L., Schmitt-Kopplin, P., & Gougeon, R. D. (2019). Impact of Oak Wood Barrel Tannin Potential and Toasting on White Wine Antioxidant Stability. *Journal of Agricultural and Food Chemistry*, *67*(30), 8402–8410.

Romanet, R., Bahut, F., Nikolantonaki, M., & Gougeon, R. D. (2020). Molecular Characterization of White Wines Antioxidant Metabolome by Ultra High Performance Liquid Chromatography High-Resolution Mass Spectrometry. *Antioxidants*, *9*(2), 115.

Romanet, R., Gougeon, R. D., & Nikolantonaki, M. (2023). White Wine Antioxidant Metabolome : Definition and Dynamic Behavior during Aging on Lees in Oak Barrels. *Antioxidants*, *12*(2), 395.

Pharmacologie

Design, synthesis and evaluation of novel arginase inhibitors from pharmacomodulation of Piceatannol

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Arginase is the metalloenzyme that hydrolyses L-arginine into L-ornithine and urea whose biogenesis ensures ammonia detoxification. However, L-arginine is also the substrate for NO-synthase which catalyses the production of nitric oxide (NO), an endogenous regulator, strongly involved in endothelial stability, control of infectious diseases, tumors, and immune processes.

In dysfunctions, the upregulation of arginase results in L-arginine depletion that decreases NO levels involved in endothelial dysfunction. L-arginine deficiency also affects an immune response in the tumor environment as it provokes the inactivation of T-cells. Furthermore, regarding parasitic infections, L-ornithine can be a precursor of polyamines which could promote cellular growth and therefore parasite replication.

Despite high therapeutic potentials, only few arginase inhibitors have been developed and none has been approved for clinical use. Our aim concerns the synthesis of small molecules, inspired by natural polyphenols bearing catechol moieties as potential arginase inhibitors. The present work is focused on the synthesis and evaluation of derivatives of the natural arginase inhibitor, Piceatannol. Specifically, the replacement of the central double bond in Piceatannol's molecule with other rigid systems and the change of position of hydroxy moieties on the aromatic ring has been performed to improve the biological activity.

Keywords: piceatannol, polyphenol, pharmacomodulation, biological evaluation, molecular modelling.

Additive effect of SGLT2 inhibition and CB1R antagonism in the fight against diabetic nephropathy

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Introduction: Diabetic nephropathy (DN) is one of the most common complications of diabetes. While pharmacological approaches exist, including renin angiotensin aldosterone system (RAAS) blockers and sodium-glucose cotransporter type 2 inhibitors (SGLT2i), the cannabinoid 1 receptor (CB1R) has emerged as a new potential therapeutic target. Since SGLT2i has become the new standard of care for DN, we evaluated if combining CB1R antagonism with SGLT2i leads to better reno-protection than SGLT2i or CB1R blockade alone.

Methods: 40 C57BLKS-Leprdb/db mice and 6 control non-diabetic mice were fed a high protein diet for 9 weeks. After 5 weeks, diabetic mice were divided into 4 groups and were treated either with control vehicle, the SGLT2i empagliflozin (0.3 mg/kg/day), the CB1R blocker INV-202 (0.5 mg/kg/day), or a combination of both by oral gavage for 28 days. We then analyzed the diagnostic parameters for DN (albuminuria, glycemia, and urinary albumin to creatinine ratio (ACR)). Moreover, we assessed general kidney state by evaluating the parameters associated with RAAS activation, oxidative stress, inflammation and renal fibrosis.

Results: Both SGLT2i and INV-202 alone significantly improved albuminuria and ACR while the combo was significantly more effective. Interestingly, similar observations were noted for inflammatory and for oxidative stress markers. Furthermore, we observed an additive protective effect of the combo regarding the normalization of renal histopathology features and injury markers such as KIM1 and DKK3 urinary excretion.
Moreover, tubulointerstitial fibrosis was also significantly reduced after combo compared to single approach and vehicle-treated mice in a TGF-β/SMAD3 pathway dependent manner.

Conclusion: A poly-pharmacological approach combining both SGLT2i and CB1R antagonism might represent a promising therapeutic strategy for the management of DN.

Keywords: diabetes, nephropathy, CB1 receptors, SGLT2 inhibition, poly-pharmacological

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Development of a method to analyse the behaviour of rapidly dissolving films in contact with liquids

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An oral film is a drug delivery system that consists of a thin layer of hydrophilic polymer designed to be rapidly disintegrated and dissolved in the mouth upon contact with saliva without drinking water or chewing. It, thus, allows a fast release of the drug. The disintegration time of an oral film is a critical quality and safety feature, so it is essential to know the behaviour of the film in contact with water or aqueous liquids.

Two types of disintegration test methods are generally used for the following products oral films: the disintegration test method prescribed in the tablet' pharmacopoeia and the Petri dish method. However, these methods only indicate partial information of the film' disintegration

time (which is usually between 30 seconds and 1 minute). The aim of this study is to develop a new analytical method to study the behaviour of oral film in contact with a liquid for very short periods (from few seconds to minutes).

The setup of a methodology based on goniometry (contact angle measurement) techniques allows to follow the evolution of the contact angle, the volume, the wetting, and the swelling of the drop over time in a reproductive way. By following the kinetics of these parameters, the wettability, hydrophilicity, the disintegration time, and surface free energy of the films can be properly determined.

Keywords: oral film, analytical method, contact angle meter, disintegration time, wettability

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Exploring the chemical diversity of essential oils in Armenian markets: a comprehensive analysis of composition profiles

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Due to its location at the convergence of multiple biogeographical regions, Armenia experiences significant variations in climate and soil conditions, resulting in a diverse range of plant chemotypes. However, there has been a lack of recent reports on the biological activity of plants found in Armenia's flora. There are few with well-described essential oil profiles, despite the vast biodiversity of Armenian flora. This study aimed to analyse the chemical composition of essential oils used by the population and found in the Armenian market. Unfortunately, only essential oils of foreign origin can be found, like Russia. Three essential oils of *Lavandula angustifolia*, *Abies sibirica*, and *Rosmarinus officinalis* were selected, and analysed by GC-MS and GC-FID. Based on a comparison with relevant literature and prior GC analyses, it was found that the essential oil of *Lavandula angustifolia* product exhibited similar chromatogram to *Lavandula* x *intermedia* "grosso", mainly because of the high amount of camphor (6.98%). Similarly, the GC of the essential oil of *Rosmarinus officinalis* showed some similarities with a *Rosmarinus officinalis* cineol chemotype profile, with a surprising higher amount of α- (24.86%) and β-pinene (10.62), compared to the cineol amount (19.51%). In contrast, the GC of the *Abies sibirica* conformed to the classical standards. These data are very important for a safe and therapeutic use of these essential oils.

Keywords: Essential oils, GC-MS, GC-FID, *Lavandula angustifolia, Abies sibirica, Rosmarinus officinalis*

Environnement et Santé

Proposed phylogenetic inference and haplogroup determination in *Echinococcus multilocularis* from whole mitochondrial DNA sequencing

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Echinococcus multilocularis is a flatworm of the family Taeniidae responsible for alveolar echinococcosis, a rare but severe disease mimicking a liver cancer. The disease usually occurs in the cool and high regions of the northern hemisphere, mainly in China but also in the historical European cradle including the Franche-Comté Region. The study of the genetic polymorphism of this parasite has so far been carried out on the basis of a few mitochondrial/nuclear genes or nuclear microsatellites.

We propose to establish phylogenetic inference from whole mitochondrial DNA sequencing of *E. multilocularis* samples from various endemic areas worldwide and to define haplogroups in French patients in order to make comparisons between genetic and clinical data.

The French human samples were collected by the National Reference Center for Echinococcoses, the other samples (human, monkeys, rodent, dog and fox samples) came from worldwide collections (Alaska, Canada, Japan, China, Spitzberg-Norway, Switzerland, Belgium, Germany, Sweden, Luxembourg and Poland). Sequencing was performed by Illumina technique. The analysis of the raw data was performed using a workflow created on the Galaxy platform.

One hundred and one samples were sequenced; 51 haplotypes were emphasized from haplotype network analyses and three major haplogroups stand out (named Arctic, Asia-North America and Europe); three subgroups can be distinguished in France, one corresponding to the most recent cases found in the west of the country.

Genetic polymorphism analysis performed on the whole *E. multilocularis* entire mitochondrial DNA allowed to reach a better definition of the existing groups at the continental level. For French patients, three groups stand out and will permit in a second time to compare genetic and clinical data.

Keywords: *Echinococcus multilocularis*, NGS, Illumina technique, mitochondrial genome, phylogenetic inference

Transcriptomic integrity of human oocytes used in assisted reproductive technologies: technical and intrinsic factor effects

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Millions of children have been born throughout the world thanks to assisted reproductive technologies (ART), the harmlessness of which has not yet been fully demonstrated. For years, efforts to evaluate the specific effects of ART have focused on the embryo, however it is the oocyte quality that dictates first and foremost the developmental potential of the future embryo. Controlled ovarian hyperstimulation (COH), cryopreservation, and *in vitro* maturation (IVM) are sometimes necessary steps to obtain a mature oocyte, but they could alter the appropriate expression of the oocyte genome. Besides, it is likely that environmental factors and lifestyle have a significant influence on oocyte transcriptomic quality that may interfere with the outcome of an ART attempt. Using an in-depth literature search performed on PubMed, we identified transcriptomic changes in the human oocyte caused by interventions specific to ART but also intrinsic factors such as age, reproductive health issues and suboptimal lifestyle. Specifically, maternal aging, lifestyle factors (smoking, BMI) and infertility due to endometriosis or polycystic ovary syndrome increase oxidative stress and alter mitochondrial processes in the foreground. Concerning ART techniques themselves, there is evidence that IVM, cryoconservation and different COH regimens shape the oocyte transcriptome. For other ART laboratory factors such as temperature, oxygen tension, air pollution, light, the evidence remains scarce. Focusing on genes involved in chromatin-based processes such as DNA methylation, heterochromatin modulation, histone modification, and chromatin remodeling complexes, but also genomic imprinting, we observed systematic dysregulation of such genes either after ART intervention or lifestyle and environmental exposure. Alteration in the expression of such epigenetic regulators may be a common mechanism linked to adverse oocyte environments and explaining global transcriptomic modifications. Fortunately, it is likely that dysregulations in oocyte transcriptomic integrity can be minimized by adapting ART protocols or reducing adverse exposure.

Keywords: assisted reproductive technologies, human oocyte, RNA-seq, transcriptome

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Impact of the environment on the level of risk in pregnancy

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Pregnancy is a vulnerable period where the occurrence of complications can have major consequences on the outcome of the mother and/or the newborn. Multiple factors are responsible for these complications, such as medical or obstetrical history and sociodemographic characteristics. However, there is an unexplained proportion of complications and adverse pregnancy outcomes. PreCEE 2.0 is a research program on perinatality, its complications and exposure to multiple factors.

It will fill gaps in the current literature by contributing to the understanding of the impact of co-exposure to pollution (noise, air (PM2.5, PM10, NO2, O3), green and blue spaces), on the occurrence of complications and adverse pregnancy outcomes (fetal growth retardation, hypertensive pathologies of pregnancy, prematurity, gestational diabetes...), as well as by exploring how all these factors combine and accumulate.

The objective of the project is to evaluate the relevance of integrating the environmental exposure of the pregnant woman in the definition of the level of risk in pregnancy. More specifically, to study the relationship between complications and adverse pregnancy outcomes and markers of pregnancy vulnerability (medical-obstetrical, demographic, behavioral and environmental dimensions), and to describe their potential cumulative effect.

The study population will consist of 21,000 women, for more than 31,000 deliveries that took place at the Besançon University Hospital maternity hospital (level 3 maternity hospital) during the period 2011 to 2021.The daily air pollution data provided over a period of 11 years and a fine spatial resolution are a strong point of the methodology of this project. The diversity of the living territory of the studied population (Franche-Comté region) is characterized by a strong urbanization gradient (urban, peri-urban and rural) responsible for marked exposure contrasts. Through a better knowledge of the dose-effect relationships characterizing the environment-maternal-fetal health relationship, this project will contribute to a potential adaptation of pregnancy monitoring.

<u>Keywords:</u> perinatality, exosome, pregnancy risk level, complications and adverse pregnancy outcomes

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Role of MexXY/OprM efflux pump in polymyxin resistance in *Pseudomonas aeruginosa*

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Among bacterial species, *Pseudomonas aeruginosa* has been considered a critical pathogen by the World Health Organization due to its high level of antibiotic resistance. As a last resort, colistin (polymyxin class) is administrated to treat clinical isolates of multidrug resistant *P. aeruginosa*. Unfortunately, some isolates resistant to this antibiotic may emerge. Polymyxin resistance is mainly due to the addition of 4-amino-4-deoxy-L-arabinose (Ara4N) to lipid A of

the lipopolysaccharide, resulting in a modification in outer membrane charges. Ara4N synthesis depends on a large operon *arnBCADTEF-ugd,* which is under the control of several two-component systems including PmrA-PmrB. We have previously shown that the MexXY/OprM efflux pump participated in the resistance to colistin in a mutant with an amino acid substitution in the histidine kinase sensor PmrB, which leads to colistin resistance. The aim of this study was to decipher the role of MexXY/OprM in colistin resistance in *P. aeruginosa*. Using a RNA-seq transcriptomic approach, we determined the genes whose expression was modulated in the mutant *pmrB* deleted from the *mexXY* operon in comparison with the *pmrB* mutant. The analysis revealed that 54 and 14 genes were up- and down-regulated when the efflux pump was deleted. Interestingly, several of these genes are involved in polyamine catabolism. Then, analysis of the polyamine composition of the supernatant and membrane cell surface of both mutants will be performed by a global method using a polyamine detection kit and by mass spectrometry (ESI-MS) to identify and characterize the types of polyamines that may can alter polymyxin susceptibility. In parallel the genes involved in polyamine catabolism will be explored by genetic experiments. All these results will improve the knowledge on the MexXY/OprM efflux pump.

Keywords: *Pseudomonas aeruginosa*, polymyxin resistance, efflux, PmrAB, MexXY/OprM

Botanique 2

Nouveaux outils en bioremédiation : prédiction du potentiel de dégradation d'une communauté à partir de sa composition et création de communautés multidégradantes par coalescence

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En bioremédiation, la bioaugmentation consiste en l'introduction de microorganismes dans un milieu contaminé afin d'augmenter et/ou de suppléer la population bactérienne en place, dans l'objectif de le dépolluer. Cette approche est cependant limitée par la difficulté de choisir des microorganismes efficients - communauté ou souche spécifique – à inoculer, en lien avec les conditions abiotiques et les microorganismes indigènes du milieu pollué.

Dans ce travail nous avons cherché à prédire le potentiel microbien de dégradation de deux pesticides, le glyphosate et l'isoproturon, de communautés microbiennes telluriques en utilisant des méthodes statistiques issues de la prédiction génomique. Pour cela nous avons obtenu des variants compositionnels de communautés dégradant ces deux herbicides (une communauté par herbicide) *via* une approche couplée de dilutions et de traitements biocides. Ensuite, dans le but de relier la composition en OTU de ces variants avec leur capacité de dégradation, nous avons appliqué 3 méthodes de prédiction : *Ridge Regression, Lasso,* et *Random Forest*. Les résultats indiquent une corrélation de plus de 80 % entre capacité de dégradation prédites et mesurées.

Nous avons ensuite construit des communautés multidégradantes par une approche de coalescence en basant nos choix sur des propriétés intrinsèques des communautés dégradant fortement l'isoproturon pour certaines et le glyphosate pour d'autres. Finalement, nous avons évalué l'efficacité de ces nouvelles communautés multidégradantes dans un sol pollué non dégradant. Les résultats montrent le transfert des capacités de dégradation des herbicides, et ceci même à faible dose d'inoculation dans le cas de l'isoproturon.

Keywords: bioremédiation, communautés cicrobiennes, pesticide, coalescence, prédiction génomique

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Dynamic of soil microbial communities in response to long-term repeated organic or inorganic fertilizations

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Within the soil biodiversity reservoir, the microbial community is essential for ecosystem functioning and resilience. Applications of organic and inorganic products in agriculture could improve soil microbial quality and increase crop productivity. However, little is known about the dynamic of the soil microbial communities after several years of repeated fertilizer inputs. In this study, we take advantage of a long-term field experiment in Rennes (SOERE PRO – EFELE), Brittany region (France). The EFELE experiment was set up in 2012 and has been cropped with wheat-maize rotation since the beginning of the trial. A mineral fertilizer (MIN), and three different organic amendments: cattle manure (CM), pig slurry (PS), and anaerobic digestate (DIG), were applied once a year from 2013 to the present. These treatments were compared to a control (CON) that has not received any organic or inorganic input. To monitor soil microbial community changes throughout 10 years of repeated fertilization practices, every two years (on wheat culture), soil samples were collected twelve months after the last organic or inorganic material application. We used high-throughput sequencing targeting 16S and 18S ribosomal RNA genes to describe the evolution of microbial soil communities. DNA extractions of all soil samples were performed in 2022. Results showed that the soil molecular biomass remained stable over 10 years of repeated fertilization practices, except for the CON treatment where a decrease (~58%) was observed. Interestingly, regardless of the sampling time considered, soils treated with CM displayed 20% higher soil molecular biomass compared to those that received DIG. The richness diversity index based on operational taxonomic units (OTUs) remained stable for both prokaryotic and fungal communities over time for all treatments. The Non-Metric multiDimensional Scaling approach (NMDS) showed that the structure of the prokaryotic community changed over time depending on the treatment.
Regarding the fungal community structure, a time-dependent effect was also observed, although the discrimination between different treatments seemed less pronounced than the one observed for the prokaryotic structure. To conclude, the present study highlights that the soil microbial community could be lastingly modified after 10 years of repeated fertilization practices. These changes depend on the nature of the treatment applied.

Keywords: Organic and inorganic fertilization, high-throughput sequencing, soil microbial Community

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Characterisation of the vacuolar sulfate transporter *SULTR4* in pea: role in the establishment of seed yield and protein composition

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To investigate the role of vacuolar sulfate in seed yield and quality, we have targeted the single pea *SULTR4* gene *(PsSULTR4),* which encodes a transporter homologous to Arabidopsis SULTR4;1 and 4;2 that allow sulfate efflux from the vacuole to the cytosol. By simulating the 3D structure of PsSULTR4, we observed that it is similar to that of SULTR4;1 in Arabidopsis. Furthermore, a phylogenetic analysis revealed a high level of conservation of SULTR4 protein motifs across land species. A fluorescent protein fusion experiment confirmed that PsSULTR4 localizes to the vacuolar membrane.

Five *sultr4* mutants were identified by TILLING (Targeting Induced Local Lesions IN Genomes), two of which showed a reduced seed yield under sulfur deficiency. These mutants are currently being characterized by studying SULTR4 mRNA and protein stability, and the effect of the mutations on the simulated 3D structure. Seed yield of these two mutants was not affected under sulfur-sufficient conditions but changes in seed protein composition were observed. In particular, less sulfur-rich PA1 albumins accumulated in mature seeds. This is likely to be associated with a reduced utilization of sulfate within the seeds, since the total seed sulfur content was unchanged compared to the wild-type, whereas the seed sulfate concentration was significantly higher in both mutants. This highlights the crucial role of vacuolar sulfate in maintaining seed quality, but also seed yield when sulfur is limiting.

Keywords: *Pisum sativum*, sulfate transporter SULTR4, vacuolar sulfate, sulfur deficiency, seed yield, seed quality, storage proteins, sulfur amino acids

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Identification of Phosphodiesterase 5 inhibitors from *Dalbergia cochinchinensis* using at-line LC-QTOF-MS micro-fractionation

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Dalbergia cochinchinensis, belonging to the Fabaceae family, is a tree widely distributed in Southeast Asia and commonly known as Thai Rosewood in English or "payoong" (พะยูง) in Thai. Furthermore, bioactivities such as anti-oxidant, anti-inflammation and 5α-reductase have been reported for this plant. Following a phosphodiesterase 5 (PDE5) inhibitory activity screening, *D. cochinchinensis* leaf extract showed promising activity (IC$_{50}$ value 0.88 ± 0.03 µg/ml). But there is still no report on responsible chemical constituents in this plant.

Thus, our study aims to identify the compounds which support PDE5 inhibitory activity from *D. cochinchinensis* leaf extract. However, conventional bioassay guided fractionation method has major drawbacks such as time-consuming and dereplication. In order to avoid these problems, the at-line coupled liquid chromatography quadrupole time-of-flight mass spectrometry (LC-QTOF-MS) micro-fractionation with bioassay can be used. The concept of at-line bio affinity screening is the combination of traditional fractionation approach with MS,

and pharmacology together (Figure 1). This technique can be one powerful tool for rapid identification of PDE5 inhibitors in *D. cochinchinensis* leaf extract in single run.
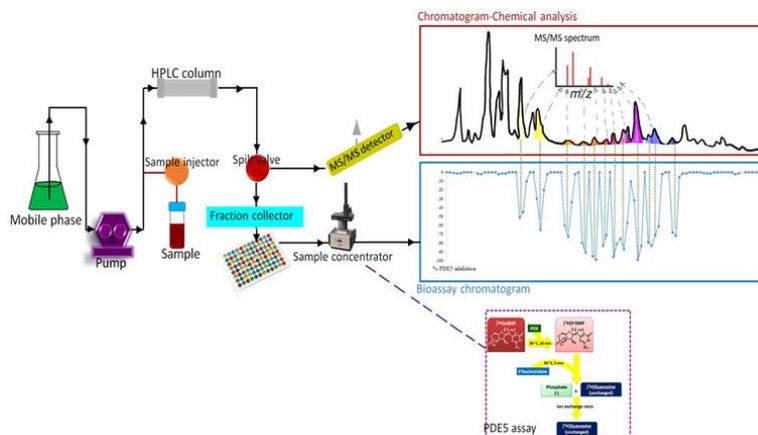

Figure 1: At-line coupled LC/MS scheme for identification of PDE5 inhibitors in crude extract

Keywords: *Dalbergia cochinchinensis,* Phosphodiesterase-5 inhibition, At-line technique

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 Immunologie

Production of functional plasmacytoid dendritic cells-targeted CAR-T cells from patients with immune-mediated inflammatory diseases

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Increasing evidence suggests that plasmacytoid dendritic cells (pDCs) are involved in the development of different IMID (immune-mediated inflammatory diseases), especially through the overproduction of proinflammatory cytokines such as type I interferons. Several studies are investigating the therapeutic suppression of pDCs in these diseases using monoclonal antibodies. Mainly developed in the field of oncology, Chimeric Antigen Receptor T-cell (CAR-T cell) therapy has been extended more recently to other areas such as infectious diseases, cardiac fibrosis or autoimmune diseases. CD123 is the α-subunit of the heterodimeric IL-3 receptor and it is expressed strongly on pDCs. To the best of our knowledge, no CD123-targeted CAR-T cells (CAR123) have yet been developed for IMID treatment. Here, we demonstrate the first preliminary results of capacity to produce CAR123 from patients' T-cells with systemic or cutaneous lupus erythematosus, systemic sclerosis, dermatomyositis, psoriasis and hidradenitis suppurative and their *in vitro* efficacy.

PBMCs from either patients or healthy donors (HD) were isolated using Ficoll-Paque density gradient. pDCs and T-cells were isolated using magnetic cell sorting. Two days after activation T-cells were transduced with the lentiviral vector encoding the CAR123. Proliferation and

transduction efficiency of CAR123 were evaluated after *in vitro* culture. Cytotoxic activity was assessed by flow cytometry 6 hours after co-culture with autologous pDCs or CAL-1 cell line (positive control).

T-cells were genetically engineered to express CAR123 in both patients and HD (66.9% ± 16.0%, n=23 and 79.4% ± 15.4%, n=5, respectively, p=ns). After 15 days of culture, CAR123 expression was stable in both cases. Patients-derived CAR123 were able to lyse autologous pDCs *in vitro* (85.9% ± 10.6%, n=20) as well as HD-derived CAR123 (87.4% ±6.9%, n=5) (p=ns).

Our preliminary results demonstrate the feasibility of CAR123 production from patients' T-cells with IMID and their *in vitro* efficacy towards circulating autologous pDCs.

Keywords: Plasmacytoid dendritic cells, immune-mediated inflammatory diseases, CAR-T cell therapy

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Febrile temperature decreases efferocytosis and increases the pro-inflammatory phenotype of murine macrophages

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Inflammation is a natural protective response to fight against any aggression, such as infections. Under physiological conditions, the resolution phase of inflammation allows the body to stop inflammation, and promotes tissue repair. A critical step in the switch from the onset phase to the resolution one is mediated by macrophages performing the elimination of apoptotic neutrophils (a process called efferocytosis). Efferocytosis stimulates macrophage reprogramming from a pro-inflammatory to a pro-resolving phenotype. Fever is a defense mechanism encountered in different inflammatory settings, including infectious diseases. This mechanism is an advantage for the host, since fever reduces pathogen proliferation and increases the efficacy of immune response. However, few studies focussed on the link between fever, macrophages and the resolution of inflammation. To study this aspect, bone marrow-derived macrophages were exposed to heat (39.5°C for 2 hours) or not before co-culture with apoptotic thymocytes. After 1 hour of co-culture, cells were washed to remove uncleared apoptotic cells. Then, macrophages were cultured at 37°C or 39.5°C for one to 24 additional hours. The febrile temperature reduced the efferocytic capacity of macrophages generated from bone marrow cells using M-CSF and then LPS plus IFN-γ. Exposure of macrophages to febrile temperature was attested by RT-quantitative PCR analysis with an increased expression of heat shock protein (HSP) genes.The relative expression of pro-inflammatory genes (e.g., *il1b, il6, cox2 and inos*) increased 24 hours after exposure to 39.5°C. Efferocytosis assays performed using either life cell microscopy (Incucyte, Sartorius) or flow cytometry showed a diminution of the macrophage efferocytic capacity at 39.5°C. Furthermore, gene expression of efferocytic factors (e.g., *axl and mertk*) was also reduced in macrophages. These preliminary data should be confirmed at protein levels and the inhibition of efferocytosis needs to be further explored.

Overall, this suggests an enhancement of the pro-inflammatory profile of macrophages by febrile temperature.

Keywords: fever, efferocytosis, macrophages, heat shock response

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Interaction entre la voie de signalisation STAT1 et le métabolisme du NAD dans les cellules myéloïdes au cours du vieillissement : impact sur les processus inflammatoires et l'athérogénèse

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L'athérosclérose est l'une des principales causes de décès dans le monde. Son incidence augmente en lien avec le vieillissement de la population. Le vieillissement est un facteur de risque de cette pathologie du fait de son association avec un état pro-inflammatoire. Le facteur de transcription STAT1 (Signal Transducer and Activator of Transcription 1) contribue à l'activation des macrophages. Celle-ci intimement liée à leur reprogrammation métabolique. De manière intéressante, des travaux de la littérature font état d'une chute des niveaux intracellulaires de NAD dans les macrophages chez les sujets âgés. La restauration des niveaux intracellulaires de NAD pourrait donc constituer une piste pour limiter l'activation des macrophages au cours du vieillissement.

Des travaux préliminaires de notre laboratoire ont mis en évidence une interaction entre STAT1 et CD38 dans le contexte d'une inflammation septique. CD38 est une ectonuclétotidase consommant du NAD. Il a récemment été mis en évidence qu'elle pourrait contribuer à la chute des niveaux de NAD intratissulaires au cours du vieillissement chez la souris. Nos travaux menés sur des macrophages primaires humains ou murins issus de sujets jeunes ou âgés confirment l'altération de la voie de signalisation STAT1 au cours du vieillissement dans le contexte de l'athérosclérose en lien avec un changement du profil inflammatoire et des niveaux intracellulaires de NAD. Néanmoins, ces modifications ne semblent pas associées à un changement de l'activité de CD38.

Des approches de biologie intégrative basées sur des technologies à haut débit sont actuellement en cours sur des macrophages primaires humains et chez la souris (sujets jeunes et âgés) pour étudier en détail le métabolisme et les voies de signalisation altérées dans les macrophages au cours de l'athérosclérose liée à l'âge. Ces travaux nous permettrons de confirmer le bien-fondé du ciblage de la voie de signalisation STAT1 et du NAD dans ce contexte.

Mots-clés : Macrophages, NAD, STAT1, Athérosclérose, Vieillissement, Immunométabolisme

Impact différentiel de l'élongase ELOVL5 sur le remodelage des acides gras insaturés oméga 6 et oméga 3 au sein des macrophages et des hépatocytes.

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Contexte. Les acides gras polyinsaturés (AGPI) oméga 3 et 6 sont impliqués dans de nombreux processus cellulaires, et pourraient moduler le développement de maladies cardiométaboliques notamment via le contrôle de fonctions cellulaires clés des macrophages. Le but de cette étude est d'élucider le rôle d'ELOVL5, enzyme clé dans la biosynthèse des AGPIs, et de comparer les altérations du profil lipidique induites par le déficit d'ELOVL5 dans les macrophages, les hépatocytes ou le tissu adipeux (TA), afin d'identifier des fonctions d'ELOVL5 spécifiques du type cellulaire considéré.

Méthodes. Des prélèvements de foie et de TA ont été effectués à partir de souris Wild type et Knockout pour ELOVL5, et des macrophages ont été généré in vitro à partir de moelle osseuse de ces souris. Ces prélèvements ont ensuite fait l'objet d'analyses lipidomiques GC- et LC-MS/MS, afin d'établir un profil précis des altérations lipidiques au niveau des acides gras totaux et des différentes classes de phospholipides.

Résultats. Les analyses confirment le rôle central d'ELOVL5 dans la synthèse des AGPIs n-3 et n-6 avec une diminution des AGPIs à longue chaines. Dans le TA et dans le foie, le déficit d'ELOVL5 se traduit par une accumulation des précurseurs n-3 et n-6 en C18 au détriment des produits en aval, tels que l'acide arachidonique et l'acide docosahexaénoïque. Spécifiquement dans les macrophages, le déficit d'ELOVL5 se traduit par une accumulation importante d'acide eicosapentaénoïque.

Conclusion-Perspectives. Nous avons pu mettre en évidence des altérations des profils lipidiques tissus-spécifiques, en lien avec le déficit d'ELOVL5. L'accumulation d'EPA dans les macrophages suggère une action tissu-spécifique d'ELOVL5. Des études cliniques récentes ont mis en évidence un effet protecteur de l'EPA chez les patients à haut risque cardiovasculaire. Les conséquences de l'accumulation d'EPA dans les macrophages, secondaires au déficit en ELOVL5, seront donc intéressantes à explorer dans des modèles expérimentaux d'athérosclérose.

Keywords : maladies cardiométaboliques, ELVOL5, AGPI, lipidomique.

Nutrition 1

Sustainable food, what does matter when experiencing food insecurity? Understanding the social representations of food aid users

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A transition towards more sustainable eating patterns is necessary as our current food system represents a threat for human and environment health. However, in order to be efficient, interventions aiming to improve eating behaviours have to be suited to the target population. In particular, populations with a low socioeconomic status should not be left aside from this transition, especially since diet-related socioeconomic health inequalities are striking in high-income countries. Their specific constraints and representations should therefore be more properly studied. The present study aims to investigate the social representations of sustainable food among users of food aid in France. Twenty-nine individual semi-structured interviews were conducted with users of an urban social grocery store in order to explore food practices as well as motives and beliefs regarding food. In particular, specific aspects of food sustainability such as healthy and environmentally-friendly eating were examined. Findings indicate high heterogeneity among the participants. Social representations of "eating well" were in line with previous results in the French population and mainly associated to nutritional guidelines, naturalness, pleasure and meal structure. However, participants had specific concerns on trust and distance to food systems, and showed positive attitudes about sobriety and food solidarity. Though some participants were satisfied with their diet, they had little control and self-efficacy. Participants had variable knowledge about sustainable food systems but were either indifferent or anxious to environmental issues, resulting in a feeling of powerlessness. These results call for interventions empowering populations with a low socioeconomic status. Further qualitative and quantitative data are needed to understand more precisely the practices and representations of sustainable eating in Europe, including underprivileged consumers.

Keywords: food insecurity, sustainable diet, social representations, healthy eating, socioeconomic status, semi-structured interviews, food banks, health inequalities

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Prognostic role of polyunsaturated fatty acids in the adipose tissue of colorectal cancer patients

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Nutritional intake and dysregulation of fatty acid metabolism play a role in the progression of various tumours. The consumption of different types of fatty acids is difficult to assess accurately by dietary questionnaires. Biomarkers allow objective assessments of intake, storage and bioavailability. We studied the association between risk of death and the polyunsaturated fatty acid (PUFA) composition of abdominal subcutaneous adipose tissue (a good indicator of dietary intake over 2-3 years).
In the multicentre AGARIC study, among 203 colorectal cancer (CRC) patients undergoing curative surgery, subcutaneous adipose tissue was sampled and analysed for PUFA composition. Multivariate Cox proportional hazards models were used.
After a median follow-up of 45 months, 76 patients had died. These patients were more often men (72,4% vs 57,5%, p=0,04), diabetic (32,9% vs 13,4%, p=0,001), older (median: 74,5 vs 66,6 years, p=<0,001) and with high alcohol consumption (47,4% vs 30,7%, p=0,005) compared to survivors. Significant positive associations with all-cause mortality were observed for 20:2 n-6 (hazard ratio$_{tertile3\ vs\ tertile1}$ (HR_{T3vsT1}) = 2.12 [95% confidence interval: 1.01-4.42], p-trend=0.04), 22:4 n-6 (HR_{T3vsT1} = 3.52 [1.51-8.17], p-trend=0.005), and for 22:5 n-6 (HR_{T3vsT1}=3.50 [1.56-7.87], p-trend=0.002). Significant negative associations with all-cause mortality were observed for 18:3 n-6 (HR_{T3vsT1}=0.52 [0.27-0.99], p-trend=0.04) and for the essential fatty acid, α-linolenic acid 18:3 n-3 (HR_{T3vsT1}=0.47 [0.24-0.93], p-trend =0.03). The estimated δ-6-desaturase & elongase 5 enzyme activity (20:3 n-6/18:2 n-6) was found to be positively associated with all-cause mortality (HR_{T3vsT1}=2.25 [1.03-4.90], p-trend=0.04).
In our study, the risk of death in CRC patients was increased in those with higher concentrations of certain n-6 PUFAs and lower concentrations of α-linolenic acid in their subcutaneous adipose tissue. These results reflect both dietary habits and altered fatty acid metabolism. Nevertheless, our exploratory results need to be confirmed in larger studies with further exploration of the mechanisms involved.

Keywords: colorectal cancer, polyunsaturated fatty acids, mortality, adipose tissue, prognosis

Activation of a Sweet Taste Receptor by Oleanane-Type Glycosides from *Wisteria sinensis*

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The phytochemical study of *Wisteria sinensis* (Sims) DC. (Fabaceae), commonly known as the Chinese *Wisteria*, led to the isolation of seven oleanane-type glycosides from an aqueous-ethanolic extract of the roots. After successive purifications by various chromatographic methods, like solid/liquid chromatographic methods, vacuum liquid chromatography (VLC), medium pressure liquid chromatography (MPLC), on normal and reverse phase (RP-18 silica gel), and size exclusion chromatography on Sephadex L, their structures were elucidated by an extensive 600 MHz NMR analysis including 1D and 2D NMR experiments as well as ESI-MS. Among the seven isolated saponins, two have never been reported before: 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranosyl-22-*O*-acetylolean-12-ene-3β,16β,22β,30-tetrol, and 3-*O*-β-D-xylopyranosyl-(1→2)-β-D-glucuronopyranosyl wistariasapogenol A. Moreover, five additional known compounds were obtained, namely 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl-(1→2)-β-D-glucuronopyranosyl wistariasapogenol A (wistariasaponin A), 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl-(1→2)-β-D- glucuronopyranosyl soyasapogenol E (wistariasaponin D), 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranosyl soyasapogenol E (dehydroazukisaponin V), 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl-(1→2)-β-D-glucuronopyranosyl 3β,22β,24-trihydroxyolean-12-ene (astragaloside VIII) et 3-*O*-α-L-rhamnopyranosyl-(1→2)-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranosyl 3β,22β,24-trihydroxyolean-12-ene soyasapogenol B (azukisaponin V). Based on the close structures between the saponins from *W. sinensis*, and the glycyrrhizin from licorice, the stimulation of the sweet testing receptors hTAS1R2/TAS1R3 by these latter was evaluated.

Keywords: *Wisteria sinensis,* Fabaceae*,* Sweet taste receptors, TAS1R2/TAS1R3, 2D-NMR

Olfaction

Role of oral bacterial glycosidases in human flavour perception

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Taste perception is a complex mechanism generated by instructions from gustation and olfaction along with oral and nasal somatosensory inputs. This process includes the integration of different modalities such as aroma, taste, trigeminal sensations, texture and visual. There is relationship between how we perceive taste and oral microbiota diversity. Flavor perception is different among individuals and this dissimilar sensibility could be explained by the oral

microbiota composition. Glycoside-derived aroma compounds are mainly produced by bacterial glycosidase enzymes in the mouth. These bacterial families mainly represented as *Prevotella*, *Streptococcus*, *Veillonella*, *Neisseria*, and *Haemophilus*. Qualitative distinctions among oral bacteria may bring to different metabolizations of aroma compounds and their precursors, thus leading to different retronasal olfactive responses. There are few researches focused on studying the oral microbial communities associated with β-glucosidase activity and the release of volatiles from flavor precursors.

Aim of the present research is to show the ability of mouth bacterial glycosidase to release aroma from food product. For that, specific oral glycosidases are recombinantly produced in *Escherichia coli*, purified, characterized and applied within a model food product to analyse full aroma profile released under enzyme treatment. New insights gained on oral microbial enzymes will be useful to design molecular tools optimized for aroma compound production or enhancing the flavor intensity of specific food products, as well as for certain food manufactures to optimize and modulate food processing.

Keywords: glycosidase, β-glucosidases, flavor, glycoconjugates, aroma, taste, microbiota, food

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Culinary traditions and weight status impact on odor-induced taste enhancement: A cross cultural study between Mexican and French population across different weight status.

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Overconsumption of sweet, salty and fat-rich foods associated with a sedentary lifestyle has been proven to contribute to overweight-obesity. One strategy to reduce those ingredients consists in using odorants that compensate for taste reduction. Odorants are frequently associated with taste and can even produce taste enhancement (odor-induced taste enhancement, OITE). OITE likely depends on the previous experience of odor and taste together. Furthermore, OITE depends on congruence and familiarity between odor and taste, which both depend on culinary traditions.

Our study aimed to compare two different body mass index (BMI) based populations; normal weight (NW) and obese (OB) from two different countries; France (FR) and Mexico (MX), to understand OITE's similarities and differences, through descriptive analysis across cultures and considering body composition.

147 participants performed a ranking task to evaluate the perceived sweetness or saltiness intensities of different culturally familiar (CF) or culturally unfamiliar (CU) water-based solutions with or without aroma.

Our results showed that for sweet samples, vanilla aroma enhanced the sweetness of Hibiscus water (MX-CF & FR-CU) in both French and Mexican NW and OB. Also, vanilla aroma

enhanced the sweetness of apple juice (MX-CU & FR-CF) in both French NW and OB, but only in Mexican OB.

In the salty samples, bacon aroma enhanced the saltiness of green peas (MX-CU & FR-CF) in both French NW and OB, but only in Mexican NW. Coriander aroma enhanced the saltiness of Cacahuazintle corn (MX-CF & FR-CU) only in French OB and Mexican NW. Finally, onion aroma enhanced the saltiness of Cacahuazintle corn only in Mexican NW.

In conclusion, we shed light on the critical impact of previous food experience and food culture on OITE thus demonstrating that this phenomenon depends not only on the congruency between odor and taste but on consumer's history and BMI as well

Keywords: obesity, flavor, cross-cultural, France-Mexico

Odor hedonic perception in humans: characterization of the flexibility

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In human olfaction, hedonic evaluation (pleasant/unpleasant character) is the first response to any olfactory stimulation. It appears that this perception is highly variable and depends on several factors related to the stimulus (physico-chemical properties…), individual characteristics (age, state of satiety…), and the experimental context (frequency of exposure, semantic context…). This variability is difficult to study and remains poorly documented. However, hedonic perception is essential as odors play a key role in many basic behavioral responses (e.g., food intake). The present work focuses especially on stimulus and individual characteristics in order to contribute to the characterization of the flexibility of hedonic odor perception in humans.

Firstly, the relationship between the odorant concentration and the hedonic estimation has been widely studied. However, few studies have examined odor hedonic ratings in relation to individual detection thresholds. Therefore, the aim of this first study was to determine odor detection thresholds and to measure hedonic rating variations from individual thresholds to higher concentrations. The results show the existence of a relationship between individual olfactory sensitivity and hedonic evaluation, which is dependent on the odorant used.

Secondly, as hedonic perception of food odors is considered to be one of the most important dimensions in eating behavior, the question of hedonic variability in this context arises. Thus, the aim of the second study was to compare odor hedonic ratings for different odor categories (meat, vegetables…) in three diets (omnivore, vegetarian, and flexitarian). Data reveal that vegetarians and flexitarians specifically rate meat odors as more unpleasant than omnivores.

Considering these data and the existing literature, it appears that individual characteristics are likely to be the main factor involved in the flexibility of hedonic odor perception. The results are also discussed from a functional point of view, especially in relation to induced behaviors.

Keywords: Olfaction, Odor hedonic, Perception, Variability, Diet, Odor detection threshold

Effect of a relaxing odor on neural entrainment to an isochronous beat in a synchronization-continuation paradigm

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Both music and odors have the ability to modulate arousal level and are commonly used for relaxation or stimulation. Whereas numerous studies have explored the relaxing effects of music or odor when presented alone, only a few tried to combine them in order to evidence a potential cumulative effect. Surprisingly, we recently showed a detrimental effect of multimodal presentation compared to monomodal conditions (Baccarani *et al*., 2023). The relaxing effects of musical (slow-paced classical pieces) or olfactory stimuli (lavender essential oil) disappear when presented simultaneously. Since entrainment of cerebral activity to the music beat is known to be one major factor underlying music-induced relaxation, this study aims to understand this olfactory-musical paradox by asking if a non-temporal stimulus such as an odor could disturb neural entrainment to a beat. To answer this question, a synchronization-continuation paradigm was used in the presence or absence of an odor. Participants (N=20) listened to isochronous pure tone sequences at 3 different Inter-Onset Intervals (225 ms, 600 ms and 1000 ms respectively fast, moderate and slow tempo condition) for 12 seconds (listening phase), then they were asked to tap on a force sensitive resistor on each beat for 20 seconds (synchronization phase) and finally had to continue to tap for another 20 seconds after the sounds had stopped (continuation phase). Meanwhile, a relaxing odor (lavender essential oil) or a blank (odorless oil) were presented to the participants. Electroencephalogram (EEG) was recorded to measure neural entrainment to the beat, using the frequency tagging method. Preliminary results on the amplitude of the resonance peaks showed an interaction effect between phase (listening vs. synchronization) and odor (lavender vs. blank) conditions, suggesting reduced neural entrainment in the presence of lavender during the listening phase. Moreover, this effect seems to be modulated by the tempo of the beat.

Keywords: tapping, neural entrainment, crossmodal, olfaction, EEG

Sport et Motricité

A Cluster Analysis of Multielectrode LFPs in the Motor Cortex During Reach and Grasp

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There is experimental evidence of a low dimensional organization of both the neuronal and muscular components of the neuromuscular system for the reach-and-grasp task. This would provide one way for restricting the number of degrees of freedom in a system which is very high dimensional. Given this, the aim of this study was to investigate if such an organization can be seen in the local field potentials (LFP) recordings of multielectrode arrays in the motor cortex during the same task. The data investigated consisted of LFP recorded from the motor and premotor cortex of two macaque monkeys as they reached to grasp vertically or horizontally oriented target.

We found very robust changes in the correlations of the multielectrode LFP recordings which corresponded to task epochs. Mean LFP correlation decreased significantly during reaching and then increased during grasp. This pattern was very robust and found to be true for both left and right arm reaches irrespective of target orientation. A hierarchical cluster analysis was found to give results that went in the same direction – a decrease in cluster number during reach and an increase during grasp. A sliding window computation of cluster number was then done in order to probe the predictive capacities of these LFP clusters to predict upcoming events. For a very high percentage of trials (94%), the start of grasp was preceded by a global minimum with delays between 20 and 880 ms of the start of grasp. This is promising for future attempts of online prediction of the start of grasp.

Keywords: Local Field Potential, Multielectrode array, Machine Learning, Motor control, Reach-and-Grasp task

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The impact of local vibration condition on wrist corticospinal excitability

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Aims: Local vibrations (LVs) applied over the musculotendinous unit of a target muscle constitutes a powerful stimulus to activate the muscle spindle primary (Ia) afferents that project at both spinal and cortical levels. Depending on the vibration condition used, LVs can induce a tonic vibration reflex (TVR) of the vibrated muscle or an illusion of movement due to the integration of afferent feedback by the brain. No study to date has measured the influence of vibration condition on changes in corticospinal excitability for vibrated and non-vibrated muscle.

Methods: LVs were applied to the Flexor Carpi Radialis (FCR) muscle (Duration: 6', Frequency: 80Hz). The 12 subjects performed one session with *TVR* and one with *Illusion*. For each session, Motor-Evoked Potentials (MEPs) of the FCR and Extensor Carpi Radialis (ECR) muscle were measured before LVs (PRE) and at 0' (P0), 10' (P10), 20' (P20) and 30' (P30) after vibrations were stopped. All measurements were performed at rest.

Results: In the *Illusion* session, the MEPs responses decrease for the FCR muscle at P0 (p = .014) while responses increase for the ECR muscle at P0 and P10 (p < .012). In the *TVR* session, MEPs increase significantly for both FCR and ECR muscle at P20 (p < .041). Compared to PRE, the FCR MEPs responses in the *TVR* session were significantly higher than in the *Illusion* session (p = .005). Regarding the ECR muscle, MEPs were higher at P0 in the *Illusion* session compared to the *TVR* session (p = .003).

Conclusions: 6' of LVs do not induce prolonged modulations of corticospinal excitability. The presence of illusion combined with the absence of TVR reduces the increase in corticospinal excitability for the FCR muscle and increases that of the ECR muscle compared to the condition performed with the presence of the vibratory reflex.

Keywords: Tendon vibration, Corticospinal excitability, Tonic Vibration Reflexes, Illusions

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Interactions between emotions, sleep and the autonomic nervous system in high-level female cyclists: effects of hypoxia

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Introduction: "Living High-Training Low and High" (LHTLH) is an altitude training method used by high-level athletes for its positive effect on performance [1]. However, as any hypoxic method, it may alter sleep [2] and heart rate variability (HRV) [3]. Moreover, intense emotions impair sleep in normoxia [4] even more in high-level athletes [5]. Therefore, the aim of this

study was to determine the possible relationships between sleep, HRV and feelings during training (FDT) in high-level cyclists before or after 14 days of LHTLH.

Method: Ten high-level female track cyclists (age: 17,3 ± 1,2 year; VO$_2$ max: 54 ± 6.9 ml.min.kg-1) were invited for 5 training days in normoxia followed by 14 days of LHTLH in normobaric hypoxia. During LHTLH, they spent ~14 h per day in an altitude simulated 2800m and performed a normal training program between 150 to 2800m. Before and during LHTLH, morning HRV, sleep recording (Dreem® EEG headband), sleep disturbance (Groningen) and night peripheral oxygen saturation were monitored. From 5 days before and during LHTLH, the participants were asked to record their FDT [6][7][8]. A Pearson correlation coefficient was used to determine possible relationships between sleep, HRV and FDT. Statistical significance was set at p < 0.005.

Results: In normoxia, no significant relationship was observed between sleep, HRV and FDT. However, during the acclimatization phase, we observed i) a negative sleep influence on FDT (significant correlation between REM and preferred arousal); ii) a negative and a positive influence of FDT on HRV or sleep with a significant correlation between goal reaching in training and HRV (RMSSD) and between mental toughness and sleep efficiency.

Conclusion: Overall, our results suggest that LHTLH exacerbates emotions particularly during the first days in hypoxia. These finding are of practical interest for coaches to optimize athletes' training and recovery in hypoxic environment.

1. Brocherie *et al.* (2015) 2. Roach (2013) 3. Schmitt *et al.* (2018) 4. Vandekerckhove & Wang (2017) 5. Fullagar *et al.* (2014) 6. Svebak & Murgatroyd (1995) 7. Clarck & Malecki (2019) 8. Gucciardi *et al.* (2014)

Keywords: Hypoxia, Sleep, Emotions, Cycling, Training

An Upper Limbs Plyometric Performance Comparison between Experienced and Non-Experienced Athletes.

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Although far less studied than in lower limb, upper limbs explosive movements are important in many sport activities. Here, we aimed at comparing the ability to perform the classic exercise of push-up in an explosive way, of Street Workout (SW) athletes and athletes from various sports, by adapting classical tests usually performed on lower limb. 18 participants took part to this study; 9 of them practiced Street Workout for a long time, and 9 others practiced various team and individual sports. As it is for lower limb jumps, they performed 3 different forms of the push-up, one was done only in a concentric way (equivalent to squat jump), the 2 others were done in plyometric way (counter movement jump and drop jump), and they did a fatigue-inducing set. Jump heights, myoelectrical activities (through electromyography) and muscle architecture (through ultra-sonography) of pectoralis major, anterior deltoid and triceps brachii were measured. Results showed no difference in jump height between types of push-ups, but SW athletes performed better (approximately 60% batter) than control athletes in all performances. There was no major difference of EMG between groups, but on average, SW

athletes had a greater pectoralis major and anterior deltoid thickness. The results suggest that classical plyometric performances studied in the lower limb are not observed in the upper limb in the same way. The greater capacity in doing explosive push-ups in SW could be attributed to a greater upper body muscles hypertrophy, as well as a more efficient execution of the movement.

Keywords: Street Workout, Push-up, Plyometrics, Concentric, Electromyography, Echography.

Les compétences techniques et tactiques dictées par les demandes du jeu ou par les contraintes du joueur ?

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La réussite des joueurs de football repose sur des combinaisons variées d'habilités motrices, des compétences techniques (CT) / tactiques (CTa) et des traits psychologiques [1]. Les variations des compétences entre les joueurs sont expliquées par la fatigue, le score pendant un match ou bien le niveau de pratique [2]. Les réflexes primitifs (RP) non intégrés pourraient être un facteur supplémentaire de variations des CT et CTa. Ils sont actifs durant la première année de vie, puis intégrés lors du passage de la motricité involontaire à une motricité volontaire [3]. Non intégrés (actifs), ils peuvent altérer des compétences motrices [4]. L'objectif de cette étude était d'observer les corrélations entre le profile réflexe primitif (PRP) des joueurs de football et le taux de réussite des CT et CTa. Les tests des RP ont été effectués en suivant la méthodologie de Sally Goddard-Blythe [5] et les recherches de Capute et al. [6]. Ils ont été classés en cinq catégories allant de nul à maximale selon l'activité des réflexes. Les matchs de l'académie (U17 ; U19 ; national 3) ont été analysés avec 18 joueurs avec un PRP nul, 21 avec un PR faible, 15 avec un PRP moyen et trois avec un PRP sévère. Les CTa ont été catégorisées par les passes en fonction de la zone où elles ont été réalisées et l'équipe adverse. Les CT ont été catégorisées par les actions techniques ciblées. Les résultats montrent que le taux de réussite des CTa est diminué lorsque le PRP est faible ou supérieur dans les ZF et ZD. Cependant, le taux de réussite des CT ne diminue pas entre les joueurs ayant un PRP nul et faible. Seuls les PRP moyens ou supérieurs diminuent significativement le taux de réussite. Il apparaît essentiel d'étudier les liens entre ces profil réflexes et les CT et CTa afin d'améliorer le développement individuel et collectif.

Mot clés : contrôle moteur, réflexes, football, compétence technique, compétence tactique

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Biologie animale

Spatial response of a specialist opportunist to variations in the abundance of its main prey: the importance of within-territory movements

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Animal populations can exhibit large inter-annual variations in abundance, with predation being one of the main drivers behind these dynamics. Predators specialising on cyclic preys face alternations between periods of food abundance and shortage, with significant consequences on their biology and ecology at both short and large spatio-temporal scales. Specifically, some species adjust their movements and foraging behaviour in times of food scarcity. According to the Optimal Foraging theory, predators should increase their territory size when preys are rare in order to fulfil their nutritional needs. Yet, this spatial response is not consistently observed or not as extensive as predicted. This could be because predators can also adjust their movements at a small spatial scale, i.e. changing their spatial behaviour within a stable territory. However, how opportunistic specialist predators use and move within their territory in years of prey abundance versus scarcity is currently unknown. Using GPS data collected on 22 Arctic foxes (*Vulpes lagopus*) between 2017-2021 under varying lemming (*Lemmus spp.*) densities in Nort-East Greenland, we describe these spatial responses of foxes to changes in their main prey availability. Dynamic Brownian Bridge Movement Models (dBBMM) were fitted to calculate the utilisation distributions of these foxes and to compare their respective sizes under different lemming densities. In this presentation, we will present the first results from these analyses. Our study helps understanding how specialist predators adjust their movements to changes in the availability of their main prey. In the fast-warming Arctic, this knowledge could help predicting the consequences of the ongoing fading of the rodent cycles.

Keywords: *Vulpes lagopus,* Specialist, Predator-prey cycles, Optimal Foraging theory, Spatial behaviour, Telemetry, Arctic.

Efficiency of immune priming by oral route or septic wounding in *Tenebrio molitor*

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Since the discovery of immune priming in arthropods, many studies (mainly concerning insects) have focused on the ability of these animals to resist infection following a non-lethal contact with the same pathogen as that involved in the infection. The demonstration of this phenomenon often relies on an immunisation procedure of individuals by septic wounding; however, the natural route of infection may also include an oral contamination route by pathogens. Furthermore, as juvenile insects tend to invest more in immunity than adults due to their much higher residual reproductive value, the effectiveness of immune priming should be age-dependent. In addition, an adult that has already reproduced (and therefore has a low residual reproductive value) should invest less in priming compared to a virgin adult of the same age.

The experiments we conducted on the mealworm beetle (*Tenebrio molitor*) aimed to compare the efficiency of the immune priming response considering two routes of contamination in larvae: wounding with dead bacteria, or orally with food contaminated with either live or dead bacteria. We also compared the efficiency of the immune priming response by septic wounding in larvae, virgin adults and reproducing adults. We observed that consumption of contaminated food only protects larvae for a very short period, and that the effectiveness of this protection varies according to the pathogen involved. Priming by wounding is effective in protecting adults from subsequent reinfection, but less effective in larvae. However, contrary to predictions, we did not find any effect of the reproductive status of adults. Moreover, larvae showed a much stronger constitutive resistance than adults, and were therefore better protected from injuries. These results seem to confirm that the effectiveness of immune priming depends on the developmental stage at which the first infection occurs, but also on the route of infection.

Keywords: cost of reproduction, immune priming by septic wounding, oral immune priming, developmental stage, *Tenebrio molitor*

North African Houbara bustard reproductive tract anatomy and histology in relation to breeding season

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The North African Houbara bustard (*Chlamydotis undulata*) is a seasonal breeder (spring) endangered bird and part of a large captive breeding program. Knowledge in reproductive physiology in wild species is mandatory especially in captive breeding context. The aim of this study is to describe the anatomy and histology of males and females and compare it during and out of breeding season (BS).

Reproductive tract of males and females were collected during (21 males; 14 females) and out of the BS (4 males; 2 females). Pictures and measurements of testis and oviduct were taken, and testis color was graded from 1 (black) to 6 (white). Organs were fixed and later processed for histology, scanning and transmission electron microscopy. Testis and oviduct size and seminiferous tubules (ST) diameter were compared during and out of the BS.

Overall anatomy and histology of male and female reproductive tract were similar to what is known for others avian species. A regression of testis (BS: mean length right/left =15.91 ± 2.95 mm / 16.65 ± 3.22 mm; out of BS: mean length right/left = 13.66 ± 4.09 mm), oviduct size (BS: mean length = 420.48 ± 70.52 mm; out of BS: 64,66 and 87.96 mm) and ST diameter (BS: mean diameter = 131.66 ± 23.45 µm; out of BS: mean diameter = 97.86 ± 13.87 µm) out the BS was recorded. Sperm storage structures were located inside the oviduct. Melanin granules were observed in the interstitial space of the seminiferous epithelium explaining the testis pigmentation. Melanin was also found in the ovaries and the uterus.

This work gave a first anatomical and histological description of male and female reproductive tract in bustards. Further investigation on melanin function in the testis will be of interest.

Keywords: Houbara bustard, seasonal reproduction, anatomy, histology, melanin, testis, oviduct

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Do sheep differentiate emotional cues conveyed in human body odour?

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Humans are significant sources of stimuli for domestic animals, especially by visual/vocal cues. Evidence that horses, dogs, and cattle do react to cues carried in human body odors is recent. Sheep perception of human visual/vocal cues has been previously reported, their reactivity to human body odor is yet to be demonstrated. We assessed whether sheep detect human odors and differentiate stressed vs. non-stressed individuals.

Axillary secretions were sampled from 34 students (age: 23 y, 31 ♀) before an oral examination vs. a standard class, conveying stress (SO) and non-stress (nSO) odors, respectively. These samples were frozen until testing that consisted in a habituation-dishabituation procedure (n=29 sheep, age: 7-8 m, 14 ♀). An odour n°1 (habituation stimulus) was presented one minute four times at animal, then odour n°2 (dishabituation stimulus) was presented one minute once time. Sheep were either habituated with nSO and dishabituated with SO or the reverse (ability to detect and discriminate human nSO/SO). Tests were video recorded to blindly code behaviors indicating attraction, aversion or indifference (i.e. approach/withdrawal, locomotor spatiality, sniffing, ingestion, vocalization).

Ewes (8.4; p=0.038) and rams (8.6; p=0.037) displayed more avoidance/stress (frequency of ears pointing backwards) when facing the dishabituation odour, but again regardless of its assumed cueing of human stress. While sheep were expected to express specific different behaviors when exposed to nSO and SO, these results ultimately suggest that sheep avoid the odors of unfamiliar humans (although the discrimination of familiar/unfamiliar humans remains

to be tested). Overall, further studies are required to unveil ovine olfactory performance toward humans along dimensions of familiarity and emotionality, and to provide a better understanding of subtle aspects of the human-animal relationship.

Keywords: Olfaction, Human-animal relationship, Sheep, Stress

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Maladies

The glucagon-like peptide 1: a role in the intestinal barrier function?

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Background and aims: Bowel infarction, also named mesenteric ischemia, is an absolute medical emergency. During this ischemia, the intestine is no longer irrigated, the intestinal permeability is highly disturbed, allowing the passage of lipopolysaccharides (LPS) into the bloodstream. These LPS are able to increase rapidly the secretion of an incretin, the GLP-1, in mice or humans[1,2]. Thus, this GLP-1 could be a biomarker, allowing an early diagnosis of this pathology, and therefore a rapid medical care. In this project, we study the role of GLP-1 in the intestinal barrier function.

Materials and methods: Gut permeability was investigated in vivo or ex vivo in mice pretreated with GLP-1 agonists and challenged with an inflammatory stimulus.

Results: Pretreated mice with GLP-1 agonists, showed an increase in the gut permeability, measured in vivo or ex vivo, after an inflammatory stimulus, but does not seem to be altered without inflammation. The ARNm expression of occludin, a tight junction protein, and many pro-inflammatory cytokines, is respectively reduced and increased. Also, the expression of the glucagon, the gene that codes for GLP-1, and the secretion of GLP-1 are reduced.

Conclusion: In order to understand this contradiction with the anti-inflammatory properties of GLP-1[3], we are looking currently to understand the role of GLP-2, which is co-expressed and co-secreted with the GLP-1, and has demonstrated trophic effects on the intestine[4]. We are also studying the effect of these agonists on the barrier function after chronic treatment. Finally, we will study the role of endogenous GLP-1 in this context, using a genetic approach (Cre/lox mice), invalidated for the glucagon gene, and a pharmacological approach using an antagonist for the GLP-1 receptor.

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[4] Kaori Austin, Melanie A Markovic, et Patricia L Brubaker, « Current and potential therapeutic targets of glucagon-like peptide-2 », *Gastrointestinal • Endocrine and metabolic diseases* 31 (1 décembre 2016): 13-18.

Keywords: Intestinal ischemia, gut, glucagon-like peptide 1, lipopolysaccharides, inflammation, gut permeability, barrier function

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Interaction between geological and ecological factors in the determinism of cholera epidemics along the African Rift: case of lakes Kivu and Tanganyika

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Cholera is a highly pathogenic bacillus that has been endemically affecting African Rift populations since the 1970s. Despite significant advances in the role of volcano-tectonic activity and lakes in the dynamics of cholera epidemics, the mechanisms that allow *Vibrio cholerae* 01 to sustain itself during inter-epidemic periods and to spread along the hydrological continuum of the Great Lakes Kivu and Tanganyika remain unclear.

The objective of this study is to investigate the geological (including geomorphological, hydrogeological, and volcano-tectonic activity) and ecological causalities of the temporal dynamics and spatial distribution of cholera outbreaks along Lakes Kivu and Tanganyika.

The study will first synthesize existing data on the chemistry of the large lakes (temperature and salinity/conductivity, the two key parameters for the survival of the bacillus), the planktonic communities (phytoplankton and zooplankton, host organisms of the bacillus in its aquatic phase) and the cholera cases, on both sides of the lake.

In parallel, a physico-chemical, planktonological and cholera monitoring is planned. We plan to conduct transects to measure temperature, conductivity, planktonic biomass and bacilli concentration of surface waters from west to east during outbreaks and in the lull phase. This will be done on Lake Tanganyika (selected according to its accessibility), from Uvira (in DRC, west side of the lake) to Bujumbura (in Burundi, east side of the lake).

The link between the number of cholera cases and environmental variables will then be investigated, explicitly considering the upstream-downstream continuum and the eastern and western shores of the lakes.

Keywords: Cholera, Health ecology, Hydrogeology, Volcano-tectonism, Lake Kivu, Lake Tanganyik

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Omega-3 fatty acid/Resveratrol disrupt VEGF-A secretion in an *in vitro* model of Age-related Macular Degeneration by promoting VEGFR2/caveolin-1 interaction in lipid rafts

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Age-related macular degeneration (AMD) is an eye disease that impairs vision in the centrer of the visual fields due to macular damage. Among the different forms of the disease, neovascular AMD is the most severe and is the only one that is characterized by an abnormal formation of blood vessels due to an excessive synthesis of vascular endothelial growth factor A (VEGF-A) by retinal pigment epithelium (RPE) cells among others. Although intravitreal injections of VEGF inhibitors are now the standard treatment for neovascular AMD, many patients do not respond adequately to this therapy. In order to identify new therapeutic candidates, we explored whether supplementation with Resvega®, a nutraceutical formulation composed of omega-3 fatty acids and resveratrol, a polyphenol in grapes, is able to counteract VEGF-A secretion, in context of AMD. We highlighted that Resvega® significantly reduces VEGF-A secretion in human RPE cells. This effect is related to the relocalization of VEGF receptor 2 (VEGF-R2) in lipid rafts (LR), which promotes its interaction with caveolin-1 (CAV-1). The depletion of LR by a cholesterol-chelating agent blocked the VEGFR2/CAV-1 interaction and Resvega®-mediated impaired VEGF production. These *in vitro* findings pave the way for further preclinical and clinical investigations on the health benefits of omega-3 fatty acids and polyphenols.

Keywords: AMD; angiogenesis; omega-3 fatty acids; resveratrol; lipid raft

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Implicit visual statistical learning during aging

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This study investigated the effects of aging on implicit visual statistical learning using behavioral and eye-tracking measures. Three groups of participants were included: 21 young adults (Mean age: 19.73), 20 young-old adults (Mean age: 67.22), and 17 old-old adults (Mean age: 79.34). The same implicit visual statistical learning paradigm as Fiser and Aslin (2001) was used to compare implicit learning performance across age groups. Participants were presented with 12 arbitrary shapes, organized into 6 base pairs, which were arranged in different spatial relationships and orientations (horizontal, vertical, and oblique). On each trial, 3 different pairs were presented in a 3×3 grid. The base pairs were not explicitly disclosed to the participants, who were instructed to attentively observe 144 grids presented sequentially on a computer screen for 7 minutes. This exposure phase was followed by a test phase, in which participants performed a two-alternative forced choice task. They had to choose the most familiar pair compared to what they had seen during the exposure phase, out of 48 trials, consisting of the presentation of one of the 6 base pairs and a nonbase pair.

Behavioral results revealed that the learning performance of the young and young-old adults was significantly above chance, whereas the learning performance of the old-old adults did not differ from chance. These results indicated that implicit visual statistical learning was absent in the old-old group and suggested an impairment of implicit visual statistical learning with increasing age. Ongoing analyses

of eye movements and performance on psychological tests (visuospatial memory and time processing) should provide further insight into the underlying mechanisms of these age-related changes in implicit visual statistical learning.

Keywords: Implicit visual statistical learning, Aging, Eye tracking

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Access to optimal treatment among AML patients is affected by non-biological factors: analysis using machine learning algorithm

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AML patients not admitted to specialised haematology unit (SHU) during their care pathway have less access to curative treatment. Our aim is to determine whether access to optimal curative treatment is affected by non-biological factors.

We included 1,033 patients from 3 French departments. We assumed that patients managed in academic hospitals by haematologists within 5 days of their diagnosis (n=297) received the best treatment (gold-standard patient). Patients were categorised by their treatment modality ("curative treatment" if intensive chemotherapy and "non-curative treatment" if other). Firstly, we used 80% (n=238) of the gold-standard patients to train a Gradian Boosting Machine (GBM) algorithm in order to learn how clinical and biological characteristics are associated with receiving each treatment modality. The model was validated on the remaining 20% (n=59) of gold-standard patients. Next, the GBM was used to predict the treatment modality for all patients given their clinical-biological characteristics and contrasted it with the actual treatment. Using a multivariable logistic regression, we then examined how non-optimal treatment (discrepancy between predicted curative and observed non-curative treatment) was associated with any non-biological factors (sex, diagnostic department, EDI quintile, city of residence, distance between city of residence and academic hospital and the corresponded travel time).

We repeated the analyses for 1,000 bootstrap samples to account for uncertainty in the predicted treatment outcome. Patients with predicted non-curative treatment were not included in this analysis as uninformative (n=471).

Access to "curative treatment" was 84.8% (252/297) for gold-standard patients compared to 33.5% (247/736) for the others patients. The three most influential factors related to treatment modality among gold-standard patients were age (68.3% influence), secondary aspect of AML/MDS (15.8%) and presence of the AML-others subtypes (5.4%). In total, we identified n=460 (44.5%) and n=102 (9.9%) patients in respectively, optimal and non-optimal treatments. Living in Basse-Normandie (0.65 times; 95%CI [0.5,0.8]) and living in a municipality more than 10 kms from an academic hospital were strongly associated with a non-optimal treatment. There are geographical disparities in access to optimal treatment. This could be related to the medical desert situation, or to disparities in medical organisation.

Keywords: Acute Myeloid Leukaemia, Machine Learning algorithm, Optimal curative treatment, Non-biological factors

Communications orales – Session 6 : 13h30-14h50

Nutrition 2

Impact of parental feeding practices on eating in the absence of hunger in toddlers: protocol presentation and preliminary results

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Infants have an innate ability to self-regulate their food intake. As they grow older, they are more likely to be influenced by external factors related to their food environment, such as parental controlling feeding practices or food availability. Hence, the emergence of "eating in the absence of hunger" (EAH) behaviours has recently been demonstrated as early as in toddlerhood with links to parental controlling practices. However, the influence of parental use of food as a reward (FaR) and use of food to regulate emotions (FRE) on EAH remains poorly studied at this early age.

The primary objective of this study is to evaluate the association between toddler EAH and parental FaR and FRE. Secondary objectives include assessing (1) general toddler temperament as a potential moderator of this relationship, (2) associations between food accessibility and toddler EAH. Toddler EAH is expected to be positively correlated with parental FaR and FRE and food accessibility.

This cross-sectional observational study involves 64 parent-toddler dyads (child age 24-36 mo) living around Dijon, France. During a laboratory session, the child eats an *ad libitum* meal until satiation. Five minutes after the meal, together with a manual activity, the child is offered eight finger foods of different tastes and energy densities. The food choices and intake (kcal) are recorded as an experimental measure of EAH. The other outcomes are reported by parents in a questionnaire. Regression analyses will be run to assess the associations with EAH.

This study is expected to be launched in April 2023. Preliminary results will be presented.

This study will help to identify optimal feeding practices and habits to promote the development of healthy eating behaviours from an early age.

Keywords: Eating in the absence of hunger, Appetite control, Regulation of food intake, Early childhood, Parental feeding practices, Food accessibility, General temperament.

Evaluation of a short sensory education program at school canteen on liking and children's eating behavior of plant-based food: a quasi-experimental study

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Dietary transition towards more plant-based foods is needed to improve nutritional quality and reduce carbon footprint. Since 2018, the French school meal guidelines imposed vegetarian meals once a week yet children may not like them. A short sensory education program (SSEP) targeting plant-based foods was developed in collaboration with school canteen staff. This study evaluated the effects of this program on food liking and on children's eating behaviour.

Two school canteens were selected to co-create and implement a SSEP (intervention group) and two similar school canteens were selected as control group. Two target recipes were selected (green cabbage and red beans) and two two-week sequential SSEP were carried out at school canteens: SSEP1 on cabbages and SSEP2 on pulses. The outcome measures were food liking, knowledge about cabbages and pulses, willingness to taste and identification of green cabbage and red beans, attitudes towards food and food neophobia. Liking data were collected through connected feedback devices installed in the canteens. Other outcome measures were collected by asking children to self-complete paper-based questionnaires at school during lunch break. Independent T-tests were used to test the effect of the interventions on children's liking between pre and post-SSEP, in control and intervention groups separately. Linear mixed models were used to investigate whether changes in measured outcomes pre and post-SSEP differed significantly between the intervention and control groups.

After SSEP1, the knowledge score on cabbages increased significantly but not liking nor willingness to taste and identification of green cabbage. After SSEP2, the knowledge score on pulses, willingness to taste and identification of red beans increased, but not liking. A significant time effect was observed for the hedonic and food neophobia scores.

The evaluation of the SSEP showed encouraging effects in increasing the acceptance of one of the two target recipes. The implementation of this type of short program during lunch time could allow to develop a shared food culture in both school catering staff and children around healthy and sustainable food consumption.

Keywords: Children, School canteen, Sensory education, Eating behaviour, Sustainability

Evolution dynamique des populations microbiennes thermophiles apportées par les levains lactiques au cours de l'affinage du Comté

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Le microbiote des fromages traditionnels au lait cru tel que le Comté présente une diversité résultant d'interactions entre les populations microbiennes endogènes du lait et les populations microbiennes apportées au cours du procédé de fabrication, cas des levains lactiques. En technologie fromagère Comté, des levains artisanaux préparés à température ambiante par culture naturelle sur lactosérum cru issu de la fabrication de la veille et appelés levains ambiants connaissent un regain d'intérêt. Les principales populations microbiennes apportées par ces levains sont des bactéries lactiques thermophiles.

Les travaux présentés ont pour objectif de suivre la dynamique des populations thermophiles apportées par les levains lactiques dans les Comtés au cours de leur affinage.

Au total 24 Comtés ont été fabriqués, dans deux fromageries, sur trois jours consécutifs, en été et en hiver, soit avec un levain ambiant soit avec un levain témoin. Le suivi des populations thermophiles a été réalisé par une double approche : une approche culture-dépendante pour quantifier les populations cultivables sur milieux de culture et une approche PCR (qPCR et viabilité-qPCR) pour quantifier les populations viables.

Les dynamiques microbiennes obtenues par dénombrements sur milieux indiquent une diminution importante des populations thermophiles cultivables au cours de l'affinage (de 8 à 2 log ufc/g pour *Streptococcus thermophilus* ; de 9 à 3 log ufc/g pour les lactobacilles thermophiles). Le suivi de ces mêmes populations par qPCR montre cependant une diminution bien moins importante. La combinaison de ces résultats avec ceux obtenus par viabilité-qPCR, a permis de mettre en évidence différents états physiologiques (viables cultivables, viables non cultivables et non viables) au sein des populations thermophiles et de suivre leur évolution à différents stades d'affinage des Comtés.

Mots clés : Comté cheese, thermophilic lactic acid bacteria, bacterial viability, natural whey starter

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Which behavioural determinants predict a healthier or more environmentally friendly diet in French students?

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Students are building their adult dietary behaviours and the period of academic study is thus sensitive to shape sustainable eating habits. This study aimed to identify the behavioural determinants that could be levers or barriers to adopt healthier and more environmentally friendly diets.

A representative sample of French students (N=582) retrospectively reported their food consumption over the past month using an online 125-item food frequency questionnaire. We evaluated the nutritional quality (adherence to French national recommendations, sPNNS-GS2 score [-17;11.5]) and the dietary greenhouse gas emissions (GHGE/2000 kcal) of students' diets. Behavioural determinants were selected based on a literature review and classified thanks to the COM-B framework (capacity: nutritional and environmental knowledge, cooking skills, opportunity: availability of cooking equipment, motivation: perception of cooking and food choice motives). Two linear models were run to identify the predictors of nutritional quality

and GHGE of the diets, adjusted for socioeconomic characteristics (age, gender, scholarship status and living condition).

Higher cooking skills (β=0.38, p=0.010), health motives (β=0.91, p<0.001) but less cooking equipment (β=-0.08, p=0.032) were associated with higher nutritional quality. Higher knowledge about the environmental impact of food was associated with lower GHGE (β=-0.07, p=0.002) but being motivated by health and weight control was associated with higher GHGE (β=0.26, p= 0.020 and β=0.39, p<0.001).

These results show that enhanced cooking skills and environmental knowledge could be levers for the adoption of healthy and environmentally friendly diets respectively. However, health motives had conflicting effects on nutritional quality and environmental impact and appears a lever or a barrier.

Keywords: Diet, nutritional quality, environmental impact, students.

Cancérologie 2

Rapport bénéfice-risque et gestion de l'incertitude dans un contexte d'innovation thérapeutique en cancérologie digestive : perception, positionnement et décision des patients et des médecins

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L'innovation thérapeutique est fortement influencée par l'évolution technologique. C'est cette évolution qui a permis l'émergence de médecine dite "de précision" qui repose actuellement sur deux grands types de traitement : les thérapies ciblées et l'immunothérapie. Ces traitements ont changé le paradigme du traitement du cancer, le faisant sortir d'une approche des cancers "par organes" pour évoluer vers une classification "moléculaire", permettant d'aboutir à une personnalisation de plus en plus complexe de la prise en charge des cancers, du diagnostic à la mise en place du traitement. Si ces traitements se différencient des traitements conventionnels par leurs mécanismes d'action, ils sont également associés à des modalités de prescription différentes et des modalités d'évaluation spécifiques avec la mise en œuvre d'essais d'un nouveau type : "basket" et "umbrella".

Comme pour n'importe quel autre traitement la décision de prescrire une thérapie ciblée ou une immunothérapie doit être réalisée au regard de leur rapport bénéfice-risque et de l'incertitude qui y est associée. Cette incertitude varie selon le niveau d'information disponible, accessible et maîtrisé. Elle est aussi fonction de caractéristiques plus personnelles du patient (caractéristiques socio-économiques, aversion au risque) et du médecin (formation, expérience professionnelle, vécu personnel, relation au patient). Cette incertitude peut rendre difficile la relation patient-médecin et la prise de décision.

Ce changement de paradigme et la spécificité de ces traitements nécessite de se questionner sur le rapport des médecins et des patients à ces thérapies nouvelles et à l'incertitude du rapport bénéfice-risque qui en découle, ainsi que sur l'impact de cette incertitude sur la relation

médecin-patient dans ce contexte. Peu d'études semblent s'être intéressées à cette question. C'est ce qui justifie l'intérêt de conduire une étude qualitative reposant sur des entretiens semi-directifs auprès d'oncologues et de patients atteints de cancers recevant ces traitements.

<u>Mots-clés :</u> cancérologie, innovation, rapport bénéfice-risque, incertitude

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Développement d'une nouvelle stratégie thérapeutique des hémopathies malignes : les immunoliposomes contenant la Valrubicine

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Malgré les succès des thérapies actuelles, entre 20 et 30 % des enfants qui développent une Leucémie Aiguë Lymphoblastique (LAL) vont connaître une rechute thérapeutique. C'est pourquoi la découverte et la mise en place de nouvelles stratégies thérapeutiques est encore nécessaire. Depuis leur découverte, les liposomes sont considérés comme un outil de transport prometteur des prodrogues. Nous avons donc créé des immunoliposomes contenant la Valrubicine (ILs-Val), un analogue lipophile de la Daunorubicine actuellement utilisé pour la thérapie des LALs et possédant à leur surface un anticorps dirigé contre les biomarqueurs spécifiques des leucémies aiguës.

Nous avons généré des modèles de souris xénogreffées avec des cellules leucémiques humaines. Lorsque les ILs-Val, couplés aux anticorps αCD19, αCD7 ou αCD33 sont respectivement injectés *in vivo* pour le traitement des souris qui développent des leucémies aiguës lymphoblastiques à cellules B, à cellules T ou une leucémie aiguë myéloïde, une chute de la viabilité de plus de 90% de cellules cancéreuses est observée. Seulement 5 nmol de Valrubicine encapsulée dans les ILs injectés aux souris ont permis d'induire cette diminution du nombre des cellules leucémiques.

De plus, les Val-ILs affectent spécifiquement les cellules leucémiques et ne ciblent pas les cellules souches hématopoïétiques saines. Ils représentent donc un outil intéressant pour éliminer les cellules leucémiques *ex vivo*, avant une greffe autologue associée à un risque de contamination du greffon par des cellules cancéreuses.

Dans l'ensemble, nos résultats démontrent que la vectorisation de la Valrubicine ainsi que le ciblage spécifique des cellules cancéreuses permettent de réduire la quantité de drogue utilisée sans pour autant réduire l'efficacité du traitement. Les ILs-Val peuvent donc être utilisés comme nouvelles stratégies pour le traitement des leucémies aiguës.

<u>Mots-clés:</u> immunoliposomes, leucémies, cancer

Control of Chimeric Antigen Receptor T-cell by Tyrosine Kinase Inhibitors

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Chimeric Antigen Receptor (CAR) T-cell therapy consists of repurposing T-cells' ability to kill cells against tumoral cells. Expression of a CAR allows T-cells to recognize and kill cells expressing the antigen of the CAR. A CAR T-cell targeting CD123 could be a therapeutic solution for Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) and Acute Myeloid Leukemia (AML): two leukemias that have strong CD123 expression on leukemic cells. Despite CD123 high expression on leukemic cells, it should be noticed that a low expression on endothelial cells, monocytes and a subpopulations of hematopoietic stem cells, may result in an on-target/off-tumor effect. Moreover, CD123 expression is increased on endothelial cells by the pro-inflammatory environment induced by CAR T-cells' activation. Dasatinib and ponatinib, two tyrosine kinase inhibitors (TKI), could help to control these toxicities by reversibly inhibiting CAR T-cells.

In this study, we showed that dasatinib and ponatinib, with sub-micromolar concentrations (100 to 250nM), can modulate CD123 CAR T-cell functionality, successfully inhibiting activation (CD25/CD69), degranulation (CD107a) and cytokine secretion (TNF-α and IFN-γ) after contact with leukemia cell lines. These two TKI inhibit the cytotoxic function of CD123 CAR T-cells on leukemia cells and this inhibition is lifted upon withdrawal of the molecules.

Together, these preliminary data show that the use of pharmacological molecules such as dasatinib or ponatinib could inhibit reversibly the functionality of CAR T-cells once deleterious effects appear. After showing on an endothelial cell model that CD123 expression is raised by TNF-α and IFN-γ, we will confirm that a low concentration of these two TKI allow a reduction of the pro-inflammatory environment and of the toxicity on endothelial cells, without decreasing the anti-tumoral effect. Finally, these two TKI will be evaluated *in vivo* in mouse models to confirm their pharmacological potential.

Keywords: Immunotherapy, CAR T-cell, TKI, CD123, Leukemia,

Role of immune cells in the anti-tumor response following an immune checkpoint and anti-angiogenic combination therapy

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Immune checkpoint inhibitors have powerful and lasting effects but only on a small percentage of patients. This can be explained by a lack of immune cell in the tumours. In order to increase immune cells in the tumor, it is possible to target angiogenesis. Angiogenesis induce the formation of blood vessels to transport nutrients and oxygen to expanding tumors. However, within tumors, blood vessels are abnormal and disrupts the migration of immune cells into the tumor. This combination has been the subject of clinical studies in solid cancers and is now

approved by the FDA. However, the consequences of this combination on the immune system are still poorly known.

By combining these treatments, we have shown that anti-tumor responses are improved in a mouse model of colorectal cancer. This is explained by the importance of LT-CD8+ and NK whose number and cytotoxicity are increased. We have shown that dual therapy induces an increase in the expression in the tumor microenvironment of chemokines such as CXCL10 and CXCL11. Then, we demonstrated, by qPCR, a rapid increase mRNAs coding for CXCL10 and CXCL11 in macrophages after treatment.

We observed that dual therapy promotes a polarization of macrophages towards an M1 phenotype. This polarization can be induced by cytokines including GM-CSF. We observed an increase in GM-CSF production in the tumors of the mice treated with the dual therapy. In parallel, in a tumor growth assay, using an antibody blocking GM-CSF, we observed a loss of the anti-tumor effect of the dual therapy indicating that this cytokine is essential in the response to the dual therapy. Early on, we identified that NK cells produce GM-CSF in response to dual therapy. Moreover, in mice lacking NK and treated with the dual therapy, the macrophages no longer show polarization towards the M1 phenotype

Keywords: cancer, immunotherapy, angiogenesis, immune cells, immuno-oncology

Divers

New insights on the mechanical properties of cork in compression

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Cork is a lightweight natural material with good chemical stability, low liquid permeability, a fairly high gas barrier and thermal-acoustic insulation properties. It also has remarkable mechanical behaviour, especially in compression, enabling it to undergo large deformations up to 80 % strain. All these properties have led to the use of cork for various material engineering applications, but its main use obviously remains the manufacturing of cork stoppers for wine. Due to its specific alveolar structure, cork displays a mechanical behaviour typical of a cellular material.

Despite the fact that the mechanical behaviour of cork has already been described in many works related to its properties in compression, some fundamental aspects still need to be clarified. Firstly, the relationship between the structure and the mechanical behaviour in compression, as evidenced by the strain-stress curve, requires a better understanding. Secondly, the interpretation of the elastic modulus and, in particular, the contribution of lenticels and phellem to the stiffness of the material still have to be investigated. To that purpose two methods were applied: a quasi-static test and a repeated loading test in compression. The elastic modulus was also determined using different devices: the crosshead, the extensometer and the digital image correlation (DIC).

Molecular dynamics studies of platelet plasma membrane based on lipidomics

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The plasma membrane of platelets plays a major role in platelet activation, particularly through the P2Y receptors, a family of purinergic G-proteins. In addition, platelet plasma membrane is enriched in arachidonic acid compared to other cells. This unsaturated fatty acid is also necessary for platelet activation, as a precursor of thromboxane A2. But its role in the plasma membrane is not known. Our aim is therefore (i) to reveal the precise content and organization of lipids inside the plasma membrane of platelets and (ii) to see how P2Y12 receptors, the target of antiplatelet drugs, embedded accommodates such complex lipid environment.

For this purpose, coarse-grained molecular dynamics was used to study the dynamics of membrane lipids and P2Y12 receptors. This work is done according to lipidomic study conducted by our group. Three models were built: a single bilayer with 10 lipid species representatives of the lipidomic results (M1), a bilayer with 9 receptors P2Y12 embedded (M2) and a control model without acid arachidonic (M3). 100 µs of each model were simulated.

Dynamic lipid microdomains containing sphingomyelin and cholesterol enriched clusters were observed in M1, M2 and M3 models. More unexpectedly, phospholipid containing arachidonic acid-rich clusters were also identified in both M1 and M2. These enrichments are particularly found near P2Y12 receptors in the M2 model (between +10% and +125% depending on the species, within 5 Å of proteins). This is not observed for the same species where arachidonic acid has been substituted by oleic acid in the M3 model. Moreover, after 50 µs of simulation, there are two dimers and one trimer in M2 model while there is only one trimer in M3 model. All together, these results show that arachidonic acid promotes the oligomerization of P2Y12 receptors, which is apparently necessary for their functioning.

Keywords: Molecular Dynamics, Platelet, Plasma Membrane, Receptor

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Interactions between vegetation and atmosphere in an urban environment: the case of trees in Dijon

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Urban areas have to deal with issues related to urban heat islands and episodes of fine particle pollution. Urban vegetation, especially trees, is capable of locally reducing air temperature and particulate pollution. However, the functional mechanisms of trees are affected by urban conditions, altering in turns the services provided by the ecosystem. The high price of instrumental devices often limits the spatial coverage of measurements and favors modeling approaches. With the emergence of reliable "low cost" sensors and the availability of very high spatial resolution remote sensing, it is now possible to obtain a large quantity of observations. This allows the application of approaches adapted to the heterogeneity of urban environments. The objective of this PhD work is to better understand the interactions between vegetation and its urban environment: what are the specificities of the environment of urban vegetated sites, how do they cool and purify their environment, at a micro-scale, and based on new technologies of in-situ micro-sensors measurements in Dijon metropolis.

Fifteen sites, located in streets or parks, were selected using tree cover, morphology, proximity to air pollution sources and more or less water stress conditions from diversified data sets among which remote sensing images. These sites will be instrumented during two campaigns (Spring to Autumn 2023, Spring to Autumn 2024). Sensors will measure local meteorological and air pollution conditions. Within certain sites, trees (*Acer Platanoides*, *Tilia Euchlora* or *Quercus Petraea*) will be equipped to measure the micro-variations in the growth of one of their branches, and the quantity of water in the soil available to them. Ultimately, these measurements will provide data (e.g. transpiring potential, water stress) which will enable to better identify and understand the criteria impacting the functioning of trees and the provided services. The construction of plant functionality indices could also be considered.

Keywords: urban trees, tree benefits, park cool island, particulate air pollution, water stress, low cost sensors, microscale

Session Poster : 14h20-15h30

Ecologie

Testing a new automated macrocharcoal detection method applied to a transect of lacustrine sediment cores in eastern Canada

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Over the past decades, the abundance and area of macrocharcoal (i.e. ≥ 150 mm in diameter) fragments from sedimentary sequences have been quantified using visual or semi-automated methods to reconstruct fire histories. However, the lack of uniformity between counting methods used in each study could introduce methodological biases influencing fire frequency reconstructions, and therefore impact their interpretation and limit their comparisons.

To overcome this issue, we have developed a new automated method to quantify the number of macrocharcoal fragments and measure their areas from high definition image capture, based on the analysis of colorimetric parameters. We tested the efficiency of our method and reconstructed charcoal influx over the last 8000 years by comparing visual and automatic counting methods along a north-south transect from eastern Canada, estimating number and size, and the associated fire frequencies. Results show that our automated method is efficient in detecting charcoal particles, except for highly minerogenic samples, and suggest that the traditional visual inspection tends to overestimate the size of macrocharcoal fragments, that could have implications for paleecological studies.

Keywords: Charcoal, Methodology, Holocene, Wildfire, Sediment core, Fire frequencies

Conservation of the Eurasian lynx (*Lynx lynx*) in Western Europe: investigation of the population viability.

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Changes in public opinion and legislation in favour of the conservation of the Eurasian lynx (*Lynx lynx*) made its return to Western Europe in the mid-20th century possible. Several reintroduction programs, particularly in the Swiss Jura, the Swiss Alps and the French Vosges, contributed to the growth and expansion of the Eurasian lynx, along with the restoration of suitable habitat and the increased density of ungulate prey. Nevertheless, the species still faces several threats, including a loss of genetic diversity and direct persecution due to conflicts with human activities. Other threats, such as the potential impact of chemicals, have never been investigated in these populations. The low population density, the large home range size of individuals and their elusive behaviour make estimating population size difficult. This study aims to investigate the viability of the lynx populations in France and Switzerland, thus providing knowledge in order to identify the main threats endangering these populations. Molecular analyses of non-invasively collected samples, such as faeces, were designed to assess the genetic structure and the level of genetic diversity in the lynx populations, as well as to characterise their diet. Estimating the impact of lynx predation on domestic and game species can help clarify debates regarding conflicts with the hunting and breeding communities. Finally, toxicological analyses are currently being conducted to investigate the exposure of the Swiss lynx population to different chemicals (mainly trace metals and pesticides) and thus identify a potential supplementary threat.

Keywords: faeces, DNA, genetic structure, genetic diversity, diet, human-wildlife conflicts, ecotoxicology

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Role of rhizospheric microorganisms from a mercury-enriched brownfield site

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In environments polluted by anthropogenic activities, the roots constitute a direct interface between soil pollutants and plants, and the microorganisms of the rhizosphere could therefore play a major role in promoting vegetation growth on contaminated soil. The objective of the thesis is to improve the phytoremediation potential of woody species that have grown on a brownfield site contaminated with mercury (Hg), one of the most toxic metals, by studying the rhizospheric microorganisms associated with them. This project will characterise these communities of microorganisms by shotgun metagenomics and isolate Hg-tolerant bacteria and fungi by culture-dependent approaches. Eventually, the objective is to reintroduce them into the root environment in order to assess their potential to promote plant growth. In this way,

soils that are economically, socially and ecologically unworkable could be rehabilitated through biomass production.

In addition, the transfer and accumulation pathways of Hg will be studied in the isolated candidates in order to improve knowledge of the mechanisms involved in Hg resistance; in particular, the genomes of interesting microbe candidates will be sequenced and RNA-Seq assays will be used to identify genes potentially involved. The project also aims to assess the potential dispersion of Hg in the environment through the development of an innovative biomonitoring method based on the engineering of fluorescent microbial biosensors.

<u>Keywords:</u> mercury soil contamination, rhizospheric microorganisms, functional characterization, metagenomic, bioremediation, environmental biomonitoring

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Valuing the DEPHY network datasets to analyze relationships between crop diversity and pesticide use, to help the design of sustainable cropping systems

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Overuse of pesticides is one of the main hanging issues which impede sustainable crop production. Many researches assessed the impact of agricultural diversification on ecosystem services provision including improvement of associated biodiversity, reduction of pest pressure, reduction of crop damage, and improvement of crop yield. Similarly, considerable research has proved that crop diversity can lead to a reduction of pesticides but most of those results are context-dependent and often not based on current farmers' practices. Therefore, a quantitative analysis is missing about the relationship between crop diversity and pesticide use, in a large range of on-farm production situations to conclude from a broader view.

This study is focusing on depicting the relationship between two major components of sustainable cropping systems, i.e., crop diversity and pesticide use, based on the French DEPHY network dataset, including data from around 3,000 French farms over ten years (Fouillet *et al*., 2022). Pesticide use will be estimated by the Treatment Frequency Index, a commonly used indicator to describe the intensity of pesticide use. Crop diversity will be described using indicators from the domains of ecology and agronomy based on a combination of divisional methods: (i) plant taxonomy (e.g., species and cultivars …), (ii) ecological functional groups (e.g. high vs low N requirements, spring vs winter vs summer crops …), (iii) agronomic practices (e.g. service plants including cover crops, species mixtures, cultivar mixtures …). Considering the temporal dimension of the dataset will allow us to analyze the variability of pesticide use due to pedoclimate conditions, crop diversity, and notably the effect of preceding crops. Similarly, the effect of market (e.g. grain vs forage production) on the relationship between crop diversity and pesticide use will be also evaluated.

Finally, this work will help in the design of low-pesticide cropping systems which simultaneously contribute to more diverse crop production.

Development of functional diversity indicators of vineyard soils in the Cognac region: impact of technical itineraries

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The development of agro-ecological practices, based on the valorisation of ecosystem services, will improve the quality of the environment. In this context, the beneficial micro-organisms that promote plant growth, nutrition and health form the basis of a functional community model useful for the development of agroecological practices. The plant-associated microbiota is a key factor in reducing the effects of biotic and abiotic stresses. However, the description of the taxonomic composition of the holobiont associated with plants remains incomplete. The holobiont consists of the host plant and all the organisms it hosts. In recent years, there has been a growing interest in understanding the interactions between the grapevine and its microbiome, especially the root microbiome. However, the microbial diversity and functions associated with grapevine roots have never been described and would be a novel result. Knowledge of biogeographical patterns and the spatio-temporal dynamics of microbial communities associated with grapevines is fundamental if grapevine growers are to be able to monitor/predict the dynamics and evolution of their vineyards and thus use microbial communities as a decision-making tool. An integrated approach carried out in plots will be used to determine the link between holobiont changes (at the taxonomic and functional level), must quality and organoleptic properties of wine and/or eau-de-vie (but not on the grape). This integrated approach will also allow the identification of AMF strains characteristic of the vineyard studied for controlled mycorrhization in the nursery. Finally, experiments under controlled conditions will enable us to define whether rootstock associations are possible, which would make it possible to consider the management of a vineyard like that of a forest with several species.

Neurosciences

Local vibrations and spasticity treatment in subacute stroke: a controlled single-blinded randomized trial.

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Stroke is a worldwide leading cause of disability with 27-40% of patients developing spasticity. Local muscle vibration (LMV) has been proposed as treatment to overcome spasticity, showing positive results in the chronic phase. However, information is still scarce about its effects on the subacute phase post-stroke, which represents the best therapeutic window to promote neuroplasticity. More, little is known about the neurophysiological mechanisms subtending these beneficial effects.

This protocol aims to evaluate the effects of 6 weeks of vibration program on the incidence of spasticity in the affected upper limb of a subacute stroke population. A secondary objective is to dissect the neurophysiological mechanisms associated with spasticity.

Participants received 18 LMV sessions on the wrist and elbow flexors: 40Hz-0.5mm through a foam band for the control group (SHAM), and 80Hz-0.5mm directly on the skin for the intervention group (INT). We evaluated spasticity (Modified Ashworth scale (MAS) and isokinetic ergometer), arm function (Fugl-Meyer Assessment for upper extremity (FMA-UE)), and corticospinal excitability (H/M ratio, H-reflex post-activation depression (H-PAD) and transcranial magnetic stimulation recorded at the flexor carpi radialis).

Our preliminary results on 9 participants showed a good adherence to the protocol. Both groups felt vibrations 100% of the time, with 0% illusions in the SHAM group and 86.3% illusions of arm movements in the INT group. We found a slim reduction in the MAS scores at the wrist and a slight improvement in the FMA-UE scores in the INT versus SHAM groups. The H-PAD and the H/M ratio seems to decrease and increase respectively, in both groups.

Patients adherence was good and the difference of illusional perception between SHAM and INT groups seemed confirmed. LMV have shown a trend to improve the patient's functional impairments.
Keywords: Stroke, Spasticity, Neuroplasticity, Vibration

The amount of post-activation depression is similar between peripheral nerve and transcutaneous spinal cord stimulation

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Transcutaneous spinal cord stimulation (tSCS) elicits reflex responses in all muscles of the lower limb by stimulating the lower thoracic level. These posterior root muscle (PRM) reflexes are sensitive to the homosynaptic post activation depression (HPAD) phenomenon, as the reflex elicited by peripheral nerve stimulation, named the H-reflex. The HPAD phenomenon stems from the repetitive activation of muscle afferents which induces a decrease in the amount of neurotransmitters available at the synapse and a subsequent decrease in the second reflex amplitude. The aim of the study was to test whether these responses share the same physiological mechanism related to HPAD phenomenon.

Twenty healthy volunteers participated in one experimental session consisting of stimulations of the lower thoracic level, to elicit PRM reflexes and tibial nerve stimulation, to elicit H-reflexes, on the right lower leg. Recruitment curves were built for tSCS and tibial nerve

stimulation. After that, six series of paired-pulse stimulations were delivered with a 50-ms or 1-s inter-stimulus interval. All conditioned responses were normalized with respect to the test responses, allowing us to determine the degree of depression of the second reflex.

H_{COND}/H_{TEST} and PRM_{COND}/PRM_{TEST} were significantly lower when they were delivered at 50ms inter stimulus interval compared to 1s (P<0.01) but they were not significantly different between them when they were delivered at the same interval (P>0.05). For the series of stimulations evoked at 1s intervals, ratios were not significantly different (P>0.05).

Present results show that PRM reflexes are sensitive to the HPAD phenomenon like H-reflexes and that the amount of inhibition due to HPAD is similar for the two types of responses. Moreover, it is shown that the inhibition is more pronounced at intervals of 50ms than at 1s. These preliminary results corroborate previous findings reporting that tSCS effectively activates Ia afferences, at least for low reflex amplitudes.

Keywords: neuromuscular, tSCS, H-reflex, HPAD, neurostimulation, spinal cord

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Impact of the deletion of endothelial brain-derived neurotrophic factor on hippocampal BDNF/Tropomyosin-related kinase B signaling-induced neuroplastic pathway elicited by physical exercise.

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Physical exercise (EX) is widely recognized as the foremost non-pharmacological approach to enhancing physical and mental health. Studies in both humans and animals identify the neurotrophin brain-derived neurotrophic factor (BDNF) as the essential molecule for proper brain function, and whose role in the beneficial effects of EX on the brain is clearly established. BDNF exerts its positive effect through its binding to the tropomyosin-related kinase B (TrkB) receptor. BDNF upregulation in response to EX is believed to be dependent of 3 main mechanisms: the increase in neuronal expression through an activity-dependent mechanism, the contribution of endothelial cells through cerebral blood flow elevation (hemodynamic hypothesis) and the recent mechanisms involving mediators originating from muscular tissue. Concerning the contribution of endothelial cells, we have previously demonstrated that the cerebrovascular endothelium is an important source of cerebral BDNF since its removing halved brain BDNF content. In this context, using an endothelial BDNF-conditional knockout mouse model submitted to 3-weeks of treadmill running, this study aims to characterize the effects of endothelial BDNF deletion on hippocampal BDNF/TrkB signaling-induced neuroplastic pathway. This research intends to shed light on the intricate interplay between endothelial-derived BDNF and hippocampal neuroplasticity, further elucidating the multifaceted mechanisms underlying the beneficial effects of EX on brain health.

Keywords: BDNF, Physical exercise, Endothelium, Neuroplasticity

New quinazoline-Donepezil hybrids as cholinesterases and tau tubulin kinase 1 inhibitors for Alzheimer's disease

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Alzheimer's disease (AD) is the most common degenerative dementia in the elderly and is characterized by a decline in cholinergic functions. AD is characterized by the presence of extracellular plaques composed of the accumulation of amyloid beta peptide (Abeta) and intracellular deposits in the form of neurofibrillary tangles of hyperphosphorylated tau protein. Recent results indicate that tau protein plays a central role in AD, with a strong correlation between neuronal death and tau aggregates in the brain of Alzheimer's patients. The study of this aggregation has already revealed several interesting partners, such as the recently discovered Tau-Tubulin Kinase 1 (TTBK1) involved in Tau phosphorylation.

Cholinergic neurons are the most damaged in AD, resulting in a low level of acetylcholine (Ach) that can be alleviated by the administration of acetylcholinesterase (AChE) inhibitors [6]. Despite significant research and an unprecedented number of publications (more than 198k in PubMed as of March 2023), the only available treatments are limited to temporary relief of symptoms.

Our objective is to develop new multi-targeted molecules with simultaneous activity on cholinesterase inhibition for symptomatic action and more specific properties to hinder disease progression, mainly targeting the Tau protein by inhibiting the promising newly identified TTBK1 target. Please refer to Figure 1 for more details.

To achieve this objective, we have prepared functionalized quinazolines in 2 steps: first, a reaction of 2 aminobenzonitrile and different orthoesters, followed by the addition of variously substituted anilines. The condensation of substituted benzylpiperidine allows the preparation of the desired compounds. These products are currently under biological evaluation.
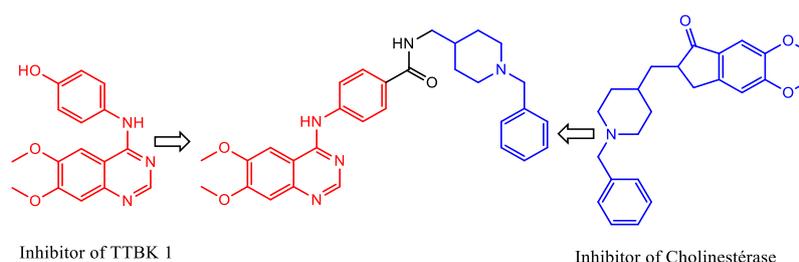

Figure 1: Designed Compounds.

Keywords: Alzheimer's disease, Tau Tubulin Kinase 1, Cholinesterase, Quinazoline, Donepezil

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The Neural correlates of apraxia: An anatomical likelihood estimation meta-analysis of lesion-symptom mapping studies

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Limb apraxia is a motor disorder frequently observed following a stroke. Patients present clinical deficits observable using three specific tasks: tool use, imitation, and pantomime. These tasks are supported by different cognitive processes, which are supported across a left-lateralized brain network including inferior frontal gyrus, inferior parietal lobe and lateral occipito-temporal cortex (LOTC).

For the past twenty years, voxel-wise lesion symptom mapping (VLSM) has been used to obtain statistical brain maps of lesions associated with tasks assessing apraxia. For the first time, we proposed a meta-analysis of studies using VLSM on tool use, imitation, and pantomime to better understand the brain regions associated with a deficit in these tasks.

We performed a literature review regrouping 3431 left brain-damaged patients from 40 papers. Data were processed with Anatomic Likelihood Estimation analyses.

Our results questioned traditional neurocognitive models on apraxia and reinforce our understanding of cognitive processes involved in action production. Interestingly, lesions within the LOTC were more associated with imitation deficits than tool use or pantomime, confirming its important role in higher visual processing.

<u>Keywords:</u> Apraxia, VLSM, tools, action, stroke patients, pantomime, imitation

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Effects of different exercise modalities on cognitive performances

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Introduction: It is well established that physical exercise (PE) positively impacts physical and brain health. More specifically, exercises performed at moderate to high intensities are highly recommended to induce greater benefits. However, reaching such intensities can be difficult for some patients due to physical limitations. Across years, electrical stimulation (ES) and functional electrical stimulation (FES) have been proposed as good alternatives to voluntary exercises in rehabilitation contexts. While their beneficial effects on physical functions have been well described, little is known regarding cognitive function. The present experiment therefore aimed to investigate the effects of ES and FES protocols on cognitive performances.

Methods: Thirteen participants were recruited and participated to seven sessions. The first-three sessions were dedicated to familiarize the subjects to ES and cognitive tasks. Then, participants underwent four sessions in a randomized order and separated by one week of rest. Sessions included: FES-assisted cycling, Cycling, ES and sitting control. Stimulation was applied to both quadriceps' muscles during 20 minutes at the maximal tolerable intensity. Cognitive perfomances were evaluated immediately before and after stimulation using the Stroop test (executive function), the Trail Making Tests (mental flexibility) and the RAVLT test (memory).

Results: Results show improved performances to the Stroop test (congruent and incongruent conditions) after FES-cycling (P<0.05). Responses were unchanged for the three other

modalities. Exercise also induced an improvement of mental flexibility as shown by greater performances to the TMT-A test (P=0.005). Memory was only improved after the ES session (P=0.007).

Conclusion: Our results suggest that exercise, even performed with ES, is effective to improve cognitive performance, even after a single session.

Keywords: Functional electrical stimulation, Electrical muscle stimulation, cognition

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Preuve de l'existence de fonctions de coûts subjectives dans une tâche de pointage verticale à vitesse libre

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Différentes lois motrices ont été décrites de façon récurrente comme la preuve de représentations corticales génériques des actions, telles que la loi de Fitt (Fitts, 1954) ou la loi de puissance 2/3 (Viviani & Flash, 1995). Notamment, les paramètres cinématiques qui varient avec la direction du mouvement (i.e., les mouvements vers le haut ont un temps plus court pour atteindre la vitesse maximale que les mouvements vers le bas, Papaxanthis et al., 1998) seraient des marqueurs de la meilleure solution motrice (Gaveau *et al.*, 2021). Ce comportement a été relié à une minimisation de la dépense énergétique à l'aide d'un modèle mathématique issu de la théorie du contrôle optimal appelé modèle "Smooth-Effort" (Berret *et al.*, 2008a). Ce modèle suggère la minimisation de deux fonctions de coût : la secousse du mouvement et la dépense énergétique. Dans cette étude, nous avons examiné la validité du modèle "Smooth-Effort" dans une tâche de pointage libre (c'est-à-dire minimisant au maximum les contraintes spatiales et temporelles). Cette libération des contraintes de la tâche a mis en évidence des différences cinématiques interindividuelles importantes, qui ne sont pas explicables par une pure minimisation de la dépense énergétique (Devemy *et al.*, 2023). Par l'utilisation d'une méthode de contrôle optimal inverse, nous avons recherché le modèle optimal le plus adapté pour expliquer la cinématique de chaque sujet. Nous avons constaté que le modèle « Smooth-Effort » n'était pas le plus approprié pour rendre compte du mouvement de la plupart des participants. Enfin un modèle optimal seul ne parvenait pas à expliquer la variété de mouvements observés. Ce résultat montre que dans un même contexte sensorimoteur, différents individus vont se référer à différents coûts optimaux (ou motivations internes) pour planifier leur mouvement.

Mots-clés : Contrôle moteur, Cinématique de pointage du bras vertical, Contrôle optimal, Signatures Motrices Individuelles

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Synthesis and biological evaluation of new Donepezil-Nifedipine hybrid for Alzheimer's disease treatment

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Alzheimer's Disease (**AD**) is the most common form of age-related dementia. This disease has a complex mechanism involving many pathophysiological processes including (*i.*) amyloid plaques, (*ii.*) neurofibrillary tangles, (*iii.*) oxidative stress, (*iv.*) increased intracellular calcium and (*v.*) neurons loss. All these dysregulations conduce to a cholinergic deficit. Current treatments can only limit the consequences of this deficit but have failed to show proof that they could limit the development of this pathology. Consequently, it is urgent to develop compounds able to simultaneously treat these dysregulations and impact pathophysiological processes (**disease-modifying drugs**).

A central element of this pathology is calcium dyshomeostasis. This increase in calcium seems to be at the origin of disturbance of the activity of the enzymes implicated in AD. Moreover, the increase of intracellular calcium concentration leads to neuronal apoptosis. Pharmacovigilance studies shown a reduction in the incidence of AD in hypertensive patients treated with dihydropyridines (in particular *Amlodipine* and N*ifedipine)*. This effect is explained by the fact that dihydropyridines are calcium channel inhibitors, they reduce the entry of calcium inside cells, which in the case of AD, prevents dysregulations.

In this study, we describe the design, synthesis and biological studies of several MultiTarget-Directed-Ligands for AD. These compounds were rationally designed from *Nifedipine* and *Donepezil*. *Nifedipine* is a calcium channel blockade and antioxidant with neuroprotective effect while *Donepezil* is a cholinesterases inhibitor. The synthesis was performed in compliance with green chemistry recommendations. These reasons lead us to use MultiComponent Reactions (**MCRs**) and with high yield reaction (**click reaction**) associated fewer toxic solvents, safe reagents under microwave irradiation.

From the preliminary biologicals' tests, we have selected 3 interesting compounds showing BuChE inhibition **C4** (40% at 10µM), **C15** (40% at 10µM) and compound **C9** which showed respectively inhibition of 32% and 43% at 10µM against both AChE and BuChE.
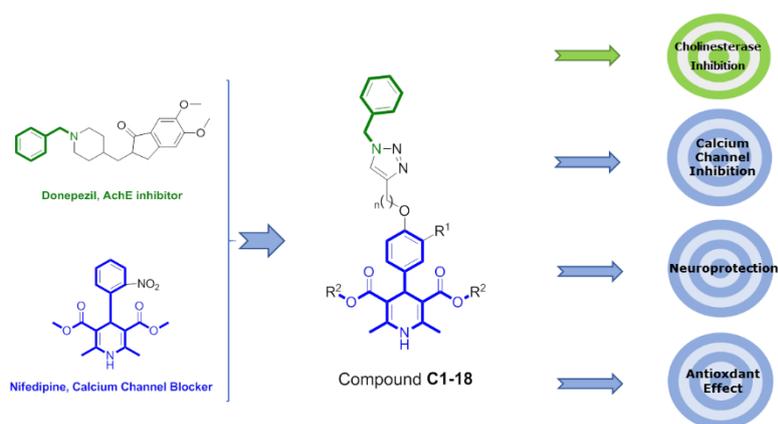
Keywords: Alzheimer's Disease, Disease-modifying Drugs, MultiTarget Directed Ligands, Dihydropyridines, MultiComponent Reaction, Click Reaction

Cancérologie et Pharmacologie

Study of a sequential therapy, chemotherapy/ Nitric Oxyde-donor, for the treatment of colorectal cancer

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The treatment of colorectal cancer at advanced stages is based on surgical excision, preceded and/or followed by chemotherapy or radiotherapy treatment. However, the resistance of cancer cells limits the effectiveness of these treatments. For this reason, combinatorial therapy strategies are currently the subject of numerous clinical studies to improve the effectiveness of standard treatment. We propose to develop a new combinatorial strategy through the association of chemotherapy with a nitric oxide (NO)-releasing drug called Glyceryl Trinitrate (GTN).

It has been shown within the tumor microenvironment that several chemo-induced cytokines contribute to tumor progression and resistance to treatment. We focused our attention on the cytokines of the *Tumor Necrosis Factor* (TNF) family such as TNFα, FasL and TRAIL. Depending on some parameters (microenvironment, stoichiometry...), cytokines display both pro-tumor and anti-tumor effects. Our laboratory has shown that NO, released by GTN, promotes the death of cancer cells in the presence of TNFα and FasL. So, we hypothesised that the GTN should be administered when an increase in the level of these cytokines is detected within the tumors and/or in the serums following a chemotherapeutic treatment. The project is based on the study of the level of these cytokines as potential biomarkers to figure out the use of a sequential therapy (chemotherapy/ NO-donor, such as GTN). To demonstrate this, our study is conducted *in vivo* via a pre-clinical syngeneic Balb/c mouse model of colorectal cancer and *in vitro* using a human colon cancer cell line (SW480). This project is structured around two main objectives: 1) To evaluate *in vivo* the effect of chemotherapy on the level of the TNF cytokines and then the anti-tumor response of sequential therapy (chemotherapy then GTN) and 2) To study *in vitro* the impact of NO on the TNF-cytokines/TNF-receptors system (Western Blot and flow cytometry analyses).
Keywords: cancer; chemotherapy; nitric oxyde; cytokines; TNF receptors; microenvironment.

In vitro evaluation of the hepatic safety of new multi-target agents for Alzheimer's disease therapy

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Alzheimer's disease (AD) is devastating neurodegenerative disorder that affects millions of people worldwide with only symptomatic therapy available. However, multi-targeted directed ligands (MTDLs), which can act simultaneously on several targets associated with AD pathology, are thought to be a prospective treatment option for this multifactorial disease. In the last decade, we have developed numerous series of MTDLs and reported multiple new hit-compounds [1-3]. Nevertheless, before their use in clinical settings it is essential to guarantee the safety of them. Hepatotoxicity is a primary concern when administered orally; moreover, the modulation of the cytochrome P450 (CYP) enzymes can lead to drug-drug interactions that might be clinically significant. Hence, the aim of this study is to evaluate the effect of these hit-MTDL compounds on 1) hepatocyte viability and 2) CYP activities in rat hepatocyte culture. Thus, different concentrations of the MTDLs were added to primary rat hepatocyte cultures for 24h, 48h and 72h. Hepatocyte viability was measured using MTT assay, and CYP1A, 2B, 2C and 3A-dependent activities were assessed by fluorescent and luminescent methods. Our findings have shown that the highest noncytotoxic concentration is 48 µM in rat hepatocytes among all the compounds with IC50 from 9 to 64 µM after 24h, 8 to 39 µM after 48h, and 8 to 34 µM after 72h of treatment. Additionally, at noncytotoxic concentrations, the compounds do not significantly alter the function of CYP1A- and 2B-dependent activities at any time point; although, there is a moderate induction of CYP3A, but only at the highest concentrations tested. Therefore, the obtained results are very promising for further investigation of these hit-MTDL compounds, particularly using human hepatocytes.

References: [1] Malek R. *et al*., J. Med. Chem. 2019; 62: 11416-11422; [2] Ismaili L. EP3929192A1 (29/12/2021); [3] Ismaili L. *et al*., ACS Chem. Neurosci. 2021; 12: 1328-1342.

Keywords: Alzheimer's disease, multitarget agents, drug safety, hepatotoxicity, cytochromes P450

Development of a CAR-NK-CD123 in the management of Blastic Plasmacytoid Dendritic Cell Neoplasm

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The plasmacytoid dendritic cell leukemia, also known as blastic plasmacytoid dendritic cell neoplasm (BPDCN), is a rare hematological disorder derived from plasmacytoid dendritic cells, and its prognosis is particularly poor (median survival of 9-13 months), with currently no consensus on its management. In young patients, only induction by acute leukemia-type polychemotherapy followed by hematopoietic stem cell transplantation allows for long-term remission. The current challenge is to develop innovative therapies targeting the CD123 marker, the main marker of this pathology.

CAR T cell-mediated immunotherapy has shown impressive results in clinical trials with response rates of up to 80%. However, the adverse effects associated with this approach and the use of the patient's own lymphocytes currently limit their use. The more recent development of CAR NK (natural killer) cells in this field is based on the fact that NK cells may be a safer

alternative and, more importantly, a "ready-to-use" therapy option as they induce little allogeneic response. In addition, their powerful intrinsic antitumor properties are an additional asset.

The first objective was to sort NK cells derived from peripheral blood or placental blood and then amplify them in culture. Indeed, the proliferation phase of these NK cells is crucial for transduction. To achieve transduction of the NK cells, a lentiviral supernatant containing the CD123 CAR must be produced. After transduction, we evaluated the cytotoxicity of this CAR-CD123 against BPDCN cell lines.

Keywords: BPDCN – plasmacytoid dendritic cell – CD123 – CAR-NK.

Rôle d'OSR1 dans la réponse immunitaire anti-tumorale des cancers du pancréas

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Le cancer du pancréas est un des rares cancers dont l'incidence et la mortalité sont en augmentation. Ces tumeurs sont caractérisées par un microenvironnement tumoral (MET) dense et abondant constituant une barrière limitant l'efficacité des traitements. Ce stroma tumoral est composé majoritairement de fibroblastes associés au cancer (CAF) capables notamment de moduler la réponse immunitaire anti-tumorale.

De plus, l'analyse par single-cell RNAseq du MET de modèles murins syngéniques de cancer du pancréas exposés à la chimiothérapie, aux anti-PD1 et aux anti-TGF-β1 a montré le rôle majeur de la neutralisation de la voie du TGF-β1 sur l'efficacité de la chimio-immunothérapie. En effet, la neutralisation de l'action du TGF-β1 permet la reprogrammation des myofibroblastes (myCAF) en CAF inflammatoires (iCAF). Ces données nous ont permis d'identifier des molécules spécifiquement exprimées dans les iCAF et corrélées au recrutement des lymphocytes T telles que CXCL9 et CXCL10. Dans ce contexte, le facteur de transcription OSR1 a été spécifiquement identifié dans les iCAF des tumeurs à évolution favorable. Notre objectif est de décrire le rôle d'OSR1 et les mécanismes induits par le TGF-β1 pour neutraliser la différenciation des iCAF.

Nos analyses in vitro montrent une expression naturelle d'OSR1 dans les fibroblastes. Cette expression est perdue dans les myCAF sous l'influence du TGF-β. La ré-expression d'OSR1 dans les iCAF est associée à l'activation de la signalisation IFN. Des analyses par RNAseq et ChIPseq mettent en évidence une interaction entre OSR1 et STAT1. Enfin, nous avons cherché à comprendre comment induire in vitro l'expression d'OSR1 à partir de myCAF. Ainsi ce travail montre l'implication d'OSR1 dans la réponse immunitaire anti-tumorale.

Mots clés : Fibroblastes, Biomarqueurs, Cancer, Chimiokines

Développement de cellules CAR-T anti-HSP70 dans le traitement de tumeurs solides

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Le traitement de patients atteints de cancer avec des cellules CAR-T (Chimeric Antigenic Receptor-T cells) est une stratégie thérapeutique qui consiste à prélever les cellules immunitaires d'un patient, les transformer *in vitro* afin qu'elles expriment des récepteurs d'antigènes tumoraux, et les réinfuser au patient. Malgré son efficacité remarquable dans le traitement de cancers hématologiques comme la leucémie aiguë lymphoblastique B et les lymphomes B, le succès des CAR-T dans le traitement des tumeurs solides reste encore très limité.

Les protéines de choc thermique (Hsp, pour Heat shock proteins), aussi appelées protéines de stress, sont surexprimées dans de nombreux cancers solides. Parmi les Hsp, Hsp70 membranaire est présente uniquement à la surface des cellules tumorales et son niveau d'expression est associé avec un mauvais pronostic. Il s'agit d'une protéine transmembranaire avec un domaine extracellulaire bien défini, ce qui fait de Hsp70 une cible de choix pour une approche CAR-T dans le traitement de tumeurs solides.

Pour combiner les avantages de la thérapie CAR-T et l'expression membranaire de Hsp70 dans les tumeurs, nous avons développé et exprimé un récepteur CAR spécifique de la Hsp70 membranaire. Nous avons démontré que les cellules CAR-T anti-Hsp70 sont activées lorsqu'elles sont mises en contact avec la protéine recombinante HSP70. De plus, ces cellules libèrent des nano-vésicules appelées exosomes, contenant le récepteur CAR. Ces vésicules extracellulaires d'origine endosomale, dont le contenu est similaire à celui de la cellule dont elles sont issues, sont impliquées dans la communication intercellulaire et dans la réponse immunitaire cytotoxique.

Nos résultats suggèrent que le développement de CAR-T anti-HSP70 permettrait l'utilisation de cette thérapie pour les patients atteints de tumeurs solides (HSP70+) à un stade avancé. Les exosomes sécrétés pourraient augmenter l'efficacité de ces cellules et être une alternative prometteuse pour limiter la toxicité des CAR-T.

Keywords: CAR-T cells, Protéines de choc thermique, Exosomes, Immunologie

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Tumor lipid metabolism: a potential target to restore the sensitivity of colorectal cancers to chemotherapy

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In the recent decades, cancers have taken the number one position in human mortality worldwide, despite screening and therapy. These therapeutic failures are linked to the appearance of resistance mechanism such as alterations of lipid metabolism, including the deregulation of phosphatidylcholine (PC) synthesis. This latter is a major phospholipid in biological membranes and in dynamic organelles, called lipid droplets (LD). Their accumulation has been observed in increasing numbers of colorectal cancer (CRC) cells, supported by overexpression of a key enzyme involved in PC biosynthesis pathway, lysophosphatidylcholine acyltransferase 2 or LPCAT2.

In this context, targeting lipid metabolism, in particular that of PC could be a promising approach to restore the sensitivity of cancer cells to treatments. In this strategy, the use of modulating agents such as lipid-lowering drugs already indicated in the clinic for dyslipidemia treatment, could be relevant.

We highlight that modulating agents exert a cytotoxic activity in CRC cells. The analysis of the combinatorial effects of these molecules with the conventional chemotherapies allowed us to demonstrate a higher cytoxicity. These preliminary data suggest that the use of lipid-lowering drugs as an adjuvant therapy is a promising approach to restore the sensitivity of colon cancer cells to treatment.

Keywords: Colorectal cancer, lipid metabolism, lipid droplets, chemoresistance, modulating agents.

Mise au point et évaluation de nanoparticules multifonctionnelles pour la radiothérapie et la chimiothérapie des gliomes

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L'utilisation des nanoparticules en santé offre des perspectives prometteuses dans la thérapie des cancers. Parmi elles, on retrouve les nanoparticules d'or qui sont utilisées comme agent radiosensibilisant afin d'améliorer les effets de la radiothérapie en raison de leur propension à absorber les rayonnements ionisants. Leur recouvrement par des ions gadolinium, un agent de contraste utilisé en IRM, permet en outre de les suivre en temps réel et ainsi de déclencher la radiothérapie au moment opportun. Cependant, la petite taille de ces nanoparticules d'or (moins de 10nm) explique leur rapide élimination systémique par excrétion rénale, minimisant leur intérêt thérapeutique. Dans ce contexte, des nanoparticules multifonctionnelles à visée thérapeutique et diagnostique seront développées dans le cadre du traitement des tumeurs solides. Elles seront constituées d'une matrice polymère biodégradable et transporteront ces nanoparticules d'or fonctionnalisées. Leur taille comprise entre 100nm et 200nm contribuera à éviter l'élimination rénale, ce qui augmentera leur temps de résidence vasculaire. Afin de renforcer le potentiel antitumoral des nanoparticules, un agent anti-cancéreux sera également

co-encapsulé dans ces vecteurs polymères. Cette stratégie visera ainsi à délivrer de façon concomitante et à des doses optimales, un agent radiosensibilisant et un agent anticancéreux au niveau de la tumeur par un ciblage passif et actif. Afin d'augmenter la concentration des anticancéreux au niveau de la tumeur et préserver le tissu sain, une biomolécule reconnaissant un récepteur ou un antigène surexprimé par les cellules cancéreuses (peptide RGD ou anticorps) sera greffée sur la surface des nanoparticules polymères.

Mots clés : Radiothérapie, Gliome, Chimiothérapie, Nanoparticules d'or

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Nutrition

Roles and Quantification of Lipids in Wines

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Lipids are essential nutrients for many organisms like yeasts and play a role in numerous biochemical reactions, particularly during the production of a food product such as wine. In fact, yeasts are main factors in the alcoholic fermentation during the winemaking process. The roles of lipids include nutrition and protection against various yeast stresses encountered during alcoholic fermentation. Lipids also have an impact on the aroma profile of the wine, as they are responsible for the production of certain volatile aromatic compounds such as ethyl esters.

Despite the significant impact of lipids on fermentation and wine aroma profile, there is currently limited data on the diversity and quantity of lipids, as well as the effect of viticultural and winemaking practices on them. It is reported that lipids can also be a limiting factor during the fermentation and lead to stopped or sluggish fermentation. Understanding and managing fermentations are crucial for ensuring wine quality.

Methods described for quantifying these lipids are liquid and gaz chromatography coupled with mass spectrometry. Mostly two families of lipids have been identified in grape musts: fatty acids and phytosterols. These lipids originate from yeasts (biosynthesis and beta-oxidation of fatty acids) and from grape skins, stems, and seeds. Other lipid families such as glycerophospholipids, sphingolipids, and glycerolipids are described as present in grape seeds and skins, as well as in yeasts (biosynthesis), but not analyzed in grape juice.

Determining the nature and concentration of lipids in the must should help to better understand the lipid requirements of different yeasts, their role in fermentation, and their impact on the organoleptic qualities of the wine.

Keywords: Yeast, lipids, wine, fermentation, must, stress, nutrition, aromatic profile

Changes in taste perception in patients with Mild Cognitive Impairment and mild Alzheimer's Disease, recorded by Gustatory Evoked Potentials

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Approximately 50 million people worldwide suffer from dementia, Alzheimer's disease (AD) being the most common cause. Efforts to counteract its expansion are increasing, so does the need for biomarkers for an early diagnosis.

The main purpose of the study was to explore gustatory functions using subjective taste tests and recordings of gustatory evoked potentials (GEPs) for sucrose solution in patients with mild AD, patients with mild cognitive impairment (MCI) and comparing them to healthy age and sex-matched subjects. The secondary objective was to evaluate the relationships between GEPs and the results of cognitive assessments and fasting blood samplings.

This study has included 45 subjects divided into three groups of 15 persons: healthy subjects, MCI, AD patients. We compared their gustatory functions using subjective taste tests (threshold detection for sucrose) and their brain activity recording GEPs in response to a sucrose stimulation. Correlations were done with their cognitive scores and eating behaviour hormone levels.

Our study showed differences in cortical taste responses after sucrose stimulation in the MCI and mild AD groups of patients in comparison to controls. Increased latencies and reduced amplitudes were observed in the two groups of patients. No correlation was observed with hormone levels. The threshold for sucrose detection was significantly higher in the group of mild AD than in the groups of controls and MCI.

The cortical processing of sensory taste information seems to be altered early in patients with AD at the prodromal stage. It could be detected with subjective detection taste tests in AD only in the mild dementia stage and not in MCI patients. Further studies are needed to understand the underlying physiopathological mechanisms. Comparison with other neurodegenerative diseases could help to understand if changes in GEPs are biomarkers for Alzheimer's disease specifically, or simply a marker of neurodegeneration.

Keywords: Alzheimer's disease, Gustatory Evoked Potentials, Taste

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Can storage stability of citrus fiber powder be explained by modifications of their physicochemical properties?

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Citrus, consisting of orange, lemon, mandarin, and grapefruit, is the most important crop in the world, with worldwide production of 144 million tons in 2019. Most of the fruits produced are used for juice production, pectin, and flavonoid extraction, which results in a huge quantity of by-products corresponding to 50-60% of the original whole fruit weight. Biopolymers are the main constituents of these agro-industrial wastes and present many properties that make them interesting for applications such as sustainability, inexpensive, biodegradability, friendly to the environment, and recyclability. Citrus fiber powders (CFP), manufactured from pectin extraction of lemon juice industry by-products, are characterized by an ability to retain moisture and good emulsifying stability and could have many food applications in baked products, meats, dairy products, sauces, and dressings. The fibers are dried to facilitate distribution and commercialization as a food ingredient. The quality of the dehydrated powder is influenced by the processing and storage condition. However, the mechanism of the modifications induced by storage on functional properties of the powders and especially rehydration properties were not understood. This study aimed at investigating the mechanisms responsible for CFP stability upon storage. Samples were stored in different conditions of temperature and humidity for 12 months. Gelation, water holding capacity, and swelling capacity were used to evaluate the effect of storage on functional properties. In addition, powder surface composition, morphology, and chemical and physical properties were analyzed to understand the modification of physicochemical properties during storage. The results highlighted that properties related to moisture retention, emulsifying stability, and rehydration decreased with increasing aging time. The loss in functionality was accelerated at 40 °C and 75%RH compared to 20°C and 30% RH. These modifications might be linked to the chemical structure of the biopolymers further than to surface composition and morphology.

Keywords: Citrus Fiber powder, biopolymers, stability, functional properties, storage

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Santé

Role of intestinal CD36 in the synthesis of triglyceride-rich chylomicrons, key parameter deregulated in obesity

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Obesity is a multifactorial disease characterized by the accumulation of body fat. Intestine absorbs dietary fats through the formation of triglycerides-rich lipoproteins called chylomicrons (CM). Quality of CM synthesis conditions their plasma residence time. In addition to triglycerides, CM also carry pro-inflammatory bacterial lipopolysaccharides in the blood. Therefore, alterations in CM clearance can increase postprandial inflammation and hypertriglyceridemia, states that are closely related to the development of obesity. Cluster of differentiation 36 (CD36) is a ubiquitous receptor implicated in CM synthesis in the gut. In humans, CD36 polymorphisms are positively correlated with an increased risk of obesity. In mice, the absence of CD36 alters postprandial consequences of lipid overconsumption such as

CM size and hypertriglyceridemia. Nevertheless, these results have been obtained in totally CD36-deficient mice. The aim of this work is to evaluate the role of intestinal CD36 in the regulation of microsomal triglyceride transfer protein (MTP), a key actor of CM synthesis.

In this study, we use transgenic mice deficient for CD36 only in the gut (*Cd36*-Ent(-/-)) and their control littermates which express CD36. *Ex vivo*, an intestinal segments model is used to determine signalling pathways kinetics downstream CD36 activation by linoleic acid (LA) at 750µM for 5, 10 and 20 minutes.

Our results show that, in control mice, LA stimulation of intestinal segments for 5 minutes upregulates MTP expression. This upregulation reaches a peak at 10 minutes and decreases to reach back basal level after 20 minutes of activation with LA. Conversely, in *Cd36*-Ent(-/-) segments, MTP expression is downregulated after 5 minutes with LA. In conclusion, we observe *ex vivo* that LA-induced MTP upregulation requires a functional CD36 receptor. Therefore, CD36 deficiency could affect CM quality. An *in vivo* model of high-fat diet is ongoing to assess physiological postprandial consequences of intestinal CD36 deficiency.

Keywords: intestine, lipids, chylomicrons, intestinal CD36, MTP, obesity

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Vasorelaxation effect of Thai medicinal plants:
Derris scandens (Roxb.) Benth, *Oroxylum indicum* (L.) Kurz, *Sesbania grandiflora* (L.) Pers., and *Ficus racemosa* L.

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Phosphodiesterase 5 (PDE5) inhibition is one of the therapeutic options to manage pulmonary arterial hypertension and erectile dysfunction. Four Thai medicinal plants including *Derris scandens* (Roxb.) Benth [1], as well as *Oroxylum indicum* (L.) Kurz, *Sesbania grandiflora* (L.) Pers., and *Ficus racemosa* L. have demonstrated high PDE5 inhibitory activity. In the present study, we investigate the pulmonary and systemic vascular effects of these plant extracts in rats.

Plant extracts were prepared by maceration of dry plant materials with 95% ethanol with a ratio of dry sample to solvent of 1:3 w/v (kg/L), then filtered and evaporated under reduced pressure until dryness. Vasorelaxant effects were evaluated by *ex vivo* technique in pulmonary arteries (PA) and aorta isolated from seven-nine weeks-old male Wistar rats. Vessels are pre-contracted with 10^{-5} M of phenylephrine and then relaxed with cumulative concentrations of extracts (0.01 to 300 µg/mL). The same experiments were performed in endothelium-denuded conditions. Nonlinear regression analyses were performed with GraphPad Prism 5 software.

In PA, *D. scandens* extract showed the highest relaxation (E_{max} = 89.9%, EC_{50} = 5.54 µg/mL), followed by *O. indicum* extract (E_{max} = 84.0%, EC_{50} = 7.13 µg/mL) and *F. racemosa* extract (E_{max} = 61.4%, EC_{50} = 5.14 µg/mL), while *S. grandiflora* displayed the lowest relaxation (E_{max} = 45.9%, EC_{50} = 0.33 µg/mL). In the aorta, the maximum effects of the extracts were 37.6% for *D. scandens*, 24.8% for *O. indicum*, 57.2% for *F. racemosa*, and 26.9% for *S. grandiflora*, giving an efficacy index (E_{max} (PA)/ E_{max} (aorta)) of 2.3, 3.3, 1.07 and 1.7, respectively. All of

these relaxant effects were attenuated by endothelial removal, except for the *F. racemosa* extract.

Extracts from *D. scandens* and *O. indicum* exhibited potent vasorelaxant effects with good efficacy for PA. Our data encourage the investigation of the precise mechanisms involved in their vasorelaxant effects.

Keywords: *Derris scandens*, *Ficus racemosa*, *Oroxylum indicum*, Pulmonary artery, *Sesbania grandiflora*, Thai herbal, Vasorelaxation

Reference:

[1] Chaichamnong N, Temkitthawon P, Khorana N, Pitpakdeeanan P, Taepavarapruk P, Nuengchamnong N, Siriwattanasathien Y, Suksamrarn A, Ingkaninan K. Phosphodiesterase 5 Inhibitors from *Derris scandens*. *Planta Med.* 2018;84(15):1134-1140.

Development of *Andrographis paniculata* extract formulations for the treatment and prevention of viral infection of the lung

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Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is the causative pathogen of the coronavirus disease of 2019 (COVID-19) that can cause respiratory and extra-pulmonary pathologies, including acidic respiratory tract microenvironment, pulmonary endothelial dysfunction, diffuse alveolar damage, lung oedema, inflammation from immune and nitric oxide dysregulation, including excessive inflammatory cytokines release, which is the main problem related to respiratory and multi-organ failure and fatality in severe COVID-19 patients.

Andrographis paniculata (AP) has been long used in herbal medicines, and the AP extract (APE) has been considered as an antiviral regimen in Thailand. However, APE, its main compound, andrographolide and its derivatives, have poor bioavailability which are limitations on their use.

In this research collaboration; dried aerial part of AP was extracted, and the compounds were isolated. From cytotoxicity and bioactivity assays using pulmonary and immune cell lines, non-cytotoxic concentration of APE and its main compounds have both anti-inflammatory and antiviral activities. An amphiphilic polymer was used in the formulation, then APE/polymer inclusion complex formation was confirmed and physicochemical properties were determined by various pharmaceutical analytics. Polymeric-based formulation showed amendments to solubility and bioactivities.

The further development of innovative nano drug delivery systems using active compounds of APE with pH-responsive polymer might improve stability, enhance pulmonary surfactant or pathologic mucous penetration and promote bioavailability, specify the targeted cells and areas for treatment, and eventually might improve therapeutic efficacy.

Keywords: *Andrographis paniculata*, Andrographolide, COVID-19, Anti-inflammatory, Antiviral, Nano drug delivery system

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Type 1 and type 2 myocardial infarction in a sub-Saharan Africa population: data from Abidjan Heart Institute

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Objective: From an observational acute coronary syndrome registry in Côte d'Ivoire, we aimed to address incidence, clinical, management and in-hospital outcomes of T2MI compared with T1MI patients.

Patients and methods: Cross-sectional monocentric study using data from Abidjan Heart Institute. All MI patients included between 2018 and 2022 who underwent coronary angiography were considered. MI cases were adjudicated into T1MI and T2MI, based on criteria defined in the fourth UDMI. For each patient, in-hospital data, and outcomes were collected and compared.

Results: 441 met the definition of T1MI or T2MI in the study population. T2MI accounted for 14.1% of cases (62/441). T2MI were slightly younger (54 versus 58 years), with a higher rate of women. Classical CV risk factors (hypertension, diabetes, dyslipidemia, and smoking) were more frequent in T1MI. T2MI patients had more frequent history of HF or LV dysfunction (p = 0.025). Prior and on admission ECG AF/flutter were much more common in T2MI (p < 0.001). Compared to T1MI, T2MI had less severe CAD, with less frequent multivessel disease (p < 0.001). The main triggering factors for T2MI were coronary embolism (24.2%), severe hypertension ± LVH (22.6%) and tachy-arrythmia (16.1%). Anemia was rarely involved (3.2%).

In agreement with history and ECG findings, AF/flutter, and stroke showed only a non-significant trend toward higher rate in T2MI. Overall hospital mortality was 2.3%. Albeit without significant difference, death rates in T1MI trend to be higher than in T2MI.

Conclusion: In a sub-Saharan Africa population, T2MI was characterized by younger age, less frequent risk factors and more frequent AF/flutter. Coronary embolism was the main triggering factor in T2MI. T2MI patients had less severe CAD compared to T1MI. It would be interesting to implement prospective and multicentric studies in sub-Saharan Africa to refine these results and assess the long-term prognosis of T2MI patients.

Keywords: Type 1 myocardial infarction, Type 2 myocardial infarction, Coronary artery disease, Sub-Saharan Africa

Co-contribution of inflammation and biomechanics during the development and persistence of keloid fibrosis

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Fibrosis is a major public health problem defined as the excessive accumulation of extracellular matrix (ECM) in tissue. All organs can be affected by fibrosis and no preventive or curative treatment is currently available. Fibrosis could be the consequence of a deregulated tissue repair process, often associated with inflammation, such as in keloid disease. Keloids are defined as a cutaneous fibrotic disorder characterized by excessive proliferation of fibroblasts and their subsequent contribution to the over accumulation of extracellular matrix in the dermis.

Recent publication reviewed the immunological mechanisms of keloids (Lee *et al*, frontier immunol, march 2023) and ECM stiffness as a central clue for skin fibrosis (Wang *et al*, Frontiers in Molecular BioSciences, march 2023). To our knowledge, the synergestic contribution of both inflammation and mechanical factors is still an opened problem in keloid research.

To adress this issue, our project aims to elucidate the cellular and tissue mechanisms responsible for skin fibrosis along a "macrophage-fibroblast-matrix" axis. Indeed, during healing, the activity of fibroblasts is regulated by immune cells, namely macrophages which are highly plastic immune cells that could present different phenotypes. Type M1 macrophages are described as pro-inflammatory and type M2 macrophages as pro-healing/pro-fibrotic, since they synthesize TGF-β1 and activate fibroblasts into myofibroblasts (synthesis of ECM and α-SMA). The ECM is also able to regulate fibrosis at the cellular level via mechano-transduction and modulation of the matrisome.

Understanding this complex interplay may ultimately lead to develop more effective treatments against keloids. In order to propose new therapeutic options for the prevention and management of tissue fibrosis, we proposed to organize our research as 4 main axes:

- Characterize *in vivo* the macrophagic and fibroblastic phenotype and functionalities associated with fibrosis;
- Model *in vitro* their mutual interactions in a microenvironment subjected to mechanical and inflammatory stimuli;
- Decode, from these models, the signalling pathways involved;
- Investigate new regulatory mechanisms at cellular and/or molecular level to resolve or prevent fibrosis.

Keywords: Keloids, Fibroblast, Macrophages, ECM, Inflammation, Mechano-transduction

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Investigating metabolic cost to probe gravity-related effort minimization

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The Central Nervous System (CNS) is thought to select movement trajectories that optimize certain criteria within the environment. For example, previous work revealed that young adults' arm movements are tuned to harvest gravity effects and reduce muscle effort, as supported by kinematic and electromyographic (EMG) parameters (Gaveau *et al.*, 2016, 2021). Also, Poirier *et al.* (2022) revealed that young adults produce sub-optimal movements with their non-dominant arm, compared to their dominant one. The present study aims to test this gravity optimization theory by examining energy consumption through exhaled gas analysis.

30 young adults (15 females; 25 years old) were divided into two groups. i) one group performed four blocks of horizontal movements and four blocks of vertical movements with their right dominant arm. ii) the second group performed four blocks of vertical movements with their right dominant arm and four blocks with their left non-dominant arm. One block consists of 120 consecutive single degree of freedom arm movements. The energy consumption was measured using a Cosmed K5 portable metabolic system using breath-by-breath mode (BxB). We also recorded EMG signals from 4 shoulder muscles (Anterior and posterior deltoids for vertical movements and major pectoral as well as infraspinous for horizontal movements) using bipolar surface electrodes (1000Hz) and the kinematics of 10 markers using a custom model from a Vicon motion capture system (200Hz).

Preliminary results tend to support the effort-optimization theory, which assumes an internal model of gravity to leverage its effects instead of compensating for them. We observed significant higher metabolic power during horizontal compared to vertical movements, as well as with the left non-dominant arm compared to the right dominant one.

Additional data are being collected.

<u>Keywords:</u> effort minimization, metabolic cost, kinematics, gravity, EMG

Study of chemical constituents and steroid 5 alpha-reductase inhibitory activities of teak leaves using metabolomics approach

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Excessive dihydrotestosterone)DHT(is an initial cause of androgenic alopecia)AGA(or male pattern baldness. DHT is metabolized from testosterone by the enzyme steroid 5-alpha reductase)S5AR(, therefore S5AR inhibition is an acceptable way for the treatment of AGA. The teak leaf extract was demonstrated to have S5AR inhibitory activity. However, teak leaves collected from different places and at different times show inconstancy in this activity. The purposes of this study were to determine the factors affecting S5AR inhibitory activity of teak leaves including leaf age, harvesting times, and plant sources as well as to identify the S5AR inhibitors using the MS-based metabolomics approach. Teak leaves were collected from 14 provinces around Thailand. The samples were divided into young and mature leaves and harvested every 3 months in 1 year. Dried leaves were extracted with ethanol. The extracts were

then investigated S5AR inhibitory activity parallel with chemical profiles by the LC-MS technique. The acquired data showing the feature intensity, retention time, and S5AR inhibitory activity were submitted to multivariate analysis. The resulting PCA)Principal component analysis(indicated no differences in terms of chemical constituents between leaf age and harvesting times. Interestingly, the sources of leaves had a significant effect on the S5AR inhibitory activity. The S-plot of OPLS)Orthogonal partial least squares(model navigated to some bioactive compounds which were then isolated, identified, and proved to have high S5AR inhibitory activity including)+(-eperua-7,13-dien-15-oic acid)$IC_{50} = 14.65 \pm 0.31$ µM(, hydroxysesamone)$IC_{50} = 127.23 \pm 0.81$ µM(and rhinocerotinoic acid)$70.45 \pm 1.38\%$ at final concentration 5 µM(compared with standard treatment)finasteride; $IC_{50} = 0.73 \pm 0.03$ µM(. Our study highlighted the application of metabolomics for navigating biomarkers which can avoid re-isolation of known bioactive compounds and reduce time consumption to discover the biomarker in complex chemical constituents.

Keywords: Teak, *Tectona grandis* L., Metabolomics, Steroid 5 alpha-reductase inhibitor

Botanique et Environnement

Study of the stress-related signalling of endoplasmic reticulum in grapevine immunity associated to LysM receptor kinases (VvLYKs)

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In the actual situation of decreasing the use of chemicals in agriculture, enhancing our understanding of plant immunity is a critical task to develop more sustainable plant health protection methods. An interesting strategy is to study how plants, and in particular grapevine, perceives and responds to different microorganisms. Microorganisms are notably recognized by LysM Receptor-like Kinase (LYKs) and previous works have identified 16 LYKs encoded by the grapevine genome (VvLYKs) (Roudaire et al. 2023). Among them, VvLYK1-1, VvLYK1-2 and VvLYK5-1 are involved in chitin perception and thus play a role in the plant immunity. Interestingly, immune responses are also involved during symbiotic interaction but the receptors involved in this process are still unknown. In addition, it has been demonstrated that the Unfolded Protein Response (UPR), which is activated when unfolded proteins accumulate in the endoplasmic reticulum, is also involved during the plant immune response. It's therefore important to improve our knowledge about the role of the different grapevine LYK receptors involved in the balance between immunity and symbiosis and in addition to determine the role of stress-related signalling of endoplasmic reticulum and the consequent activation of the UPR in these two different pathways.

In this context, we aim to characterize new VvLYKs involved in the perception of Myc-factors which allow the down-regulation of the plant immunity during the establishment of mycorrhizal symbiosis. In addition we also intend to characterize the UPR signalling pathways in grapevine which is still unknown and finally how differents biotic factors are involved in the stress-related signalling of endoplasmic reticulum.

Nuclear involvement of the Cell Division Cycle 48 protein during the plant immune response

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The control of protein homeostasis, a balance between their synthesis and degradation, also called proteostasis, is essential for cell survival. Any imbalance of the proteome, for instance triggered by a stress, leads to an accumulation of misfolded proteins leading to proteotoxic stress that can induce cell death. The ubiquitin proteasome system (UPS) is a major actor in the selective degradation of misfolded proteins to preserve proteome balance.

The chaperone-like Cdc48 is a member of the AAA+ ATPase enzyme family which is conserved in mammals (VCP), yeasts and plants (Cdc48: Cell Division Cycle 48/p97). Cdc48/VCP is a cytosolic and nuclear protein which segregates misfolded proteins from subcellular structures or protein complexes, and brings them to the proteasome to facilitate their recycling or degradation. Therefore, Cdc48/VCP is involved in numerous cellular pathways such as membranes associated degradation, cell cycle regulation, genome stability, vesicular trafficking, autophagy and apoptosis. The role of Cdc48 in response to biotic stresses has been investigated. However, nuclear function(s) of Cdc48 in plant immunity remain unclear and poorly understood.

In this project, we aimed to characterize the nuclear function(s) of the Cdc48 protein during the plant immune response triggered by cryptogein (an elicitor produced by Phytophthora cryptogea) in tobacco cells. We analyzed the nuclear dynamic of Cdc48 under normal and elicitation conditions through Fluorescence Correlation Spectroscopy analysis (FCS). This comparison has shown that during plant immune response, (i) the nuclear mobility of Cdc48 increased and (ii) Cdc48 interacted more quickly with more proteins. Then, nuclear partners interacting with the endogenous nuclear Cdc48 were identified through immunoprecipitation and mass spectrometry analysis.

To summarize, this work provides new information regarding the role of Cdc48 and its dynamic in the nucleus during plant immunity.

Adaptation of plant root exudates to a multi-contaminated soil in a context of phytoremediation

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The impacts of anthropic activities on soil, especially contamination that are resulting, has many negative consequences on ecosystem functions. To evaluate the ecological consequences of soil degradation, it is crucial to improve our knowledges on soil biota interactions and the impacts of their relations with metal and organic contaminants. The management of contaminating wasteland with nature-based solution (NBS) to limit the environmental impact of contamination is becoming attractive. To improve the efficiency of these approaches, one of the key factors is the ability of species to adapt to the local edaphic conditions. Plants are producing a wide variety of chemicals that are released to the soil compartment to recruit beneficial microbes that are able to protect plant against stress caused by contamination. If the interactions between plants and microorganisms are described in soil with mono-contamination, few data are available in case of multi-contamination. The present study aims at identifying the variation in root exudate profiles of a plant species exposed to either trace elements (TE), or polycyclic aromatic hydrocarbons (PAH) or both. Our results highlighted significant variations in the production of some organic acids, such as isocitric acid that was released in TE-contaminated soils at higher amounts as compared with PAH-contaminated soils, control or multi-contaminated soils. Moreover, fumaric and malic acid releases decreased in comparison to control under PAH exposure. These variations are linked to the modulation of rhizospheric enzymatic activities, especially protease and phosphatase. These results demonstrate the ability of plants to modulate their root exudation profile when exposed to multiple pollutants. The final outputs of this work will highlight the mains biological processes involved in the restoration of soil quality to improve the ecological parameters of contaminated soils.

Keywords: Root exudates, multi-contamination, phytoremediation, microorganisms

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Effect of fragment weight and bud number on *Elymus repens* belowground regrowth from rhizomes

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Perennial weeds have become an increasing problem with the reduction of herbicide use and tillage. Because of their capacity to regenerate from vegetative organs, such as roots and rhizomes, they must be controlled with different management techniques than annuals. To date, few studies exist on this topic and farmers often lack solutions to control perennials in their cropping systems. Management strategies must focus on the depletion of the regenerative organ reserves to hamper the production of new shoots. However, there is a need for a better understanding of belowground organs physiology and the determining factors of their regrowth capacities.

Our aim was to assess shoot elongation speed from belowground rhizome fragments of *Elymus repens* according to 1) its weight, which is related to the amount of available reserves, and 2) the number of buds initially present on it. A pot experiment was carried out in a greenhouse: fragments of rhizomes with different weights or different visible bud numbers were buried into 6-L pots, and the number and length of the produced shoots were measured dynamically during the experiment. The effects of fragment weight and the number of buds on (1) the probability

that a fragment produce a shoot, (2) shoot growth rate, (3) shoot number and (4) maximum shoot length were analyzed. Also, shoot length was quantified as a function of hydrothermal time since bud sprouting.

These results will be used to model regrowth of perennials from below-ground fragments after tillage in a cropping system simulation model (FLORSYS). This model simulates daily weed dynamics and crop production over the years from cropping system and pedoclimate. The ultimate goal will be to identify agroecological weed management strategies and to help farmers to redesign their cropping systems.

Keywords: Perennial weeds regeneration, fragment size, number of buds, vegetative organs, rhizomes, Elymus repens, shoot growth rate

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Detection of precursors to the triggering of gravitational instabilities: multi-parameter chronicles, artificial intelligence and modelling

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Landslides are gravitational movements that occur under the combined action of predisposing factors (topography, lithology, structure of the massif, etc.), triggering factors (precipitation, earthquakes) and propagation factors. With recent climate change, mountain territories have experienced an increase in the risk associated with landslides. This has led to the implementation of monitoring systems (multi-sensor probes) and forecasting models (susceptibility map, time displacement forecast) to arrive at warning systems.

Several methods of temporal forecasting landslides exist and are already employed but are limited only to landslides considered. This limitation is due to the complexity generated by the predisposition factors (varied lithology, fracking evolution) and by their relationship with the external parameters (infiltration and circulation of rain).

The acquisition of long data chronicles on many landslides now allows the use of new forecasting models such as artificial intelligence and machine learning.

The objective of this thesis is therefore to propose a model for forecasting landslides over time with artificial intelligence based on the use of long data chronicles (displacement, rainfall, conductivity, etc.) as well as physical laws and models. The aim will be to identify the precursors to the triggering of gravity instabilities and to be able to adapt to any context of landslides.

Initially, the objective will be to create a database using and analyzing raw data from long data chronicles acquired on the Séchilienne landslide. This database will aim to build a first displacement forecasting model based on machine learning using several variables (displacement-rain, displacement-rain-chemistry, displacement-chemistry, etc.).

Keywords: landslides, temporal forecasting model, machine learning, rainfall, data chronicles, multivariate analysis

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New molecular phylogeny sheds a new light on the paleobiogeographic history of the genus *Arbacia* Gray, 1835 (Arbacioida, Echinoidea)

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The echinoid genus Arbacia comprises five extant species distributed into two distinct areas: two species occur along the Central and North Atlantic coasts of America, West Africa, and Mediterranean Sea; the last three species are present along the Pacific coasts of North and South America, except for Arbacia dufresnii that occurs in the Magellanic Province, from Puerto Montt (Chile) to Buenos Aires (Argentina). Previous works suggest that Arbacia originated in temperate zones of the Southern Hemisphere and that the three Pacific species evolved isolated from Atlantic ones after the closure of the Isthmus of Panama (3 My). A new phylogenetic analysis was performed based on multiple molecular markers (COI, 16s, CRA, 18s, 28s, histone3) and reveals a topology that drastically differs from previous ones. The phylogeny shows that a species of another genus, Tetrapygus niger, is the sister species to Arbacia dufresnii, hence questioning the taxonomic status of the monospecific genus Tetrapygus. The topology also shows two well-supported subclades: one comprises the four Pacific species, A. stellata, A. spatuligera, A. dufresnii and T. niger, and the other one the two Atlantic species A. lixula and A. punctulata. Pacific species show low levels of intraspecific genetic diversity compared to Atlantic ones which have intraspecific variation levels three to six times higher than the Pacific ones. A. punctulata includes three distinct sub-entities restricted to the Caribbean Sea, the Gulf of Mexico, and the Atlantic coasts of North America respectively. These genetic differences are associated with morphological variations.

This study suggests a different evolutionary history of the genus than previously thought with two subclades having diverged well before the closure of the Isthmus of Panama. The dated phylogeny based on mutation rates provides estimated divergence times that are consistent with fossil data and raise further questions about speciation and biogeographic processes at play.

Keywords: Echinoid, Biogeography, Molecular phylogeny

Particulate pollution during the Covid period: analysis of 2020 lockdowns in Dijon and Montbéliard

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This study focuses on the characterization of particulate pollution in two medium-sized cities with a strong contrast in terms of air quality, Dijon and Montbéliard. Measurements of PM10 ($d < 10\,\mu m$) and PM2.5 ($d < 2.5\,\mu m$) concentrations were used from two reference stations over the 2015-2022 period and specifically for the 2020 year to determine the effects of governmental measures taken during the Covid-19 crisis. First results are encouraging. If the Dijon station does not experiment an improvement of its air quality during the first lockdown

due to the influence of agriculture, it seems to be particularly exposed to PM2.5 form domestic heating during the second lockdown. This characteristic is shared with Montbéliard, exposed to the same phenomenon as well as to a strong industrial activity.

"Heading for extinction" by Cyril Bousquet and Pierre Clos

La conférence « Heading for Extinction » que nous vous proposons aborde la question de l'urgence écologique en deux parties :

L'objectif de la première sera de vous informer sur les réalités climatiques et écologiques actuelles et futures. Au programme : limites planétaires dépassées, vulgarisation des derniers rapports du GIEC, présentation de graphiques sur la disparition du vivant, anticipation des conséquences géopolitiques locales et mondiales.

Dans un second temps nous aborderons la question des actions nécessaires pour lutter contre ces dérèglements avec notamment une analyse critique des actions étatiques et une remise en question des modes d'actions individuels et militants.

« Au gré du climat et des sociétés humaines,1000 ans d'évolution d'une colonie d'oiseaux à Ukaleqarteq, Groenland » by Emilie Gauthier

Les mergules nains (*Alle alle*), viennent se reproduire sur les cotes du Groenland tous les étés. Les études s'intéressant à ces oiseaux sont souvent centrées sur leur adaptation au réchauffement climatique et sur l'impact des polluants sur leur survie. Certaines colonies sont ainsi suivies depuis près de 20 ans mais nul ne sait depuis combien de temps ces oiseaux reviennent au Groenland, ni comment les variations climatiques passées ont pu affecter leur période de reproduction. Le site d'Ukaleqarteq sur la côte Est du Groenland (70°N, secteur de Liverpool land) est caractérisé par la présence d'une colonie de plusieurs centaines de milliers de mergules. Ces oiseaux sont des ingénieurs des écosystèmes : par le biais de leurs déjections, ils transforment leur environnement favorisant un flore très particulière et l'accumulation de dépôts organiques. Ces dépôts offrent aux chercheurs des archives sédimentaires riches des informations que fournissent divers paramètres (grains de pollen, graines, isotopes, éléments traces métalliques, azote, carbone…) indispensables pour comprendre, sur le temps long, l'évolution de cet environnement typique de la colonie. À Ukaleqarteq, les études en cours ont déjà montré que, depuis 1000 ans, la pression exercée par les oiseaux sur leur environnement a varié au gré des variations climatiques mais aussi des présences humaines. Au pied de l'aire de nidification se trouvent trois cabanes de chasse, dont une est actuellement utilisée par les habitants du village voisin d'Ittoqqortoormiit, les deux autres datant respectivement des années 80 et des années 30. Un peu plus loin, à environ un kilomètre, a été localisé et prospecté un site archéologique composé d'une soixantaine de structures (tentes, caches et habitats semi-enterrés). Les oiseaux sont chassés par les Inuit et l'étaient par leurs ancêtres. Les mergules ont façonné le paysage d'Ukaleqarteq et leur quantité a évolué en fonction du climat mais aussi des différents prédateurs, dont l'Homme, affectant leur survie à cette latitude.

Infos sur les partenaires de l'évènement

Ecole Doctorale Environnement-Santé : https://e2s.ubfc.fr/

UBFC : https://www.ubfc.fr/

AJC-ES : https://ub-link.u-bourgogne.fr/associations/ajc-es.html

La ville de Besançon : https://www.besancon.fr/

La médicale : https://www.lamedicale.fr/

La CASDEN : https://www.casden.fr/

Smaltis : https://www.smaltis.fr/

Chrono-environnement : https://chrono-environnement.univ-fcomte.fr/

Dimacell : https://dimacell.fr/

Le Rucher de la Brèche : 5 Le Village, 70280 Saint-Bresson

https://www.jveuxdulocal70.fr/annuaire/producteur/gaec-le-rucher-de-la-breche-121.html