Société de Physiologie

IMPACT DU MICROENVIRONNEMENT SUR LES FONCTIONS PHYSIOLOGIQUES

5EME CONGRÈS DE PHYSIOLOGIE ET BIOLOGIE INTÉGRATIVE

LYON

FACULTE DE MÉDECINE LAENNEC
22 -24 JUIN 2022

EDITORIAL

La Société de Physiologie et de Biologie Intégrative (SPBI) a le plaisir de vous accueillir à **Lyon** pour le **5ème Congrès de *Physiologie et de Biologie Intégrative* du 22 au 24 juin 2022 et le *89ème Congrès de la Société de Physiologie.***

Le thème principal du congrès sera : **« Impact du microenvironnement sur les fonctions physiologiques »**. Ce thème transversal et fédérateur sera l'occasion de revisiter le milieu intérieur de Claude Bernard en l'ouvrant au microenvironnement cellulaire et tissulaire qui impacte les fonctions. Le choix a été fait de **casser les frontières entre nos différentes disciplines**, la physiologie étant l'intégration et le retentissement de la fonction d'un organe sur les autres, **le dialogue entre organes**.

Le congrès se déroulera dans les locaux de la **Faculté de Médecine de Laennec** avec un **programme résolument tourné vers les interactions et l'innovation.** Ce congrès sera une nouvelle occasion de réunir des **étudiants**, **chercheurs, universitaires et cliniciens** dans les disciplines les plus variées de la Physiologie, autour de conférences thématiques abordées par des **invités nationaux prestigieux** !

Nous souhaitons laisser une large place **à l'interaction** au sein des sessions scientifiques et ateliers mais aussi au cours des « pauses cafés » dédiées qui permettront aux **différentes générations de physiologistes de se retrouver et d'échanger.**

Les plus jeunes physiologistes seront sollicités pour exposer leurs derniers travaux dont les résumés seront publiés dans **Acta Physiologica**, l'organe de diffusion de la « *Federation of European Physiological Societies* ». De nombreux prix et bourses de voyage seront également décernés pour les meilleures communications affichées et orales.

Des sessions seront co-organisées avec la Société d'**Ecophysiologie** et la **Société Française de Nutrition.**

Ce congrès sera également l'occasion de replacer notre discipline au centre de **l'innovation pédagogique** avec une session organisée par le **Collège des Enseignants de Physiologie en Santé** (CFEUPS) et une session dédiée à **l'actualité pédagogique** et la **License Shift**.

Nous vous attendons nombreux à ce **5ème Congrès de *Physiologie et de Biologie Intégrative*** qui vous accueillera pour des échanges fructueux dans le cadre gourmand de la Cité des gones.

Inscrivez Lyon comme destination à ne pas manquer pour 2022 !

Pour le comité d'organisation local et national
Dominique Sigaudo-Roussel (présidente du CLO et du CS de la SPBI)
Jean-Claude Dussaule (président SPBI)

Merci à nos partenaires

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PROGRAMME

WORKSHOPS (Inscription obligatoire —1 atelier au choix) - 11H—13H

⇒ **Expérimentation animale : Modérateur : B. FROMY — F. RAJAS** — Salle LA103

- Argument pour/contre l'expérimentation animale **Sabine RICHARD (Lyon)**
- Biais dans l'observance des états de stress, douleur, souffrance chez les animaux et fatigue compassionnelle **Dominique AUTIER-DERIAN (Lyon)**

⇒ **Nouveautés en Physiologie : Modérateur : S. LEMOINE—T. BOCHATON** — Salle LA106

- Imagerie multimodale des pathologies neuro-vasculaires : de l'exploration dans les modèles pré-cliniques à la translation clinique **Emmanuelle CANET-SOULAS (Lyon)**
- Que peut nous apporter la spectroscopie au sodium et au phosphore en physiologie ? **Sandrine LEMOINE (Lyon)**
- Explorations fonctionnelles: comment faire du neuf avec du vieux..... **Pierre ABRAHAM (Angers)**
- La révolution des ARN interférents **Marie COURBEBAISSE (Paris)**

⇒ **Evaluation à l'effort : Modérateur : R. RICHARD—F. COSTES** — Salle LA104

- Evaluation à l'effort couplée aux mesures non invasives hémodynamique et d'oxygénation tissulaire

Atelier sponsorisé par : Cosmed & PhysioFlow

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12 H—14H ACCUEIL ET CEREMONIE D'OUVERTURE

14H—14H45 Conférence plénière — AMPHI 1

Dialogue intestin-cerveau et régulation de l'homéostasie énergétique
Gilles MITHIEUX (Lyon)

14H45—16H Sessions jeunes chercheurs — AMPHI 1

Modérateurs: E. LETAVERNIER - D. SIGAUDO ROUSSEL

- **Titre à venir - Nahid TABIBZADEH (Paris)**
- Nouveaux rôles du cil primaire dans l'homéostasie rénal. **- Frank BIENAIME (Paris)**
- Therapeutic approach based on GDF5 to counteract age-related muscle wasting **- Sestina FALCONE (Paris)**
- Déficience en orexine / hypocrétine chez l'homme : conséquences et pathophysiologie, la Narcolepsie de Type 1 comme modèle expérimental - **Lucie BARATEAU (Montpellier)**

16H—16H30 PAUSE—VISITE DES STANDS—POSTERS — HALL A

16H30—18H Session Innovations Pédagogiques — AMPHI 1

Modérateurs: H. BENOIT *(Grenoble)* B. CHENUEL (Nancy)

- Présentation du projet SHIFT - **Henri BENOIT (Grenoble)**
- Introduction aux Learning Analytics et proposition d'une approche de design pédagogique et d'une méthodologie d'analyse pour une meilleure exploitation des traces d'apprentissage (dans le cadre du projet HyPE-13 = Hybrider et Partager les Enseignements / PIA3- Hybridation des formations) **Ernesto EXPOSITO (Pau)**
- Rôle des processus mentaux dans la conception, le développement et la validation de solutions numériques et pédagogiques pour l'apprentissage de l'anatomie et du geste médical
EL HOYEK NADY (Lyon) - B. CHENUEL (Nancy)

18H—18h45 Conférence plénière — AMPHI 1

Vers une physiologie de la conscience : du laboratoire au chevet du malade et vice-versa

Lionel NACCACHE (Paris)

18H45—19H15 — AMPHI 1

Assemblée Générale du Collège des Enseignants en Physiologie — CFEUPS

19H15-19H45 — AMPHI 1

Histoire de la Médecine Expérimentale Claude Bernard

Microenvironnements et milieux internes : la naissance d'un nouveau concept de milieu en biologie dans le contexte de la physiologie bernardienne **Emmanuel D'HOMBRES (Lyon)**

20H15—22H COCKTAIL DE BIENVENUE — HOTEL ODALYS

Mercredi 22 juin

Jeudi 23 juin

8h30-10h Conférences Plénières

AMPHI 1

- Intégration sensorielle au cours du sommeil - **Hélène BASTUJI (Lyon)**
- Détection orosensorielle des lipides - **Naim KHAN (Dijon)**

10H—10H30 PAUSE CAFE—VISITE DES STANDS—POSTERS — HALL A

10H30—12H30

Session Ecophysiologie

AMPHI 2

Modérateurs : Karine SALIN (Brest) Yann VOITURON (Lyon)

Des carences en Oméga 3 peuvent endommager la fonction cardiaque—illustration avec un modèle poisson **Marie VAGNER (Brest)**

Behavioral, physiological and metabolic responses to long-term food deprivation (18 months) and subsequent renutrition in a cave amphibian, Proteus anguinus. **F.HERVANT (Lyon)**

Les mécanismes de protection contre la dyslipidémie athérogène chez l'ours en hibernation - **Sylvain GIROUD (Vienne)**

Muscle biopsies : consequences on muscle metabolism and swimming performance in goldfish **Elisa THORAL (Lyon)**

Session sponsorisée par : pyroscience

Session Société Française de Nutrition Genre et Physiologie Métabolique

AMPHI 1

Modérateurs : Luc PENICAUD (Toulouse) - Pascal CRENN (Paris)

Métabolisme énergétique cellulaire et sexe ? - **Eric FONTAINE (Grenoble)**

Différences sexuelles dans la régulation métabolique et la susceptibilité au diabète - **Pierre GOURDY (Toulouse)**

Y a-t-il encore des raisons pour exclure un des deux genres dans les protocoles d'études ? - **Christian DUALE (Clermont-Ferrand)**

12H30—13H CAFE RENCONTRE AVEC LES ORATEURS — HALL A

12H30—14H DEJEUNER —VISITE DES STANDS—POSTERS — HALL A

14H—15H30 : Groupes Thématiques Transversaux —1ère partie

Environnement micro-inflammatoire

AMPHI 1

Modérateurs : Delphine BAETZ Jean-Sébastien SILVESTRE

Micro environnement inflammatoire et allostasie cardiaque **Jean-Sébastien SILVESTRE (Paris)**

Sonder l'environnement inflammatoire et la réponse immunitaire à l'aide de l'imagerie in vivo : applications à l'AVC **Marlène WIART (Lyon)**

Communications orales sélectionnées

Effect of Urine Alkalinization on Urinary Inflammatory Markers Analyzed by Mass Spectrometry in Patients with Cystinuria. **Caroline BERTOYE (Paris)**

Correlation between hemodynamic parameters and cytokines in a porcine model of sepsis. **C. SLEK (Lyon)**

Genetic expression and immunofluorescence mapping of Neuron Navigator 1 highlight potential therapeutic targets in anti-inflammatory treatment of aortic valves stenosis. **David HUPIN (St Etienne)**

Dill extract (Anethum graveolens) could preserve dermal elastin network during inflammation. **Géraldine AIMOND (Lyon)**

Environnement microbien

AMPHI 2

Modérateur : Filipe DE VADDER (Lyon)

Microbiote intestinal, obésité et préférences alimentaires: rôles du microbiote intestinal dans le comportement alimentaire de l'hôte. **Amandine EVERARD (Louvain)**

Comment le métabolisme énergétique et le dynamisme osseux s'adaptent à la température ambiante à travers le microbiote intestinal **Claire CHEVALIER (Genève)**

Environnement microbien et nutrition: comment façonner un deuxième cerveau dans l'intestin **Filipe DE VADER (Lyon)**

Communications orales sélectionnées

Juvenile protein malnutrition and Lactiplantibacillus plantarumWJL modulate host physiology via GLP-1-secreting cells of the mouse ileum **Amélie JOLY (Lyon)**

Environnement hypoxique

AMPHI 4

Modérateurs : Philippe CONNES Emeric STAUFFER (Lyon)

Altitude, fonction vasculaire, rhéologie du sang et mal chronique des montagnes **Julien BRUGNIAUX (Grenoble) Emeric STAUFFER (Lyon)**

Drépanocytose : physiopathologie et impact de l'hypoxémie nocturne **Elie NADER (Lyon)**

Conditionnement hypoxique et troubles métaboliques **Samuel VERGES (Grenoble)**

Communications orales sélectionnées

Modeling the oxygen transport to the myocardium at maximal exercise at high altitude **Jean-Paul Richalet (Paris)**

Heart rate variation after a 6-minute walk test during lower limb ischemia **Nafi OUADRAOGO (Burkina Faso)**

15H30—16H VISITE DES STANDS—POSTERS-CAFE RENCONTRE AVEC LES ORATEURS — HALL A

16H—17H30 : Groupes Thématiques Transversaux —2ème partie

Environnement métabolique

AMPHI 1

Modérateur : Fabienne RAJAS (Lyon) Philippe VALET (Toulouse)

Rôle des échanges calciques « réticulum endoplasmique-mitochondrie » en physiologie et pathophysiologie cardiaque **Mélanie PAILLARD (Lyon)**

Effets métaboliques de l'apeline en physiologie, perspectives thérapeutiques ? **Philippe VALET (Toulouse)**

Communications orales sélectionnées

Impact of adipose-tissue micro-environment on breast cancer progression, in obese individuals **Assia ELJAAFARI (Lyon)**

Association Between Nocturnal Blood Pressure Dipping and Chronic Kidney Disease **Justina MOTIEJUNAITE (Paris)**

A new role of endoplasmic reticulum-mitochondria contact sites in nutrient-inducedglucagon-like peptide 1 secretion by cells **Alexandre HUMBERT (Lyon)**

Environnement phospho-calcique

AMPHI 2

Modérateurs : Emmanuel LETAVERNIER (Paris) Sandrine LEMOINE (Lyon)

La phosphatase alcaline à la croisée des chemins entre syndrome métabolique et calcification cardiovasculaire **David MAGNE (Lyon)**

Homéostasie du pyrophosphate dans les maladies pro-calcifiantes **Isabelle RUBERA (Nice)**

FGF-23 : régulation de l'homéostasie du phosphate et autres rôles **Dominique PRIE (Paris)**

Communications orales sélectionnées

X Linked Hypophosphatemia, not only a skeletal disease but also a chronic inflammatory state **Candide ALIOLI (Limoges)**

Plasma oxalate concentration in enteric hyperoxaluria related to short bowel syndrome : OXAGO study **Christophe Grocholski (Lyon)**

Renal Adaptation to a Low Potassium Diet: Implication of the Growth Factor GDF15 **Samia Lasaad (Paris)**

Environnement sensoriel

AMPHI 4

Modérateurs : Bérengère FROMY Laure PETER-DEREX (Lyon)

Perception du sommeil et de la veille : comment réconcilier explorations physiologiques et subjectivité ? **Laure PETER-DEREX (Lyon)**

Rôle des phosphocholines dans les douleurs musculosquelettiques **Fabien MARCHAND (Clermont Ferrand)**

Sensorialité de la peau **Bérengère FROMY (Lyon)**

Communications orales sélectionnées

Role of TRPV3 channel in the default of cutaneous thermoregulation during aging **Lisa MARTIN (Lyon)**

Intestinal gluconeogenesis could modulate learning process **Justine VILY PETIT (Lyon)**

17H30—18H VISITE DES STANDS—POSTERS-CAFE RENCONTRE AVEC LES ORATEURS

18H-19H Conférence Plénière

AMPHI 1

Beyond to neurons in the neuroendocrine control of metabolism

Cristina GARCIA CACERES (Munich)

20H—SOIREE CONVIVIALE — LE BELLONA

Vendredi 24 juin

8h-9h Assemblée Générale SPBI — AMPHI 1

9H-10H Conférence Plénière — AMPHI 1

Maladies métaboliques, Microbiote et Vitamines B
Karine CLEMENT (Paris)

10H-12H Session Muscle et Exercice — AMPHI 1
Modérateurs : Elise Belaidi (Grenoble) - Vincent MARTIN (Clermont-Ferrand)

Bénéfices de l'entrainement en endurance sur l'aptitude physique et le muscle squelettique chez les patients drépanocytaires homozygotes - **Angèle MERLET (St Etienne)**

Myokines, exercice et métabolisme énergétique - **Cédric MORO (Toulouse)**

Neuromuscular electrical stimulation training as an innovative therapeutic strategy to minimize cancer-induced cachexia - **Julien GONDIN (Lyon)**

Communications orales sélectionnées
Characterization of the combined effects of exercise and immune-chemotherapy treatments on tumour growth in MC38 colorectal cancer mice **Manon GOUEZ (Lyon)**

Sex differences in skeletal muscle regeneration in a mouse model of lengthening contraction-induced severe damage **Charline JOMARD (Lyon)**

Exercise-induced cardiac troponin release is associated with level of exercise training **David HUPIN (St Etienne)**

12H- 13H CLOTURE ET REMISE DES PRIX — AMPHI 1

Comité d'Organisation Local

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INFORMATIONS PRATIQUES

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Communications orales

Session Ecophysiologie

Behavioral, physiological and metabolic responses to long-term food deprivation (18 months) and subsequent renutrition in a cave amphibian, *Proteus anguinus*.

Frédéric Hervant
Université Claude Bernard Lyon 1, Univ Lyon, CNRS, ENTPE, UMR 5023 LEHNA, Domaine Universitaire de la Doua, 6 rue R. Dubois, 69622 Villeurbanne.

Subterranean ecosystems are characterized by severely limited food supplies during most of the year because of the lack of autotrophic production and sporadic allochthonous input. Cave-dwelling organisms thus have to cope with fasting periods that can extend from a month to a year (Hervant et al. 1999, 2001, 2002, Issartel et al. 2010; Salin et al. 2010). The ability to withstand and recover from long periods of nutritional stress is a critical adaptation for survival in food-limited systems. Therefore, several subterranean species have evolved behavioral, physiological and/or metabolic adaptations that allow them to exploit harsh subterranean environments successfully. Thus, the groundwater crustaceans *Niphargus rhenorhodanensis*, *N. virei* and *Stenasellus virei* and the cave salamander *Proteus anguinus* can survive without feeding for periods exceeding 200 days (Hervant et al. 1999, 2001, 2002, Issartel et al. 2010).

Here we report on investigations designed to highlight behavioral (activity), physiological (oxygen consumption) and metabolic (changes in the intermediary and energy metabolism, qualitative and/or quantitative changes of body composition) responses to prolonged food deprivation (18 months) and subsequent refeeding (15 days) in the cave amphibian *Proteus anguinus*. Based on this study and previous ones, we proposed a general adaptive strategy for subterranean organisms that includes reduced activity and metabolic rates, high amounts of energy stores (glycogen and triglycerides), and low utilization rates of body stores (with successive periods of glucidic, lipidic, and finally lipido-proteic-dominant catabolism, allowing a large protein sparing). Moreover, during refeeding, these organisms exhibit a fast reconstruction of energy reserves.

MUSCLE BIOPSIES: CONSEQUENCES ON MUSCLE METABOLISM AND SWIMMING PERFORMANCE IN GOLDFISH

Lauréliane Dargère [1], Ione Medina-Suárez [2], Angéline Clair [3], Laëtitia Averty [3], Justine Sigaud [3], Elisa Thoral [1], Loïc Teulier [1]

[1] Univ Lyon, Université Claude Bernard Lyon 1, CNRS, ENTPE, UMR 5023 LEHNA, F-69622, Villeurbanne, France, [2] Instituto de Oceanografía y Cambio Global, IOCAG, Universidad de Las Palmas de Gran Canaria, Unidad Asociada ULPGC-CSIC, Parque Científico Tecnológico Marino de Taliarte s/n, 35214 Telde, Gran Canaria, Canary Islands, Spain, [3] Animalerie Conventionnelle Sauvage d'Expérimentation de la Doua (ACSED), Univ Lyon, Université Claude Bernard Lyon 1, CNRS, FR BioEEnViS, F-69622, Villeurbanne, France

In fish, red muscle is a highly oxidative tissue that is a major contributor to the aerobic metabolism of individuals. However, the study of muscle bioenergetics at the cellular level usually requires the euthanasia of individuals. To avoid this lethal issue, red muscle micro-biopsies have been performed in 12-cm goldfish under anaesthesia, in order to withdraw enough muscle fibres for bioenergetics studies. Even less invasive, such a surgical intervention could lead to severe consequences, especially in terms of swimming performance.

The main goal of this study was to highlight the putative consequences of two-times repeated biopsies on the *in vivo* performance of goldfish *Carassius auratus*. In parallel, to refine the anaesthetic procedure, effects of lidocaine (analgesic) added to MS-222 (anaesthetic) during surgery were investigated.

The results obtained at the mitochondrial level showed that the data were repeatable over time, and that the addition of lidocaine did not affect cellular respiration. However, after a second biopsy, critical swimming speed (U_{crit}) and cost of transport seem to be negatively impacted.

To conclude, even if two repeated biopsies could be deleterious for fish performance in our conditions, one single muscle biopsy could seriously be considered as an experimental procedure for investigating mitochondrial bioenergetics, and especially in an ecophysiological context, using wild fish caught in their natural environment.

Session Environnement Micro-inflammatoire

Inflammation and post-ischemic cardiac remodeling

Jean-Sébastien Silvestre
Paris Centre de Recherche Cardiovasculaire

Despite innovative approaches in the treatment of acute cardiovascular events as well as efficient interventions in primary and secondary prevention, cardiovascular diseases remain the leading cause of death in industrialized countries and are expected to become so in emerging countries by 2020. Coronary artery disease and its associated ischemic heart failure carry high mortality and morbidity. Intensive experimental and clinical research performed during the last decade has shed light on the instrumental role of innate and adaptive immunity in the cardiac response to ischemic injury. Innate and adaptive immunity coordinate distinct but mutually non-exclusive events governing cardiac repair. Among the actors of innate immunity, macrophages, whether originating from circulating monocytes or from the resident cardiac pool, appear to be major effectors of cardiac repair through their phagocytic capacity to clear damaged tissue and subsequent potential to promote inflammation resolution. Recent studies also identified intriguing roles for adaptive immune responses mediated by T and B lymphocytes in myocardial remodeling following coronary artery occlusion. Hence, various molecular and cellular interactions underlie the bi-directional dialogue between inflammatory and non-inflammatory resident cells in the cardiac tissue. Targeting these critical biological pathways holds great promise for curbing the substantial burden of cardiovascular diseases.

Probing the inflammatory environment and the immune response thanks to in vivo imaging : Application to ischemic stroke

Marlène Wiart
Univ Lyon, CarMeN Laboratory, INSERM, INRA, INSA Lyon, Université Claude Bernard Lyon 1, CNRS

Stroke occurs in 155,000 persons in France each year. Ischemic stroke, which results from the occlusion of a cerebral artery, accounts for 80% of all stroke cases. Thrombectomy has recently revolutionized the management of ischemic stroke patients. However, even in case of successful and timely reperfusion, more than half of stroke patients suffer long-term neurological sequelae. Therefore, there is an urgent need to develop new adjuvant therapies to protect the brain after an ischemic stroke. In the first hours following stroke onset, a complex ischemic cascade is setting into place including excitotoxicity, calcium overload, mitochondrial dysfunction, oxidative stress and finally cell death. The restoration of cerebral circulation, although globally beneficial, may induce reperfusion lesions that add up to initial damages. A neuroinflammatory response is rapidly building up with macrophages as first-line actors, including resident microglia and monocyte-derived macrophages. The main function of these phagocytic cells is to clean cellular debris and to ingest apoptotic cells; however, they may also engulf viable neurons thus leading to secondary brain damages. Blood-brain barrier (BBB) dysfunction and cerebral oedema also induce secondary lesion growth. Because the inflammatory response is dynamic and 3-dimensional, the development of tools dedicated to the in vivo imaging of the inflammatory microenvironment and the tracking of immune cells are paramount in order to better understand this neuroinflammatory response and to monitor the effects of treatments aiming at mitigating it. This includes two-photon microscopy and translational imaging modalities such as magnetic resonance imaging (MRI), coupled to the administration of contrast agents.

Effect of Urine Alkalinization on Urinary Inflammatory Markers Analyzed by Mass Spectrometry in Patients with Cystinuria

Caroline Prot-Bertoye [1, 2], Vincent Jung [3], Isabelle Tostivint [2, 4], Bertrand Knebelmann [2, 5], Kevin Roger [3], Ida Chiara Guerrera [3], Marie Courbebaisse [1, 2]

[1] Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Service de Physiologie – Explorations fonctionnelles, F-75015 Paris, France., [2] Centre de Référence des Maladies Rénales Héréditaires de l'Enfant et de l'Adulte (MARHEA), Paris, France., [3] Proteomics Platform Necker, Université de Paris - Structure Fédérative de Recherche Necker, INSERM US24/CNRS UAR3633, Paris, France., [4] Assistance Publique-Hôpitaux de Paris, Hôpital de la Pitié Salpêtrière, Service de Néphrologie, F-75013 Paris, France, [5] Assistance Publique-Hôpitaux de Paris, Hôpital Necker, Service de Néphrologie, F-75015 Paris, France

Introduction:
Cystinuria is the most frequent monogenic cause of renal calculi. The objectives were to investigate: i) the urinary proteomic profile in cystinuric patients without chronic kidney disease (CKD), and in a control group of healthy volunteers; ii) the potential effect of urine alkalinization on the urinary proteomic profile in cystinuric patients as this is the cornerstone of the preventive medical treatment.

Methods:
Urinary inflammatory profile was evaluated by Nano- liquid chromatography coupled to high resolution mass spectrometry at baseline in the control group and in cystinuric patients not treated with an eGFR greater than 60 ml/min/1.73m2. In cystinuric patients, change from baseline urinary inflammatory profile was evaluated after 3 months of alkalizing treatment.

Results:
Twenty-one cystinuric patients and 7 healthy volunteers were included. Healthy volunteers had no inflammatory signature. A hierarchical clustering of the cystinuric patients according to the intensity of the profile of core inflammation signature (11 proteins) was performed. The signature could separate 5 cystinuric patients with a high inflammation from other cystinuric patients and healthy volunteers. The alkalizing treatment was associated with a decrease in the intensity of the urinary inflammatory profile in all 5 cystinuric patients compared to the initial high level of urinary inflammation.

Discussion/Conclusion:
A panel of 11 proteins was found as elevated in some cystinuric patients without CKD G3-G5 and could work as an early inflammatory signature. The alkalizing treatment was associated with a reduction of this urinary inflammation signature, suggesting that it could be a new tool to monitor the treatment.

CORRELATION BETWEEN HEMODYNAMIC PARAMETERS AND CYTOKINES IN A PORCINE MODEL OF SEPSIS

Charlotte Slek [1], Mathieu Magnin [1, 2], Abdessalem Hammed [1], Jean-Yves Ayoub [1], Bernard Allaouchiche [1, 4], Jeanne Marie Bonnet [1, 2], Stéphane Junot [1, 5], Vanessa Louzier [1, 2], Tatiana Victoni [1, 3]

[1] Université de Lyon, APCSe Agressions Pulmonaires et Circulatoires dans le Sepsis, VetAgro Sup, UP 2021.A101, [2] Université de Lyon, VetAgro Sup, Physiologie, Pharmacodynamie et Thérapeutique, [3] Université de Lyon, VetAgro Sup, Pharmacologie et Toxicologie, [4] Université de Lyon, Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Réanimation Médicale, [5] Université de Lyon, VetAgro Sup, Anesthésiologie

Introduction: Human studies reported correlations between hemodynamic failures and plasmatic cytokines concentrations in patients with sepsis and septic shock. Pimobendan is an inodilator agent, calcium sensitizer and PDE III inhibitor with potentially anti-inflammatory properties. Pimobendan have produced short-term hemodynamic benefits in patients. In this study, we performed an experimental porcine model of sepsis for two aims. First, to evaluate the pimobendan effect on the release of cytokines. Then, to confirm the presence of correlation between hemodynamic parameters and cytokines concentration in this model.

Materials and Methods: Sepsis was induced in 18 anaesthetized pigs with intravenous inoculation of live Pseudomonas aeruginosa. After shock induction, animals were resuscitated with fluid bolus and norepinephrine infusion. Nine pigs were treated with pimobendan while nine received placebo. Hemodynamic parameters and cytokines (TNFα, IL-10 and IL-6 determined by ELISA) were measured before, during and after shock. Spearman correlation was performed for statistical analysis.

Results: ELISA results showed an increase of plasmatic cytokines after shock with no difference between pimobendan and control group. TNFα and IL-6 revealed no correlation with hemodynamic parameters. Positive correlations were observed between IL-10 and hemodynamic parameters (systolic blood pressure: $\rho = 0.57$, $P = 0.03$; and cardiac index: $\rho = 0.67$, $P = 0.012$). A negative correlation was found between IL-10 and lactates ($\rho = -0.58$, $P = 0.03$).

Conclusions: Pimobendan showed no anti-inflammatory properties. Only IL10 correlated with some hemodynamic parameters and lactates. This suggests that there might be a link between macrocirculation and anti-inflammatory molecules that must be confirmed with measurement of more cytokines.

Genetic expression and immunofluorescence mapping of Neuron Navigator 1 highlight potential therapeutic targets in anti-inflammatory treatment of aortic valves stenosis

David HUPIN [1, 2], Oscar PLUNDE [1], Anders FRANCO-CERECEDA [3], Magnus BÄCK [1]
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Introduction

Aortic valve stenosis (AVS) is the most prevalent heart valve disease worldwide (*Schlotter et al. 2018*). The aortic valve is innervated, but the neural regulation of these AVS processes is unknown (*Marron et al. 1996*). Recently, a transcriptome-wide analysis study associated Neuron Navigator 1 (NAV1) with AVS (*Thériault et al. 2019*).

Purpose

Since NAV1 is involved in developmental neural migration, the aim of the study was to establish the relation of NAV1 expression to AVS disease stages, and to map the neural NAV1 to demonstrate its possible role within the valvular anti-inflammatory cholinergic pathway (via the nicotinic acetylcholine receptor α7nAChR) (*Tracey et al. 2002)*.

Methods

Human aortic valves were obtained from patients undergoing surgical aortic valve replacement at Karolinska University Hospital in Stockholm (Sweden) (*Sainz-Jaspeado et al. 2021*). The valves were used for (1) RNA extraction (Affymetrix Human Transcriptome Arrays 2.0) and (2) for immunohistochemistry (tissue clearing, *Susaki et al. 2015* and immuno-staining protocols).

Results

In 74 stenotic aortic valves (56 men and 18 women, mean age 73.4±6 [62-84] years), NAV1 and α7nAChR mRNA expressions had opposite kinetics when disease stages progressed from healthy through intermediate to calcified aortic valve tissue (statistical software Qlucore, Sweden). Immunofluorescence staining with Light Sheet Microscope (MSquared Lasers, UK) confirmed this difference in healthy valve tissue.

Conclusion

These results identified differential valvular NAV1 and α7nAChR expression patterns. These results may point to NAV1 as a local valvular potential therapeutic target for future studies.

Dill extract (Anethum graveolens) could preserve dermal elastin network during inflammation.

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Introduction : During inflammation, elastin network is reduced. Dill extract is able to improve elastin network in reconstructed skin, but also to increase elastin production by smooth muscle cells and has anti-inflammatory properties. The aim of the present study was to evaluate the impact of low and high grade inflammation on the elastin network and to find a treatment to counteract them.

Methods : To mimic low grade inflammation, IFNg, TNFa, IL-1b was applied on dermal microvascular endothelial cells and the resulting conditioned medium was applied on cultured fibroblasts (2D) and reconstructed skin (3D). Then elastin network was analysed by immunofluorescence. To mimic high grade inflammation, pancreatic elastase was applied with or without dill extract on cultured fibroblasts one-week post-confluency. Then transcripts expression was analysed by RT-qPCR.

Results : In low grade inflammation, elastin expression was only decreased in the reconstructed skin. In high grade inflammation, elastin network was strongly altered in cultured fibroblasts. But the addition of dill extract, simultaneously with pancreatic elastase, counteracted elastase activity and preserved elastin network by elafin gene expression upregulation.

Discussion/Conclusion : The present study showed that, without any immune cells, the endothelial secretion in response to a pro-inflammatory stress is able to activate fibroblasts that will maintain the pro-inflammatory environment and exacerbate elastin degradation. Dill extract is able to preserve elastin degradation through elafin upregulation since it is an elastase inhibitor and an anti-inflammatory molecule. Additional in vivo data confirmed that dill treatment prevented elastase digestion allowing preservation of the cutaneous elastic network in mice.

Session Environnement Microbien

Juvenile protein malnutrition and *Lactiplantibacillus plantarum*^{WJL} modulate host physiology via GLP-1-secreting cells of the mouse ileum

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Introduction: Juvenile protein malnutrition leads to severe stunting, together with metabolic dysfunctions. Interestingly, the probiotic bacterium *Lactiplantibacillus plantarum*^{WJL} (Lp^{WJL}) has demonstrated beneficial effects on the host organism in these conditions. Enteroendocrine cells (EECs) in the intestinal epithelium respond to luminal stimuli by secreting various hormones. Notably, some EECs secrete Glucagon-like Peptide 1 (GLP-1), which regulates glucose homeostasis. We aim at understanding how EECs mediate the effects of protein malnutrition on metabolic dysfunction and how Lp^{WJL} interact with these processes.

Material and methods: Mice are fed a control diet (CD) or an isocaloric low protein diet (LPD) during five weeks after weaning to model juvenile protein malnutrition and treated daily with a Placebo or 10^8 CFU of Lp^{WJL}.

Results: LPD did not change the total number of EECs in the ileum compared to CD. However, LPD induced a 2-fold reduction in the number of GLP-1-secreting EECs, which was not affected by Lp^{WJL} intervention. Consistently, GLP-1 secretion in the portal blood was reduced in LPD condition. Glucose tolerance, reflecting the physiological function of GLP-1, was altered accordingly but partially restored by Lp^{WJL} treatment.

Discussion: Our data suggest that protein malnutrition directs differentiation of EECs towards a reduction of GLP-1-secreting cells. To investigate EEC development in these conditions, we will perform RNA-sequencing using transgenic EEC reporter mice. We aim at identifying up- or down-regulated transcripts upon protein malnutrition to better understand the role of EECs in the metabolic phenotypes observed.

Session Environnement Hypoxique

Nocturnal hypoxemia is associated with decreased erythrocyte deformability and enhanced hemolysis in sickle cell disease patients

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Sickle cell disease (SCD) is the most prevalent genetic disease worldwide. SCD is caused by a mutation in the beta-globin gene that leads to the production of abnormal hemoglobin called hemoglobin S (HbS). HbS can polymerize in deoxygenated conditions, causing red blood cell (RBC) sickling. Sickled RBCs are poorly deformable and very fragile. Indeed, patients with SCD suffer from chronic hemolytic anemia repeated vaso-occlusive crises and chronic vascular complications. Obstructive sleep apnea (OSA) that can lead to nocturnal hypoxemia, occurs at a high frequency in SCD population. OSA could act as a modulator of SCD clinical severity, however only few studies focused on the associations between the two diseases.

The aims of this study were: (1) to explore the associations between OSA, nocturnal oxyhemoglobin saturation (SpO2) and clinical complications, (2) to investigate the impact of OSA and nocturnal SpO2 on several biomarkers in patients with SCD.

Forty-three homozygous SCD patients underwent a complete polysomnography recording followed by blood sampling. No association between OSA and clinical severity was found. Nocturnal hypoxemia was associated with a higher proportion of patients with hemolytic complications (glomerulopathy, leg ulcer, priapism, or pulmonary hypertension). In addition, nocturnal hypoxemia was associated with a decrease in RBC deformability, increased hemolysis and more severe anemia.

Nocturnal hypoxemia in SCD patients could be responsible for changes in RBC deformability resulting in enhanced hemolysis leading to the development of complications such as leg ulcers, priapism, pulmonary hypertension or glomerulopathy.

Hypoxic conditioning and metabolic disorders

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Preconditioning refers to a procedure by which a single noxious stimulus below the threshold of damage is applied to the tissue in order to increase resistance to the same or even different noxious stimuli given above the threshold of damage. Environemental factors (e.g. altitude exposure) and lifestyle behaviours (e.g. physical activity) can be considered as potential conditioning mechanisms. Hypoxic conditioning consisting in sessions of intermittent exposure to moderate normobaric hypoxia repeated over several weeks may induce hematological, vascular, metabolic, and neurological effects. Hypoxic conditioning relies on complex and active defenses that organisms have developed to counter the adverse consequences of oxygen deprivation. The protection it confers has been demonstrated against ischemic attack and several metabolic disorders in animal models. Based on these data, hypoxic conditioning (consisting in recurrent exposure to hypoxia either at rest or combined with physical activity) has been suggested a potential non-pharmacological therapeutic intervention to enhance some physiological functions in individuals in whom acute or chronic pathological events are anticipated or existing. In addition to healthy subjects, some benefits have been reported in patients with various chronic diseases, including metabolic disorders (e.g. obesity, diabetes).This presentation will underline the existing evidence regarding the use of hypoxic conditioning as a potential therapeutic modality in metabolic disorders.

Modeling the oxygen transport to the myocardium at maximal exercise at high altitude

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Introduction. Exposure to high altitude induces a decrease in oxygen pressure and saturation in the arterial blood, which is aggravated by exercise. Heart rate (HR) at maximal exercise decreases when altitude increases in prolonged exposure to hypoxia. Our objective was to develop a simple model of myocardial oxygenation in order to demonstrate that the observed blunting of maximal HR at high altitude is necessary for the maintenance of a normal myocardial oxygenation.

Material and Methods. Using data from the available scientific literature, we estimated the myocardial venous oxygen pressure and saturation at maximal exercise in two conditions: 1) with actual values of maximal HR (decreasing with altitude); 2) with sea level values of maximal heart rate, whatever the altitude (no change in HR).

Results. We demonstrated that, in the absence of autoregulation of maximal HR, myocardial tissue oxygenation would be incompatible with life above 6,200m to 7,600m, depending on the hypothesis concerning a possible increase in coronary reserve (increase in coronary blood flow at exercise).

Discussion. The decrease in maximal HR at high altitude could be explained by several biological mechanisms involving the autonomic nervous system and its receptors on myocytes, mainly by a downregulation of the beta-adrenergic system.

Conclusion. These experimental and clinical observations support the hypothesis that there exists an integrated system at the cellular level, which protects the myocardium from a hazardous disequilibrium between O_2 supply and O_2 consumption during exercise at high altitude.

HEART RATE VARIATION AFTER A 6-MINUTE WALK TEST DURING LOWER LIMB ISCHEMIA

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Introduction: Increasing cardiac output by raising the heart rate (HR) is a means of meeting oxygen demand during exercise. The higher the heart rate after exercise, the greater the oxygen debt. Our objective was to study the relationship between the extent of lower limb ischemia assessed during a walking test and the variation in HR at 1 minute post-exercise (HR1).

Material and methods: We studied the relationship between the extent of lower limb ischemia assessed during a 6-minute walk test (6MWT) and the variation in HR1 in 98 arteriopathic patients from January to July 2021 in the vascular functional explorations unit of the Souro SANOU University Hospital of Bobo-Dioulasso.

Results: Four groups of patients were formed according to the importance of lower limb ischemia. Patients in the least ischemic quartile had the greatest walking distance (333.5±87 m) and the greatest decrease in HR1 (19±8 beats per minute (bpm). Patients in the quartile of most severe ischemia walked the least (224±115m) and had the smallest decrease in HR1 (11±8 bpm).

Discussion/conclusion: Change in heart rate at 1 minute post-exercise is associated with the extent of lower limb ischemia during the 6MWT.The smaller decrease in HR1 of a 6MWT in patients with more severe ischemia may be explained by a greater oxygen debt in the ischemic tissue.

Session Environnement métabolique

Impact of adipose-tissue micro-environment on breast cancer progression , in obese individuals

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Introduction Adipose tissue-derived mesenchymal stem cells from obese (ob-ASC) contribute to adipose tissue (AT) inflammation through polarisation of Th-17 cells, as demonstrated by us (Eljaafari/Diabetes-2015). Because obesity is a risk factor for a variety of cancers including breast cancer, we investigated herein the role of the micro-environment mediated by interaction of ob-ASC with immune cells, on tumor growth and migration.

Methods: An inflammatory micro-environnement was prepared from mitogen-activated co-cultures of ob-ASC and blood mononuclear cells (MNC). Conditioned media (ob-CM) was then collected and added during 24 hours to cultures of MCF-7 or MDA-MB231, two breast cancer-cell lines expressing or not estrogen receptors, respectively. Pro-inflammatory cytokine and VEGFa expressions were measured at the mRNA and protein levels. Tumor cell growth was measured through Ki67 staining, by flow cytometry. Finally, scratch tests were used to measure tumor cell migration.

Results: Ob-CM increased mRNA expression and protein secretion of IL-1b, IL-8,TNFa and IL-6 in both cell lines. Overexpression of VEGFa, and increased migration in scratch tests, were observed in ob-CM cultured breast cancer cells. Interestingly, neutralization of IL-17A during co-cultures of ob-ASC with MNC inhibited ob-CM-mediated overexpression of pro-inflammatory cytokines in breast cancer cells.

Discussion/Conclusion: Our results strongly suggest (i) the role of obese AT -micro-environment on breast cancer progression, through enhancement of pro-inflammatory cytokine secretion, angiogenesis, proliferation, and migration, and (ii) the contribution of IL-17A in this progression. As we have reported that omega-3-PUFA inhibits ob-ASC-mediated inflammation (Chehimi/Mol-Nutr-Food-Res-2019), its putative beneficial impact on tumor progression is under investigation.

Association Between Nocturnal Blood Pressure Dipping and Chronic Kidney Disease

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INTRODUCTION: Management of blood pressure (BP) in chronic kidney disease (CKD) is critical for preventing cardio-renal complications. We aimed at describing nocturnal BP dipping patterns and its predictors in patients with CKD.

METHODS: We analysed data from 642 patients with CKD stages 1 to 5 referred for kidney function testing to a single tertiary hospital, including 24-hour urine collection, measurement of glomerular filtration rate (GFR) using clearance of radioisotopic tracer, as well as ambulatory BP measurement (ABPM). Factors associated with less than 10% nocturnal BP dipping were analysed with adjusted logistic regression models including a random intercept to deal with clustering of measurements within patients.

RESULTS: Participants (mean age 56 ± 15 years; 35% female, mean GFR 49 ± 21 mL/min per 1.73 m2) consisted of 8% extreme-dippers, 37% dippers, 40% non-dippers, and 15% reverse-dippers. The prevalence of non- or reverse- dipping increased with CKD severity, from 36% in stage 1 to 65% in stages 4-5. In the multivariable adjusted regression, non or reverse dipping was independently associated with measured GFR ([OR, 95% CI] per 10 ml/min/1.73m² decrease= 1.16 [1.06 – 1.26], p=0.001), daytime ambulatory SBP (OR per 10 mmHg decrease= 1.17 [1.06–1.28],p=0.001), African origin (OR= 1.56 [1.04 – 2.34], p=0.03) and 24h Na/K (OR per 1-unit increase= 1.20 [1.06 – 1.37], p=0.006).

CONCLUSIONS: The prevalence of nocturnal non-or reverse dipping increases substantially across the spectrum of CKD. Measured GFR, ambulatory daytime SBP, African origin and 24-hour urinary sodium to potassium ratio are independent predictors of abnormal nocturnal BP decrease.

A NEW ROLE OF ENDOPLASMIC RETICULUM-MITOCHONDRIA CONTACT SITES IN NUTRIENT-INDUCED GLUCAGON-LIKE PEPTIDE 1 (GLP-1) SECRETION BY L CELLS.

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Introduction: Postprandial GLP-1 secretion by enteroendocrine L cells plays an important role in the control of glucose homoeostasis. This study evaluated the implication of contact sites linking endoplasmic reticulum (ER) and mitochondria, termed MAMs (Mitochondria-Associated ER Membranes) in nutrient-induced GLP1 secretion. MAMs indeed are dynamically regulated by nutrients, and are crucial regulators of both calcic and energetic homoeostasis important for GLP1 secretion.

Materials and Methods: Nutrient (glucose, bile acids (BA), fatty acids and amino acids) action on MAMs and GLP-1 secretion were assessed in STC-1 cells during 1-hour treatments using respectively in situ Proximity Ligation Assay and ELISA. A pharmacological approach enabled the characterisation of the signalling pathways implicated in nutrient-induced MAMs regulation. Their causal role in GLP-1 secretion was challenged by adenoviral-mediated expression of the spacer protein FATE1.

Results: All nutrients described as GLP-1 secretagogues simultaneously induced both GLP-1 secretion and MAMs after 1 hour of treatment in STC-1 cells. FATE1-induced MAM disruption prevented GLP-1 secretion in response to glucose and BA, validating the causal role of MAMs in nutrient-induced GLP1 secretion. While glucose sensing relies on an electrogenic mechanism through SGLT1 and the firing of action potentials, BA sensing rather is mediated through a cAMP-PKA pathway.

Discussion/Conclusion: Altogether, these results demonstrate a new role of ER-mitochondria contact sites in nutrient-induced GLP-1 secretion in L cells, through different signalling pathways, with an electrogenic effect for glucose and an effect mediated through the TGR5-cAMP-PKA pathway for BA. Confirmation of these data in more physiological models is currently underway.

Session Environnement phospho-calcique

X LINKED HYPOPHOSPHATEMIA, NOT ONLY A SKELETAL DISEASE BUT ALSO A CHRONIC INFLAMMATORY STATE

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X-linked hypophosphatemia (XLH) is a rare genetic disease caused by a primary excess of FGF23, which has been associated with inflammation and impaired osteoclastogenesis. These pathways have not been investigated in XLH. The aim was to evaluate whether XLH patients display inflammatory profile and increased osteoclastic activity.

We performed a prospective multicenter cross-sectional study analyzing transcript expression of 8 inflammatory markers by RT-qPCR on PBMCs purified from total blood samples (patients and controls). In addition, the effect of native /active Vitamin D on XLH patient osteoclastogenesis was assessed by quantification of multinucleated TRAP positive osteoclasts generated in vitro (patients and controls).

28 XLH patients were enrolled, 11 adults and 17 children (6 SOC (standard of care) children and 11 burosumab children); plus 19 healthy controls. The expression of all inflammatory markers (except Il6R) was significantly increased in PBMCs from XLH patients as compared to controls. No differences were observed between patients treated with burosumab or SOC. Osteoclast formation was significantly impaired in XLH patients when compared to controls; however osteoclasts derived from burosumab treated patients showed a restored response to native vitamin D. XLH mature osteoclasts displayed higher level of inflammatory markers, lower in osteoclasts from burosumab subgroup compared to SOC subgroup.

We describe for the first time a peculiar inflammatory profile in XLH. Since XLH patients have a propensity to develop arterial hypertension, obesity and enthesopathies, and inflammation can worsen these clinical outcomes, we hypothesize that inflammation may play a critical role in these extra-skeletal complications of XLH.

Plasma oxalate concentration in enteric hyperoxaluria related to short bowel syndrome : OXAGO study.

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Introduction : Short bowel syndrome (SBS) results in hyperabsorption of oxalate due to several mechanisms. Excess oxalate absorption is balanced by increased renal excretion, leading to an hyperoxaluria named enteric hyperoxaluria. This pathological state promotes nephrolithiasis, nephrocalcinosis and chronic kidney disease. Plasma oxalate concentration is usually measured for the detection and monitoring of primary hyperoxaluria ; this rare genetic disease causes a massive metabolic production of oxalate, leading to an increase of plasma oxalate concentration when kidney function decreases, usually when glomerular filtration rate (GFR) is below 45 mL/min/1,73m². Recent studies have suggested that high plasma oxalate levels could occur during enteric hyperoxaluria.

Material and Methods : OXAGO study evaluates plasma oxalate concentration during enteric hyperoxaluria secondary to SBS type 2 and 3, through an observational, descriptive, transverse and monocentric design.

Results : Plasma oxalate concentration was measured in 30 patients. Median plasma oxalate concentration was less than 5 µmol/L. High plasma oxalate levels was discovered in 10 patients (33 %), including 3 patients with measured GFR greater than 60 mL/min/1,73m².
Plasma oxalate concentration was significantly correlated with GFR ($r = -0,5494$; $p = 0,0017$). No statistically significant association was observed between plasma oxalate concentrations and urinary oxalate concentration, nephrolithiasis events, anatomy of the digestive tract, plasma citrulline, steatorrhea or oxalate metabolic precursors (vitamin C, glycine, hydroxyproline).

Conclusion : OXAGO study confirmed that high plasma oxalate levels occurs in enteric hyperoxaluria secondary to SBS type 2 and 3. The main factor associated with plasma oxalate increase is the decrease in the GFR.

Renal Adaptation to a Low Potassium Diet: Implication of the Growth Factor GDF15.

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The modern western diet is low in potassium (K^+) which may contribute to the development of cardiovascular diseases. In response to a K^+ restriction our organism will induce both the external and internal system which involve the kidney and the muscle, respectively. The kidney adapts its functions to retain K^+ by increasing the number of type-A intercalated cells (ICA). A transcriptomic analysis revealed that the growth factor GDF15 was upregulated in renal collecting ducts of K^+ depleted animals. Therefore, we hypothesize that GDF15 may impact both the external and internal balance of K^+ homeostasis.

We used C57BL6J mice wild type or knockout for the *Gdf15* gene. Metabolism cages were used for metabolic analysis. The number of ICA was determined by immunohistochemistry on microdissected distal tubule. Muscle mass was assessed by TD-NMR.
Under a K^+ depletion, GDF15 is increased along the nephron, predominantly in the collecting duct, and in the intestine, plasma and urine of mice. We confirmed the relationship between GDF15 and K^+ restriction in human healthy volunteers. GDF15-KO mice exhibit a delayed renal adaptation, leading to hypokalemia. The adaptation issue is partly explained by the absence of proliferation of ICA. The renal effect of GDF15 depends on the ErbB2 receptor. GDF15 is also a regulator of the internal balance, because it induces a loss of muscle.

Altogether, these results demonstrate that GDF15 is a key factor for both the regulation of the internal and the external balance of K^+ homeostasis.

Session Environnement sensoriel

Role of TRPV3 channel in the default of cutaneous thermoregulation during aging

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The epidermal keratinocytes ensure, by their continuous renewal, the maintenance of the functions of the skin. The latter, at the interface with the environment and our body, plays an essential role in thermoregulation. However, with aging, the defense mechanisms against heat is deteriorated, mainly due to a default of cutaneous vasodilation associated with an increase of hyperthermia risk. We recently expose the role of the thermosensor TRPV3, a calcium channel abundantly expressed by keratinocytes, in mechanisms of cutaneous vasodilation induced by heat. The vascular response after a thermal stimulation of TRPV3-KO mice mimic the thermoregulation defect observed in elderly people and mice. This therefore offers a new insight into the keratinocyte behaviour in its environment, which can indirectly act on vascular function through TRPV3. Using skin tissues (TissueMicroArray), we characterized the gene expression and subcellular localisation of *TRPV3* in young and elderly patients (RNAscope). We then assessed the functional activity of the TRPV3 channel by calcium imaging using 2D culture of primary keratinocytes (young/old donors). This work allows a first global characterization of TRPV3 in the skin during aging, and will aim to define the nature of the keratinocyte/dermal vessel dialogue.

Intestinal gluconeogenesis could modulate learning process

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Introduction - Obesity promotes the development of both metabolic and behavioral complications. In this context, intestinal gluconeogenesis (IGN) is a key beneficial function in the maintenance of energy homeostasis, which also has beneficial effects on anxiety and depressive-like behaviors. On the contrary, its absence favors these disorders, including impairment in hippocampal neurogenesis, a function linked to memory. Thus, the objective was to assess whether IGN would be able to modulate these cognitive processes.

Material and Methods - We studied behavior related to spatial memory in mice deficient in (I.G6pc-/- mice) or overexpressing (I.G6pcoverexp mice) intestinal glucose-6-phosphatase, the key enzyme of endogenous glucose production, using the Morris Water Maze test. Mice must learn the location of an escape platform (made invisible by immersion in white coloured-water). In parallel, neurobiological studies were conducted to understand the molecular mechanisms involved.

Results - The activation of IGN improves learning process, since the time to find the platform was lower in I.G6pcoverexp mice. In contrast, the increased time to find the platform in I.G6pc-/- mice suggests that the absence of IGN is sufficient to induce a learning deficit. Consistently with the improvement of learning skills, the increased expression of NeuN and the NMDA-R in the hippocampus of I.G6pcoverexp mice suggests an improvement in synaptic plasticity when IGN is induced.

Conclusion - IGN could be able to modulate the learning process. This should greatly expand the understanding of the relationships between intestinal nutrient metabolism and cognitive processes, which are still poorly understood at the mechanistic level.

Session Muscle et Exercice

Myokines, exercice and energy metabolism

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The health benefits of exercise are well-recognized and are observed across multiple organ systems. These beneficial effects reduce disease risk and mortality. The molecular mechanisms that underlie the beneficial effects of exercise, however, remain poorly understood. With emergence of –omics technologies, the number of exercise-associated signalling molecules that have been identified has rapidly expanded. Signalling moieties released by skeletal muscle are defined as myokines. They can be released during acute and/or chronic exercise and exert their effects through endocrine, paracrine and/or autocrine pathways. Myokines have beneficial effects on the immune, cardiovascular, metabolic and neurological systems. However, very few of them have been shown to target adipose tissue, in particular in humans. Our team recently identified Growth and Differentiation factor 15 (GDF15) as a novel myokine. GDF15 is rapidly released in response to muscle contraction to promote lipolysis in human white adipose tissue. Since GDF15 has emerged as an interesting antiobesity therapy through its central effects on appetite suppression, potential peripheral effects should not be neglected.

CHARACTERIZATION OF THE COMBINED EFFECTS OF EXERCISE AND IMMUNE-CHEMOTHERAPY TREATMENTS ON TUMOUR GROWTH IN MC38 COLORECTAL CANCER MICE

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Context: Physical exercise has numerous systemic effects and significantly decreases tumor growth in mouse models of cancer. The underlying mechanisms remain to be clarified. The purpose of this pre-clinical study is to assess the capacity of exercise conducted immediately prior to treatments injection to improve the efficacy of immuno-chemotherapy via modification of the tumor microenvironment.

Methods: 4 weeks mice model of colorectal cancer (MC38) have been randomly separated in 4 groups (n = 20/groups): control (CTRL), immune-chemotherapy (TRT), exercise (EXE) and combined intervention (TRT-EXE). Both TRT and TRT-EXE received immuno-chemotherapy 5 times per week for 1 week, moreover TRT-EXE and EXE have been submitted to 50 min of treadmill exercise before each treatment administration (<15 minutes). All along the protocol, tumor growth has been be monitored. At D7, tumor hypoxia and tumor immune microenvironment have been measured.

Results : will be available in May 2022. Preliminary results obtained by flow cytometry show a greater decrease in tumor development in the TRT-EXE group compared to the other groups. Indeed, it seems that this is due to changes in biomarkers such as a decrease in the percentage of PD-1 expression on T cells and a decrease in the percentage of Treg on CD4+ cells.

Conclusion: This study may provide insights on the combined effect of pre-treatment exercise and immuno-chemotherapy in colorectal cancer and will provide valuable information to design a randomised controlled trial with sufficient power to assess efficacy on clinically important endpoints (e.g. progression-free survival) in cancer patients eligible for immuno-chemotherapy.

SEX DIFFERENCES IN SKELETAL MUSCLE REGENERATION IN A MOUSE MODEL OF LENGTHENING CONTRACTION-INDUCED SEVERE DAMAGE

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After injury, skeletal muscle regenerates thanks to a dynamic interplay between satellite cells (SCs) and inflammatory cells. A higher estrogen concentration could confer a physiological advantage to females via their role in SC fate and the modulation of the inflammatory response. However, conflicting findings have been reported due to the lack of control of the ovarian cycle in direct comparisons of muscle regeneration between males and females. On that basis, the biological mechanisms involved in a (potential) sexual dimorphism are still poorly understood. We assessed the impact of sex on skeletal muscle regeneration in adult male and female C57Bl6/J mice using a standardized model of injury and controlling the ovarian cycle of the females. Severe muscle damage was induced by 30 electrically-evoked lengthening contractions on females being in the estrus phase of the ovarian cycle. Isometric force measurements, considered as the best indirect marker of muscle damage, were performed before, immediately after, and up to 14 days post-injury. The Gastrocnemius muscle was harvested at different time points to perform histological analyses by immunostaining.
Despite more severe histological alterations, isometric force recovery was faster in females than in males. Females showed a greater activation, proliferation and differentiation of SCs and a lower macrophage infiltration as compared with males.
We conclude that female showed a faster muscle regeneration which could be related to higher myogenic capacities of SCs and/or to a better regulation of the inflammatory response. Further analyses are needed to investigate the interactions between SCs and macrophages in this context.

Exercise-induced cardiac troponin release is associated with level of exercise training

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Introduction : Prevention of cardiovascular events related to exercise in middle-aged and older adults remains essential, especially since exercise-induced cTnT release still remains open to debate.

Purpose : We attempted to identify predictors of exercise-induced cTnT release, in order to support its physiological origin.

Methods : The study was performed during the world's largest cross-country running race (30 km,Lidingöloppet, Sweden). The first 100 volunteers were selected in 2018. A structured medical history (level of training in h/week), physical examination, resting 12-lead ECG (standardized criteria for athletes and ultrashort heart rate variability) and cardio-ankle vascular index were performed before the race. Blood was collected before and immediately (<2h) after the race. Multivariate logistic regression analysis was performed using cTnT at baseline (Model A), then immediately after the race (Model B) as a dependent variable.

Results : The mean age of the 83 participants who have successfully completed the race and the study, was 52 (±5) years. cTnT increased significantly in barely all participants from baseline (3.4±4.4 ng/l) to immediately after the race (45.4±32.4 ng/l, $p<0.001$). ECG signs of left ventricular hypertrophy (LVH, 35/83 participants) and level of training (4.9±32.4 h/week) were the best predictors of resting cTnT (Model A, $p=0.04$ and 0.005 respectively). RMSSD (43.6±24.9 ms) was the best predictor of cTnT release (Model B, $p=0.038$).

Conclusion

LVH on ECG (athlete's heart) and RMSSD (parasympathetic nervous system) were respectively among the predictors potentially associated with the magnitude of pre-exercise and post-exercise cTnT concentration and appeared to be driven primarily by the level of training.

Communications Affichées

Session “sensorialité”

P1-Potential role of type 1 gustatory cells in innate immunity of taste papillae

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Introduction: The sense of taste informs the organism about the quality of ingested food. This sense is exposed to many external pathogens and its dysfunction impacts negatively the quality of life. Although immune cells are rarely found in taste bud cells, while high levels of cytokines are observed in taste buds. Yet, the origin of these cytokines in the lingual epithelium remains to be determined.
Materials and methods: In this study, using an immunomagnetic approach we isolated type I gustatory cells which share many features with astrocytes. Then, immunocytochemistry, flow cytometry and qRT-PCR were assessed.
Results: We observed that the isolated type I gustatory cells express F4/80 a specific marker of macrophage. They also exhibit CD11b and CD11c founded in glial cells. Further, in inflammatory conditions, the addition of IL-4 in culture medium triggered an increase in the mRNA expression of Arginase 1, F4/80 and IL-4; and decreased the mRNA expression of TNFα. Conversely, the addition of LPS+anti-IL-4 increased the mRNA expression of TNFα, IL-1β and IL-6.
Discussion/conclusion: These findings provide evidence that type I gustatory cells share many features with macrophage and are involved in the inflammatory process with the ability to react according to the inflammatory situation.

P2-DETECTION OROSENSORIELLE DES LIPIDES ALIMENTAIRES

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Introduction: There exists five basic taste modalities, e.g., sweet, sour, bitter, salty and umami. Recent compelling studies have recently suggested that lingual CD36 and GPR120 mainly expressed by tongue papillae might be implicated in the orosensory perception of dietary fat.
Methods: We have used genetically engineered mice, lacking the expression of CD36, GPR120 and ERK1 genes. We have also conducted behavioral experiments like two-bottle preference test, licking studies etc. We have also conducted studies on obese mice and human and looked into single nucleotide polymorphism (SNP) of CD36 gene.
Results: We have observed mice and rat exhibit spontaneous preference for fat. We have shown that lingual CD36, after activation by free fatty acids, induces increases in free intracellular calcium concentrations, ([Ca2+]i), phosphorylation of protein-tyrosine kinase (PTK) and release of the neurotransmitters like serotonin into synaptic clefts. The lipid-mediated regulation of feeding behaviour which is very critical in the development of several diseases like obesity and other metabolic disorders. The genetic studies in human lean and obese subjects show the implication of altered

CD36 function in obesity.
Discussion/Conclusion: Our studies show that fat taste signaling is altered in obese subjects and there is a genetic polymorphism of CD36 in the obese.

P3-Tongue bile acid receptor TGR5 is critically involved in preference for dietary lipids and obesity in mice : role TGR5 in genetic polymorphism in human obese participants

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Introduction: Several recent reports have indicated the implication of bile acid receptor, i.e., Takeda G protein-coupled receptor 5 (TGR5), in obesity. Keeping in view the fact that obesity is associated with dietary fat preference, and lingual taste bud cells express TGR5, we undertook the present study to explore the implication of TGR5 in fat preference under normal and obese conditions in mice.
Materials and Methods: We investigated the fat preference and fat sensing in taste bud cells (TBC) in C57BL/6 wild-type (WT) and TGR5 knock out (TGR5-/-) male mice, maintained for 20 weeks on a high-fat diet (HFD). We also assessed the implication of TGR5 single nucleotide polymorphism (SNP) in young obese humans.
Results: The high-fat diet (HFD) fed TGR5-/- mice were more obese, marked with higher liver weight, lipidemia and steatosis than WT obese mice. WT obese mice lost the preference for dietary fat, but the TGR5-/- obese mice exhibited no loss towards the attraction for lipids. In lingual TBC, the fatty acid-triggered Ca2+ signaling was decreased in WT obese mice; however, it was increased in TBC from TGR5-/- obese mice. Fatty acid-induced in-vitro release of GLP-1 was higher, but PYY concentrations were lower, in TBC from TGR5-/- obese mice than those in WT obese mice.
Discussion/conclusion: We noticed an association between obesity and variations in TGR5 rs11554825 SNP. Since bile salts exhibit homology with triterpenes, it is possible that TGR5, being terpene-receptors, modulates fat eating behavior and obesity.
Key-words: Fat, taste bud, lipids, obesity

P4-ROLE OF LEPTIN IN OROSSENOSORY DETECTION OF FATTY ACID IN MICE

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Physiology, Lipids and Cancer, NuTOX
Introduction: Recent compelling studies have revealed the existence of 6th taste modalities dedicated to the perception of fatty acids. Leptin regulates energy homeostasis, and is released from adipose tissue and also in the vicinity of mice taste bud cells (mTBC), but the latter role is poorly investigated specifically in the dietary fat intake.
Materials and Methods: We used wild type, DIO, and ob/ob mice. Behavioral tests were used for the determination of gustatory and hedonic properties. We quantify the expression of genes and proteins using the techniques of western blotting, ELISA, RT-qPCR, confocal microscopy, and calcium signaling.

Results: We observed that mTBC co-express leptin and leptin receptors with CD36 and GPR120. Silencing leptin or Ob-Rb mRNA in mTBC upregulated preference for linoleic acid (LA). In isolated mTBC, leptin decreased LA-induced increases in free intracellular calcium concentrations. Leptin and LA induced the phosphorylation of ERK1/2 and STAT-3, However, leptin, but not the LA, induced phosphoinositide-3-kinase (PI-3-K)-dependent Akt phosphorylation in TBC. Furthermore, LA induced depolarization whereas leptin-induced hyperpolarization in TBC.
Discussion/Conclusion: As leptin induces the Akt phosphorylation and this phenomenon was reversed by wortmannin, a PI-3-K inhibitor, suggesting that the PI-3-P/Akt pathway might be involved in leptin's inhibitory action. Leptin-induced PI-3-P/Akt activation was responsible for TBC hyperpolarization which contributed to its inhibitory action on sweet taste perception. Interestingly, we also observed leptin-induced TBC hyperpolarization via the PI-3-P pathway.
Conclusively tongue leptin exerts an inhibitory action on orosensory detection of a dietary fatty acid in mTBC.

Session “métabolisme / nutrition"

P5-Impact of hyperhomocysteinemia on remodelling of vascular extracellular matrix

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Elastogenesis is a complex and major process for the normal development of vascular functions. Synthesis of elastic fibers, formed by a scaffold between elastin (ELN), fibrillin 1 (FBN1), fibulin 5 (FBLN5), latent TGF beta binding protein-4 (LTBP4) or lysyl oxidase (LOX), is carried out in a time-limited window. Elastogenesis performs during late fetal and early neonatal period from smooth muscle cells, fibroblasts, endothelial cells… Beyond this period, neosynthesis or repair of elastic fibers are almost nonexistent.
The aim of our study is to determine if hyperhomocysteinemia (HHCy) due to malnutrition or genetic factors could be a disruptive agent of elastogenesis and vascular function during aging.
For our study, a rat model fed with vitamin B12 and folate deficient diet (MDD) and mice deficient in cystathionine betas synthase (CBS) are used.
The moderate HHCy of mice deficient in CBS, was associated to an overexpression of ELN, LTBP4, FBN1 and FBLN5 suggesting some alterations in aorta anatomy or functions. Surprisingly, no significant modifications of vascular wall structure, blood pressure or vascular stiffening have been observed. Our second model, young rats, born from rats fed with MDD had a high blood pressure associated with aortic wall stiffening and alteration of cardiac parameters. Histological and molecular approaches showed several disrupts of elastic fiber scaffold. Interestingly, those alterations remained present after weaning and return to a normal diet.
In conclusion, neonatal development of HHCY could impact vascular function and

alterations of elastic fibers. The molecular mechanisms involved are currently under investigation by our group.

P6-Hygiene and dietary measures in the treatment of type 2 diabetes population of Chlef region (Algeria)

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Introduction

Diabetes mellitus is a chronic, sometimes silent disease that exposes cardiovascular comorbidities and macro-angiopthic complications.

Our study contributes part of the answer to the problem concerning the current state of diabetic patients in a region of the Wilaya of Chlef in west central Algeria in terms of information (therapeutic education), knowledge about disease and the rules of hygiene and dietary (RHD) to accompagny any therapeutic scheme.

In order to better understand the relationship of diabetic subjects with medical care, we were led to introduce into the interview questions focused on dietary rules and to provide an overview of patient's knowledj diabetics.

Material an methods

The survey descriptive. it aims to describe the knowledge of patient's with type 2 diabetes with regard to the rules of diet and diet.

This is a quantitative, prospective study belonging to the group of descriptive cross-sectional observation studies.

The survey took place over the second semestre 2021.

For this we printed 100 questionnaire of 73 items.

The population concerned were 57% men and 43% women and an average age of 61 years.

Results

- < 50 % of patients have a right responses about diabetes and diet
- 70 % of patients are without job and have not physical activity
- 40 % only of patients are followed by a specialist

Discussion/Conclusion

The main goal of nutritional management is to promote in diabetics a better lifestyle change (eating habit, physical activity. relaxation. leisure) to improve the metabolic control of the disease and its evolution

P7-REV-ERB nuclear receptors in the suprachiasmatic nucleus control circadian period and restrict diet-induced obesity

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Introduction

Circadian disruption, as occurs in shift work, is associated with metabolic diseases often attributed to a discordance between internal clocks and environmental timekeepers. REV-ERB nuclear receptors are key components of the molecular clock,

but their specific role in the SCN master clock is unknown.

Material and Methods

To specifically address the role of REV-ERBs in the master clock in vivo, we used a recently developed, new Rev-erb alpha f/f beta f/f mouse model to induce either whole-body or tissue-specific deletion of both REV-ERBs.

Results

We report here that mice lacking circadian REV-ERB nuclear receptors in the SCN (SCN-DKO) maintain free-running locomotor and metabolic rhythms, but these rhythms are notably shortened by 3 hours. Thus, REV-ERBs are not necessary for circadian rhythmicity of the master clock but play a major role in maintaining a free-running period close to 24 hours.

When housed under a 24-hour light:dark cycle and fed an obesogenic diet, SCN-DKO mice gained excess weight and accrued more liver fat than controls. These metabolic disturbances were corrected by matching environmental lighting to the shortened endogenous 21-hour clock period, which decreased food consumption. Thus, the increased sensitivity to high-fat diet-induced obesity of SCN-DKO mice is corrected by adjusting external LD cycles to match their malfunctioning pacemaker, providing strong evidence for the circadian desynchrony hypothesis.

Discussion/Conclusion

SCN REV-ERBs are not required for rhythmicity but determine the free-running period length. Moreover, these results support the concept that dissonance between environmental conditions and endogenous time periods causes metabolic disruption.

P8-Frequencies and distribution of APOE gene polymorphisms and its association with lipid parameters in Senegalese population

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Background : Apolipoprotein E is a multifunctional protein that plays an important role in lipid metabolism. It is encoded by APOE gene. However, APOE gene polymorphism has not been very well studied in the Senegalese population. Therefore, we studied allele frequencies, genotype distributions and the relationship between APOE gene polymorphisms and lipids parameters in the Senegalese women population.

Methodology : In this study, 110 healthy women of age between 35 - 72 years were involved. The mean age was 49.8 ± 8.1 years. For all subjects, lipid parameters were analysed from the fasting serum and APOE genotypes were identifed by PCR-RFLP based analysis.

Results : variations in the frequencies and distribution of the APOE alleles and genotypes were observed (ε3 : 47.3% ; ε2 : 43.2% ; ε4 : 9.6%) and (ε2/ε3 : 70% ; ε2/ε4 : 16.4% ; ε3/ε3 : 10.9% ; ε2/ε4 : 2.7%). Compared to the ε3ε3 genotype carriers, carriers of the ε3ε4 genotype had significantly higher rate of total cholesterol (p=0.03) and No-HDL-cholesterol (p=0.02). Univariate analysis showed that the APOE ε4 allele increases the LDL-cholesterol rate in senegaleses women (OR=3.06 [1.16-8.22] 95%

CI; p=0.02).
Conclusion : Our study has shown a difference in APOE allele frequencies and genotype distributions with a total absence of ε2ε2 and ε4ε4 genotypes in a sample of Senegelese women. We also found that APOE gene polymorphism might play a role in plasma lipid levels
Keys words : apolipoprotein E, polymorphism, lipid, women, Senegalese

P9-Human white adipose tissue mitochondrial respiration : effect of body composition

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Adipose tissue (AT) plays an important role in health and diseases, but unlike skeletal muscle, some aspects of its energy metabolism have been under investigated due to technical limitations. According to recent studies, mitochondria could play a role in the expression of AT disorders and their activity could be associated with level of adiposity. This study aims to evaluate the metabolic flexibility of human visceral and subcutaneous white AT and its relationship with body mass index (BMI). The hypotheses are that mitochondrial function is 1) dependent of the anatomical location of AT depot and 2) that there is a relationship between BMI and mitochondrial parameters. To date, 35 out of 90 patients undergoing digestive surgery have been included in the study with BMI ranging from 15.1 to 35.5 $kg \cdot m^{-2}$. To complete characterization, body composition was assessed by regional computed tomography scan analysis at L3. Mitochondrial function was measured *in situ* in permeabilized adipocytes using high resolution respirometry and a substrate/inhibitor titration approach. Preliminary results show a negative correlation between maximal mitochondrial respiration and BMI ($p<0.05$) regardless of the anatomical location, though, respiration is significantly higher in visceral (2.39 ± 0.20 $pmol \cdot sec\text{-}1 \cdot mg^{-1}$) than in the subcutaneous AT (1.68 ± 0.16 $pmol \cdot sec\text{-}1 \cdot mg^{-1}$). Thus, mitochondrial function can be studied with small amount of AT despite its low mitochondrial density and can be discriminated according to AT depot and BMI. Further analyses are required to know whether the observed differences are quantitative and/or qualitative, as well as to identify the mechanisms involved.

P10-Impact of adipose-tissue micro-environment on breast cancer progression , in obese individuals

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Introduction Adipose tissue-derived mesenchymal stem cells from obese (ob-ASC) contribute to adipose tissue (AT) inflammation through polarisation of Th-17 cells, as demonstrated by us (Eljaafari/Diabetes-2015). Because obesity is a risk factor for a variety of cancers including breast cancer, we investigated herein the role of the micro-environment mediated by interaction of ob-ASC with immune cells, on tumor growth and migration.
Methods:. An inflammatory micro-environnement was prepared from mitogen-activated co-cultures of ob-ASC and blood mononuclear cells (MNC). Conditioned media (ob-CM) was then collected and added during 24 hours to cultures of MCF-7 or MDA-MB231, two breast cancer-cell lines expressing or not estrogen receptors,

respectively.. Pro-inflammatory cytokine and VEGFa expressions were measured at the mRNA and protein levels. Tumor cell growth was measured through Ki67 staining, by flow cytometry. Finally, scratch tests were used to measure tumor cell migration. Results: Ob-CM increased mRNA expression and protein secretion of IL-1b, IL-8,TNFa and IL-6 in both cell lines. Overexpression of VEGFa, and increased migration in scratch tests, were observed in ob-CM cultured breast cancer cells. Interestingly, neutralization of IL-17A during co-cultures of ob-ASC with MNC inhibited ob-CM-mediated overexpression of pro-inflammatory cytokines in breast cancer cells . Discussion/Conclusion: Our results strongly suggest (i) the role of obese AT -micro-environment on breast cancer progression, through enhancement of pro-inflammatory cytokine secretion, angiogenesis, proliferation, and migration, and (ii) the contribution of IL-17A in this progression. As we have reported that omega-3-PUFA inhibits ob-ASC-mediated inflammation (Chehimi/Mol-Nutr-Food-Res-2019), its putative beneficial impact on tumor progression is under investigation.

P11-Impact of CD36 gene polymorphism and methylation on soluble CD36 during type 2 diabetes

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Background : Several predisposing factors for diabetes mellitus have been identified as CD36 receptor expression. Our aim was to see the effects of CD36 gene polymorphisms and methylation on the plasma CD36 during type 2 diabetes.
Materials and methods : Circulating CD36 level were determined by ELISA. CD36 gene polymorphisms and methylation were explored by qRT-PCR and MS-PCR.
Results : We didn't find any difference in the CD36 protein level in type 2 diabetic compared to control (p=0.48). CD36 gene methylation had no impact on the CD36 protein in type 2 diabetes (Chi^2=3.56 ; p=0.05 ; OR=3.56 [0.96–5.20]). The polymorphisms studied had no influence on the CD36 protein level in type 2 diabetics. However, the control subjects of the rs3211867 CC genotypes had a significantly higher CD36 protein level than control of the AA/AC genotype (p=0.02). CD36 protein level was correlated positively with LDL-cholesterol (r=0.24 p=0.02) and negatively with body fat (r=-0.22 p=0.03), rs2311867 A allele (r=-0.24 p=0.01), HDL-cholesterol (r=-0.27 p=0.008). After linear regression, sCD36 was associated with HDL-cholesterol (p=0.01) and LDL-cholesterol (p=0.03).
Conclusion : The observations support that CD36 gene polymorphism and methylation wouldn't have no impact on the protein CD36 level during type 2 diabetes.
Keywords : CD36 protein, genetic polymorphism, DNA methylation, type 2 diabetes

Session “cardio-vasculaire”

P12-Effects of glyphosate and Roundup on kidney and heart mitochondrial respiration

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Introduction. Glyphosate and Roundup (glyphosate associated with surfactants) are the most commonly used herbicide class worldwide. We investigated their potential toxicity on kidney and heart mitochondria.

Material and Methods. Rats hearts and kidneys, separating cortex and medulla, were obtained. Isolated mitochondria were exposed to either glyphosate, Roundup or solvent (30 minutes, 37°C, 500µM). Then, mitochondrial respiration and H2O2 production were determined by high-resolution respirometry.

Results. Glyphosate alone did not modulate kidney nor heart mitochondrial respiration. In the heart, the roundup significantly decreased mitochondrial respiration (OXPHOS by complex I -46.9%, $p<0.01$), and by CI+II (-51.5%, $p<0.01$)). H2O2 increased particularly during OXPHOS CI+II (+73.9%, $p<0.05$). In renal cortex, OXPHOS by complex I and OXPHOS by complex I+II were significantly decreased with roundup compared to control (-13.4%, $p<0.05$ and -20.1%, $p<0.01$, respectively). In the medulla, the decrease was significant when investigating complexes I+II (-24.5% $p<0.01$). Mitochondrial production of H2O2 increased (+14.3%, $p<0.05$).

Discussion. Unlike glyphosate alone, at a dose found in human, Roundup significantly impaired cardiac and renal mitochondrial function together with an increase in mitochondrial reactive oxygen species. These data highlight the potential toxicity of such herbicide in organs suspected to be sensitive to Roundup in humans and suggest participation of oxidative stress.

Conclusion: studies will be useful to further investigate the mechanisms involved and whether such mitochondrial alterations might be associated with impaired integrative cardiac and renal functions.

P13-Heparin-mediated release of Hepatocyte Growth Factor at the acute phase of STEMI

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Hepatocyte Growth Factor (HGF) is a cytokine promoting cell survival. In preclinical studies HGF may have a cardioprotective effect. Heparin injection is known to induce a massive release of native HGF in blood. However, HGF release at the acute phase of myocardial and its potential cardioprotective effect is unknown. We aimed to assess HGF kinetics and its potential role in myocardial ischemia reperfusion injury.

We prospectively included STEMI patients admitted in our hospital from 2016 to 2019. Sera were collected at 5 time points (admission, 4 hours (H4), H24, H48 and 1 month after STEMI). HGF levels were assess by ELISA. We also used a mouse model of myocardial ischemia reperfusion to evaluate HGF effect.
We included 251 patients. We observed an intense and early peak of HGF as early as admission (8750 pg/ml, IQR [8021-9492]) followed by a rapid decrease within the first 48h. We demonstrated that this rapid increase was induced by heparin administration. Then, we administrated HGF or placebo in mice during reperfusion. In the HGF group infarct size was significantly smaller compared to the control group (52% of left ventricle vs 58%; p = 0.0023).
In this study we showed an early HGF peak at the acute phase of STEMI, induced by heparin. In our preclinical mouse model, HGF had cardioprotective effect after MI. Thus we may suppose that heparin-mediated release of HGF at the acute phase of STEMI have cardioprotective effect. We also propose that HGF confer a basal cardioprotection in all patients.

Session “exercice et muscle”

P14-ACCEPTABILITY OF WEARING MASK DURING A 5-WEEK TRAINING COURSE FOR HEALTH CARE PERSONNEL IN THE CONTEXT OF COVID-19

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Introduction: Wearing a mask is one of the least costly measures for containing the spread of the Covid-19. This is one of the protective measures put in place by the coordinating team of the inter-university diploma on Antibiology and Antibiotic Therapy in Sub-Saharan Africa for its 2021 session. The objective of our study was to evaluate the acceptability of wearing a mask by health personnel from sub-Saharan Africa during the 05-week training course.
Methods: A descriptive cross-sectional study was conducted from July 15 to November 15, 2021. The survey was the study method, using individual interview and observation as study techniques. During the individual interview it was administered a semi-structured questionnaire including the aspects related to observation.
Results: A total of 58 people were interviewed (35 ± 0.83 years, 75.86% males). The most represented professions were medical specialists 31.03%, biologists 29.31% and general practitioners 18.27%. 56.90% of the participants wore the mask systematically, 34.48% wore it often with an average of 7h24 of daily wear and 58.6% respected the instructions on the proper use of masks. The main inconvenience of wearing the mask was the problem of comfort for 46.55%. For 12.07%, the respiratory history (asthma, pneumonia, tuberculosis) contributed to the discomfort of wearing the mask, with respiratory difficulty being the discomfort felt.
Conclusion: The wearing of masks during the 5-week training in the context of Covid-19 is globally accepted by the health personnel. The health personnel have a fairly good knowledge of the interest of this measure.

P15-RESTING ELECTROCARDIOGRAPHIC ASPECTS OF HIGH-LEVEL SPORTSWOMEN: A COMPARATIVE STUDY BETWEEN SENEGALESE FEMALE BASKETBALL PLAYERS AND SEDENTARY WOMEN

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Introduction: Women's participation in competitive sports has progressively increased. Several studies have been carried out worldwide on the particularities of the heart of top athletes. However, there is very little works on the electrocardiographic specificities of black African sportswomen. The aim of our study was to examine the resting electrocardiogram of high-level female basketball players compared to healthy Senegalese sedentary subjects. **Material and methods:** A descriptive and comparative cross-sectional study was conducted from February 16 to December 20, 2020, including high-level female basketball players and sedentary subjects. All our subjects benefited a clinical examination followed by a resting ECG recording. **Results:** Thirty basketball players and thirty sedentary subjects, all female, were recruited. The mean age of female basketball players and sedentary subjects was 16.93±1.41 years and 17.33±1.44 years, respectively. Sportswomen presented coronary sinus rhythm (3.33%), sinus bradycardia (13.3%), and LAE (3.33%). No cases of atrioventricular block or short PR interval were observed. No subject presented an aspect of incomplete or complete bundle branch block. Electrical LVH was only found in sportswomen according to the Sokolow-Lyon, Lewis, and Cornell indices: 10%, 10%, and 16.66%, respectively. The early repolarization pattern was found only in 5 female basketball players (16.67%) at precordial leads V4, V5, and V6. We did not note a long QT syndrome in either group. **Discussion/Conclusion:** Regular, intense and prolonged sports practice induces electrically adaptive physiological changes in female basketball players. These changes are important to know by the sports physician in order to differentiate them from cardiac pathology.

P16-Walking while working increase EE above sedentary level with no food intake compensation

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Introduction: Sedentary behaviors, as sitting time have been recognize as an independent factor for mortality. Moreover, intense cognitive work can lead to an increase in food intake. Active workstations such as treadmill desks provide the opportunity to replace prolonged sitting at work with light intensity physical activity. The aim of this study was to compare effects of sitting vs standing vs walking during a cognitive task on energy balance, appetite sensation and food reward. Methods: Fifteen normal weight young men were assigned to three condition: Sit, Stand and Walk during which they were submitted to a 45-min cognitive task. For each condition, energy expenditure was measured during cognitive task, appetite sensation, energy intake, relative energy intake were recorded after an ad libitum meal test. Food reward were investigated before and after the meal test.

Results: Energy expenditure was significantly higher in Walk than in Sit and Stand

condition (p≤0.05). There was no difference in absolute energy intake. Relative energy intake decreased by 75kcal in Stand and 150kcal in Walk compared with Sit, however it did not reach statistical significance. There was no difference in appetite feelings or food reward between de three conditions.
Conclusion: Walking Desk use increase energy expenditure while working without any energy compensation in food intake. Walking while working induce a decrease of 150 kcal in energy balance that could become significant if cumulated every working days. Future studies need to clarify if active desk strategies could be of relevance in weight gain prevention.

P17-Central command contribution to cardiac adaptations to exercise

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Background: Understanding how physical exercise solicits the autonomic nervous system is fundamental to maximizing its protective effects. We studied the interaction between autonomic activity, central motor command, respiratory rate and expiration timing during movement.
Material and Methods: Fifteen volunteers (30.9 ± 7.2 years, 8 women) underwent twelve randomized 3 min-tasks of leg extension in sitting position. The type of movement (passive or active), the respiratory rate (spontaneous, 12 or 6 cycles per minute) and the expiration time (exhale during extension or return) were manipulated. Electrocardiography was monitored, RRI intervals (RRI) and its variability were calculated in time (SDNN: standard deviation of RRI, RMSSD: square root of the mean difference of successive RRI, pNN50: percentage of successive RRI (> 50 ms)) and frequency (Ptot: total power, LF: low-frequency power, HF: high frequency power, and LF/HF ratio) domains.
Results: We observed that: 1) active movements was associated with lower RRI (p<.0001), Ptot (p=.0280), SDNN (p=.0207) and pNN50 (p=.0041) than passive; 2) controlled slow respiratory rate was accompanied by increases in pNN50 (p=.0001), SDNN (p<.0001), RMSSD (p<.0001) and Ptot (p<.0001); 3) expiration during return was accompanied by higher pNN50 (p=.0006).
Conclusion: These results suggest that: 1) central motor control contributes to autonomic cardiac modulations and parasympathetic withdrawal during movement whatever respiratory control and 2) expiration during the return could preserve parasympathetic control during exercise. This could be considered in cardiac rehabilitation.
Key words: Autonomic Nervous System, Physical Activity, RR Variability, Movement, Respiration, Parasympathetic Control.

P18-CHARACTERIZATION OF A MOUSE MODEL OF ALLOWING THE MODULATION OF EXERCISE INDUCED MUSCLE DAMAGE SEVERITY AND STUDYING THE CELLULAR EVENTS INVOLVED IN SKELETAL MUSCLE REGENERATION

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Skeletal muscle has the capacity to regenerate after an injury thanks to satellite cells (MuSCs). Myogenesis is strongly influenced by interactions between MuSCs and their microenvironment including fibro-adipogenic precursors (FAPs), endothelial cells (ECs) and macrophages (MPs). Currently, knowledge on the regeneration process is mainly based on toxic, chemical and physical models of injury but remains poorly understood in response to exercise-induced muscle damage (EIMD), i.e., when muscle is rapidly stretched beyond its optimal length.
We aimed at developing a standardized mouse allowing the modulation of exercise-induced muscle damage severity through the application of one or thirty electrically-evoked lengthening contractions. Maximal isometric torque production was recorded before and from 1 to 14 days post-EIMD. Gastrocnemius muscle was harvested to perform histological analyses such as evaluation of necrosis/regeneration and quantification of the number/type of MuSCs, FAPs, ECs and MPs.
Isometric torque recovery was faster (i.e., at day 2-3 vs. day 7) and the extent of necrosis was lower after one than after thirty lengthening contractions, illustrating mild and severe EIMD, respectively. Although the kinetics of changes in the number of cells involved in muscle regeneration was similar between the two protocols, severe EIMD was associated with a larger number of differentiating MuSCs, macrophages and FAPs and a lower number of ECs as compared with mild EIMD.
This mouse model allows to easily modulate the level of muscle injury (i.e., from mild to severe). This model will be useful to further investigate cellular and molecular events in physiological muscle regeneration.

P19-Exercise oximetry (but not ankle brachial index nor walking time) correlates with exercise-induced lactate increase in patients with limiting claudication.

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INTRODUCTION
In claudicants, the correlation between walking-induced biomarkers and the clinical severity of ischemia as assessed with walking distance or ABI, is fair at best. We hypothesized that, a correlation exists between the clinical estimation of ischemia severity with exercise transcutaneous oximetry (Ex-TcpO2) and lactate increase in patients with limiting claudication.
METHODS
A study was performed among 377 patients with arterial claudication. We recorded smoking habits, presence of diabetes mellitus and ongoing treatment including metformin intake. ankle to brachial index (ABI) body mass index (BMI) age and gender, systolic brachial pressure (SAP), and glycemia. Capillary blood lactate was measured at rest and 3 minutes after a constant load treadmill test. We recorded maximum walking time (MWT), heart rate (HRmax), the sum of minimal decrease from oxygen values for buttocks, thighs and calves Ex-TcpO2 (DROPmin), as well as the amplitude of chest-TcpO2 decrease as an index of exercise-induced hypoxemia. A multilinear regression model was used to assess the variables associated to lactate increase.
RESULTS
BMI, SAP, HRmax, the amplitude of decrease in chest-TcpO2 and DROPmin, but not age, sex, ABI, MWT, diabetes mellitus nor glycemia, were significantly associated to lactate increase in the model.

CONCLUSION
Because it accounts for the severity and diffusion of lower-limb exercise-induced ischemia and detects exercise induced hypoxemia, TcpO2 is preferable to ABI or MWT to estimate the mechanisms underlying metabolic consequences of walking in patients with claudication. Estimating changes in exercise-induced lactate increase under treatment is easy with capillary sampling andwarrants future investigations.

P20-VERTICAL JUMP PERFORMANCES: A PILOT STUDY ABOUT THE EFFECT OF ANTHROPOMETRIC FACTORS, MAXIMAL POWER AND ETHNIICITY

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Introduction: Previous studies have shown an ethnicity effect on vertical jump (VJ) performances. We investigated the effects of anthropometric factors [body height (BH), sitting height (SH), foot length (FL), leg length (LL), Body Weight (BW), BMI, Body fat (BF), BF/BW and Skelic (Sk=LL/SH) or Cormic (Co=SH/BH) indices], and ethnic origins (Caucasians and West-Africans) on VJ performances [Squat Jump (SJ), Countermovement jump (CMJ) and Countermovement jump with arm swing (CMJA)] on a force-platform.
Methods: 55 physical education students [32 Caucasians (C) and 23 West-Africans (WA)] participated in this study. The correlation coefficients between VJ and an anthropometric factor (A) were studied with linear and multiple linear regressions including one A and a dummy variable E corresponding to ethnic origin.
Results: Only the anthropometric factors SH, Sk and Co were significantly different in groups C and WA. All VJ were higher in WA. The ethnic difference in SH could partly explain the higher values VJ in WA because the multiple regression between VJ and SH and E were significant. Similarly, BH was negatively correlated with SJ, CMJ and CMJA but the ethnic differences in VJ could not be explained by BH because it was not statistically different in C and WA. Countermovement (CMJ-SJ) and arm-swing (CMJA-CMJ) were significantly correlated with LL.
Conclusion: The optimal protocol to study the effects of anthropometric factor on the ethnic difference in VJ should be performed with subjects whose ranges of maximal power (in W.kg-1) and BF/BW are small because VJ performances also depend on these parameters.

P21-IMPACT OF FASTING-RAMADAN AND SPORT PRACTICE ON THE REACTION TIME AND ON THE INHIBITORY CONTROL IN CHILDREN AND ADOLESCENT BOYS

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Introduction. Cognitive-function can be influenced by Ramadan-fasting(RF) modifications such as dehydration, food intake and sports-practice. Athletes practicing open-skill-sports may develop better inhibitory-control, decision-making and execution of actions.
Aim. Compare RF' effects and open-skill sports practice on reaction time and

inhibitory control in athlete and non-athlete children and adolescent boys.
MaterialandMethods. Comparative study was conducted among eleven basketball-players (least five-years of club membership) and thirteen non-athlete aged between eleven and fifteen years old. The experimental protocol included two sessions, before Ramadan(BR), and at the beginning of the second week of Ramadan(R2). During each session, simple(SRT), choice(CRT) and negative priming(NPRT) reaction time were evaluated using validated software Superlab-4.5. These test provides valuable information about the perceptual-motor function(SRT), decision-making(CRT) and inhibitory-control(NPRT).
Results. No significant intra or inter group effects between the different sessions for different tests.

Session	BR		R2		p1	p2	p3
GROUP	NonAthlete	Athlet	NonAThlete	Athlete	NS	NS	NS
SRT(ms)	345±35	367±34	369±44	373±48	NS	NS	NS
CRT(ms)	470±68	452±48	468±60	452±63	NS	NS	NS
NPRT(ms)	474±82	469±69	496±86	446±77	NS	NS	NS

Data expressed as mean±SD. p1(Mann-Whitney-test analyzing the Ramadan effect for both groups); p2(ANOVA analyzing the practical effect); p3(MANOVA-analyzing the Ramadan effect versus the Practical effect); p <0.05; NS:not significant. BR:Before Ramadan; R2:Ramadan session

Discussion/conclusion. We found that neither fasting nor the open-skill sports had significantly affected cognitive tasks obtained through the various tests. It is assumed that the superiority of athletes can be observed in specific cognitive tasks related to the sport context and not to the general context.

P22-The assessment of submaximal aerobic capacity in North-African patients with chronic hepatitis B (CHB): a case-control study

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Introduction. Studies evaluating aerobic capacity in CHB are scarce.
Aim. Evaluate the submaximal aerobic capacity of non-cirrhotic CHB patients.
Material&Methods. This case-control study includes 54 Tunisian participants: cases(n=26;15M) were untreated CHB patients, and controls(n=28;15M) were healthy participants. Anthropometric data[sex,age(Yr),height(m),weight(kg) and body-mass-index(kg/m2)] and biological data(complete-blood-count,erythrocyte-sedimentation-rate,prothrombin-level,glycaemia,uraemia,creatinemia,gamma-glutamyl-transpeptidase,alkaline-phosphatase,bilirubin,transaminase,total-cholesterol,high and low-density-lipoproteins-cholesterol, and triglycerides) were collected. The physical activity level was estimated by the Voorrips questionnaire. The submaximal aerobic capacity was evaluated by the 6-minute walk test(6MWT) and the following data were determined: 6-minute walk distance(6MWD)(m,%),number of stops while

walking,heart-rate(HR)(bpm,%),Oxy-sat(%) and ΔOxy-sat(=Oxy-sat$_{end}$-Oxy-sat$_{rest}$),dyspnoea and blood-pressure. Dyspnoea was assessed via the visual analogue scale. The following definitions were applied: signs of walking intolerance(6MWDend>5/10),a ΔOxy-sat>5points was defined as a clinically significant desaturation; a HR$_{end}$<60% was considered as a sign of chronotropic insufficiency. Specific North-African 6MWD norms were used and 6MWD-LLN was calculated.
Results. The two groups had similar biological data and profiles,different physical activity scores, and percentages of subjects with a sedentary status. Compared to the control-group,the CHB-group had statistically lower 6MWD expressed in absolute value(702±60 *vs* 641±57m,respectively) and as a percentage of predicted value(112±11*vs* 99±15%,respectively). Compared to the control-group, the CHB group have statistically significant lower values of HR$_{end}$(bpm,%) and ΔOxy-sat, and included a significantly higher percentage of subjects with an abnormal 6MWD.
Discussion/Conclusion. Despite the similarity of profile in the two groups, the CHB group had a lower aerobic capacity than control-group. This result supposes that CHB infection alters the aerobic capacity.

P23-Sarcopenia in myositis patients: a marker of muscle damage associated with myositis severity and disability

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Introduction. Myositis are systemic diseases characterized by muscle inflammation and weakness. Even when disease activity has been resolved, myositis patients frequently present decreased physical performance and disability (coined as “damage”).
Sarcopenia is a skeletal muscle disorder characterized by low muscle strength and mass leading to disability, decreased quality of life and increased mortality.
The aim of this study was to investigate prevalence and significance of sarcopenia in myositis patients with low or no disease activity.
Methods. Adult myositis patients according to 2017 ACR/EULAR criteria with low or no disease activity were enrolled. 30 healthy controls paired for age and sex were also included. At the enrolment, total (LM) and appendicular lean mass (ALM) were measured using dual-energy X-ray absorptiometry and muscle grip strength using Jamar dynamometer. Sarcopenia was defined according to EWGSOP2. Extension and severity of damage were assessed according to IMACS, muscle strength by manual muscle test and hand-held dynamometer, physical performance by 6mWT and quality of life by HAQ.
Results. 34 patients, average age 59.9 years (±14.1), were prospectively enrolled. 7 were sarcopenic (20.6 vs 0% in controls, p=0.03).
At the enrolment, sarcopenic patients were globally weaker; they had a lower physical performance (p<0.0001), and a poorer quality of life (p=0.002). Muscle mass positively correlated with dynamometer measures and 6mWT score. Damage score was significantly higher in sarcopenic patients.

50% of sarcopenic patients had myocarditis (vs 3.7%, p=0.002). Consistently, they required more frequently aggressive therapy.
Conclusion. Sarcopenic myositis patients are a subgroup with important muscle damage and disability.

Session “rein”

P24-Mild therapeutic hypothermia during renal ischemia mitigates systemic and local renal inflammation after reperfusion in mice

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Introduction

Ischemia-reperfusion (IR) triggers systemic and organ inflammation. Mild therapeutic hypothermia (mTH) has been suggested to protect against IR lesions, however its mechanisms are unclear. We aimed to show that mTH attenuates systemic and local inflammation after renal IR.

Methods

A 20-minutes bilateral renal ischemia by clamping (or a sham procedure) was performed on C57BL6 mice with body temperature maintained at 37°C (normothermia) or 34°C (mTH). Inflammatory markers were assessed by ELISA and qRT-PCR, 2h and 24h after reperfusion. Plasma urea was dosed at 2h and 24h, acute tubular necrosis (ATN) was scored (0 to 4) at 24h.

Results

Renal IR compared to Sham was associated with urea elevation as soon as 2h after reperfusion (median urea 18.7 vs 11.7 mmol/L, p=0.02), even more pronounced 24h after reperfusion (median urea 60.8 vs 6.2 mmol/L, p=0.004), and with ATN at 24h (median score 2.23 vs 0.80, p<0.001). Renal IR led to peaks of plasma IL-6 and IL-10, respectively 2h and 24h after reperfusion. Tissue expression of IL-6 was increased at 2h and 24h, so was IL-1β at 24h.
Applying mTH during renal ischemia significantly reduced plasma urea (median 22.7 mmol/L, p=0.001), ATN score (median 1.45, p=0.03) at 24h, inhibited IL-6 and IL-10 secretions, lessened IL-6 and IL-1β renal tissue expressions, but increased TNF-α renal expression at 24h.
MCP1, NFkB or TGF-β expressions were unchanged.

Conclusion

Protection against renal IR injuries offered by mTH applied during ischemia was associated with decreased plasmatic levels of inflammatory markers and mitigation of their renal expressions.

P25-MALIGNANT HYPERTHERMIA OBSERVED DURING THE ESTABLISHMENT OF A NEW PORCINE MODEL OF ACUTE KIDNEY INJURY INDUCED BY ISCHEMIA-REPERFUSION

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Introduction: Acute kidney injury (AKI) is one on the main complication of bypass surgery and can affect severely survival of patients. To investigate AKI physiopathology, we purpose a new swine model of AKI induced by ischemia-reperfusion, one of the main causes of AKI.
Material and Methods: After tranquilization, five pigs *sus scrofa* between 30 and 50kg were intubated and anesthetized with halogenous gas (sevofluran). Analgesia was assured by morphine. After surgical opening of the retroperitoneal space, vascular pedicles of each kidney were clamped for 90min and measures were followed during next 8h.
Results: On average, plasmatic creatinine and plasmatic urea increased by 197% (+/-8%) and 350% (+/-30%). Glomerular filtration rate and diuresis decreased, varied but never reached the basal state. Surprisingly, three of five pigs seems to develop a malignant hyperthermia characterized by an increase of body temperature, muscle rigidity, spasms, a major increase in exhaled C02 and an exacerbate hyperkaliemia. Two swines exceeded 40°C and could not reach the end of the protocol because of précoce euthanized with T61. One of them started a hyperthemia but was treated with dantrolen (2mg/kg IV) which stop the rise of temperature. For pigs which not develop hyperthermia, the mean kaliemia raise by 50% whereas for others raise by 100%.
Discussion/Conclusion: The primary results are promising for a future validation of this porcine model of AKI. However, malignant hyperthermia may have contributed to the onset of renal failure. Thus, a new anesthesic protocol without halogenous gas must be considered to validate this model.

P26-Which GFR estimation formula should be used in patients followed in pediatric nephrology?

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Introduction:
Estimation of Glomerular Filtration Rate (GFR) using formulas (eGFR) is a major component of renal function monitoring. New formulas have recently been proposed for children and adolescents. The aim here is to evaluate the performance of different formulas in patients followed in pediatric nephrology.
Methods:
Creatinine levels were measured (IDMS standardization), mGFR by iohexol plasma clearance in a cohort of 307 "renal risk" patients (sex ratio1/1, 31%renal transplant, 40%non-renal transplant, 29%nephropathy) aged 12.1±0.3 years [2-19], mean mGFR of 86±1 mL/min/1.73m² [15-175]. The eDFG is calculated with different formulas (Results). The performance of the formulas is evaluated: bias measure and accuracy (accuracy, P30% and P10%). Results expressed as mean±SEM.
Results:

	Schwartz 2009	Schwartz-Lyon	CKiDU25 creatinine	EKFC creatinine	CKiDU25 cystatin	FAS cystatin	Schwartz combined	Mean EKFC-FAScys
All patients	20,1±1,3 63,2 20,5	10,6±1,2 77,9 34,5	14,2±1,1 73,6 31,6	11,2±1,0 78,5 31,9	-7,0±0,8 95,8 46,6	2,8±0,8 90,2 49,2	-0,04±0,68 95,4 52,4	7,0±0,7 86,0 45,0
mGFR > 75 mL/min/1,73 m²	23,8±1,8 65,3 19,7	12,6±1,6 78,8 37,3	15,9±1,6 76,7 34,7	8,8±1,2 89,6 37,3	-10,9±1,0 96,9 41,5	-0,1±1,1 94,3 51,8	-2,2±0,9 98,4 56,5	4,4±0,9 94,8 52,3
mGFR < 75 mL/min/1,73 m²	14,0±1,6 59,6 21,9	7,3±1,4 76,3 29,8	11,3±1,4 68,4 26,3	15,2±1,6 59,6 22,8	-0,3±0,9 93,9 55,3	7,6±1,1 83,3 44,7	3,6±0,9 90,4 45,6	11,8±1,5 71,1 32,5

Discussion:
In our population, the performance of creatinine-based formulas is inadequate with significant overestimation of GFR mainly in patients with GFR>75. CystatinC-based or combined formulas have acceptable performance with a P30%>90%, and allows better estimation of GFR in this population.

P27-Association Between Nocturnal Blood Pressure Dipping and Chronic Kidney Disease

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INTRODUCTION: Management of blood pressure (BP) in chronic kidney disease (CKD) is critical for preventing cardio-renal complications. We aimed at describing nocturnal BP dipping patterns and its predictors in patients with CKD.
METHODS: We analysed data from 642 patients with CKD stages 1 to 5 referred for kidney function testing to a single tertiary hospital, including 24-hour urine collection, measurement of glomerular filtration rate (GFR) using clearance of radioisotopic tracer, as well as ambulatory BP measurement (ABPM). Factors associated with less than 10% nocturnal BP dipping were analysed with adjusted logistic regression models including a random intercept to deal with clustering of measurements within patients.
RESULTS: Participants (mean age 56 ± 15 years; 35% female, mean GFR 49 ± 21 mL/min per 1.73 m2) consisted of 8% extreme-dippers, 37% dippers, 40% non-dippers, and 15% reverse-dippers. The prevalence of non- or reverse- dipping increased with CKD severity, from 36% in stage 1 to 65% in stages 4-5. In the

multivariable adjusted regression, non or reverse dipping was independently associated with measured GFR ([OR, 95% CI] per 10 ml/min/1.73m² decrease= 1.16 [1.06 – 1.26], p=0.001), daytime ambulatory SBP (OR per 10 mmHg decrease= 1.17 [1.06–1.28],p=0.001), African origin (OR= 1.56 [1.04 – 2.34], p=0.03) and 24h Na/K (OR per 1-unit increase= 1.20 [1.06 – 1.37], p=0.006).
CONCLUSIONS: The prevalence of nocturnal non-or reverse dipping increases substantially across the spectrum of CKD. Measured GFR, ambulatory daytime SBP, African origin and 24-hour urinary sodium to potassium ratio are independent predictors of abnormal nocturnal BP decrease.

P28-Consequences of Lithium Exposure on Mineral Metabolism in Rats on a Low Calcium Diet

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Introduction. Lithium represents the first-line treatment of bipolar disorder. However, prolonged therapy may induce mineral metabolism disturbances such as hypercalcemia, hyperparathyroidism and decrease in bone mineral density (BMD). These adverse effects suggest an alteration of the calcium-parathyroid hormone (PTH) relationship, which has been poorly investigated in experimental models. **Objective.** The present study aims to develop an animal model characterizing lithium-induced mineral disorders. **Material and methods.** Rats on low calcium diet (0.01%) were divided into two groups : controls (N=9) and lithium-treated (N=9), and followed-up during one month. Mineral metabolism and renal function were characterized by measurements of calcium, PTH, calcitriol, creatinine and lithium in blood and urine. BMD was determined after sacrifice using shinbones. **Results.** Compared with baseline values, serum calcium decreased significantly (p<0,005) on low Ca diet in controls whereas it remained stable in lithium-treated rats. Lithium-treated rats presented higher plasma PTH values than controls (p<0.05). BMD was significantly lower in both groups than in rats fed with normal calcium diet (controls, p<0.0001; lithium, p<0.05), but the difference was less marked on lithium. **Discussion.** Low calcium diet induced hypocalcemia and lower BMD in control rats. Lithium treatment was associated with hyperparathyroidism, prevented hypocalcemia and less marked decrease in BMD, likely explained by increased renal tubular calcium reabsorption. **Conclusion.** Our findings are consistent with clinical observations in chronically lithium-treated patients, thus validating our experimental model and allowing a better understanding of lithium-induced mineral disturbances. However, underlying mechanisms remain to be elucidated.

Session “autres”

P29-EVALUATION OF BIOLOGICAL PARAMETERS IN PATIENTS CURED OF COVID-19 IN THE REGION OF THIES (SENEGAL)

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Introduction: COVID-19 can alter many systems, including causing crucial hematological and biochemical changes in patients. COVID-19 survivors report persistent symptoms after discharge from hospital. No studies in Senegal are available on this stage of recovery. The aim of our study was to evaluate biological parameters in patients cured of COVID-19. **Material and methods:** A descriptive cross-sectional study was conducted from April 1 to July 31, 2021. Patients cured of COVID-19 after infection confirmed by real-time PCR for SARS-CoV-2 were recruited. The time from hospital discharge to the start of our study ranged from 1 to 14 months. The study included a questionnaire and a clinical examination followed by blood and urine sampling. **Results**: Fifty patients cured of SARS-CoV2 were recruited with a sex ratio of 1.63. The mean age was 49.74 ± 12.35 years. The majority of patients had presented a moderate symptomatic form (76%). Only ten patients (20%) were placed on oxygen therapy. The most common hematologic abnormalities were hyperlymphocytosis (52%), hyperbasophilia (48%), and neutropenia (42%). Anemia and leukopenia were found in 8% and 2% of patients respectively. The most frequent biochemical abnormalities were a decrease in HDL-cholesterol (40%), an increase in LDL-cholesterol (32%), a high atherogenicity index (36%) and an increase in D-dimer (3%). An increase in the proteinuria/creatinine ratio was observed in 24% of patients. **Discussion/Conclusion:** Biological changes were observed in patients cured of COVID-19 due to viral infection and medical treatment. Knowledge of the biological profiles of COVID-19 would help advance infection control strategies.

P30-Association of Forced Oscillation Technique measurements with respiratory system compliance and resistance in a 2-compartment physical model

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Background. The forced oscillation technique (FOT) is a lung function technique that does not require patient participation and may be useful for diagnosis and follow-up in a range of respiratory diseases. Interpretation of FOT requires caution in the absence of data on how global or regional alterations in airway resistance (Raw) and lung compliance (CL), which are key pathophysiological characteristic of obstructive and restrictive lung disease, translate into variation of FOT measurements.
Methods. A 2-compartment physical model of the respiratory system allowed to simulate variations in Raw (0.067 to 11.16 cmH2O.L-1.s), CL (0.026 to 0.312 L.cmH2O-1), and their heterogeneity. The model was activated to simulate tidal breathing in an adult human. Five-Hz respiratory system resistance (Rrs5) and reactance (Xrs5), area of reactance, resonance frequency and intrabreath variation in Rrs5 and Xrs5 were measured by FOT. Relationships between model characteristics (Raw, CL, heterogeneity) and FOT measurements were explored by multiple regression.
Results. Rrs5 and intrabreath variation in Rrs5 and Xrs5 were strongly associated with model characteristics (R2=0.753, 0.5 and 0.658, respectively). By contrast, Xrs5, AX, and Fresp only weakly associated with model characteristics (R2=0.214, 0.349 and 0.076, respectively). Raw heterogeneity was the main determinant of Rrs5 (Coeff=0.594), AX (Coeff=0.566) and intrabreath variation in Rrs5 and Xrs5 (Coeff=0.586 and 0.732). Regional extremes in Raw strongly determined Rrs5

(Coeff=1.006).
Conclusion. Raw heterogeneity and maximal regional Raw were the main determinants of FOT measurements, in particular Rrs5. Associations between lung compliance and FOT measurements were weak.

P31-Minocycline Counteracts Ectopic Calcification in a Murine Model of Pseudoxanthoma Elasticum

Elise Bouderlique [1], Lukas Nollet [2], Ellie Tang [1], Jeremy Zaworski [1], Letavernier Emmanuel [1], Olivier Vanakker [2]
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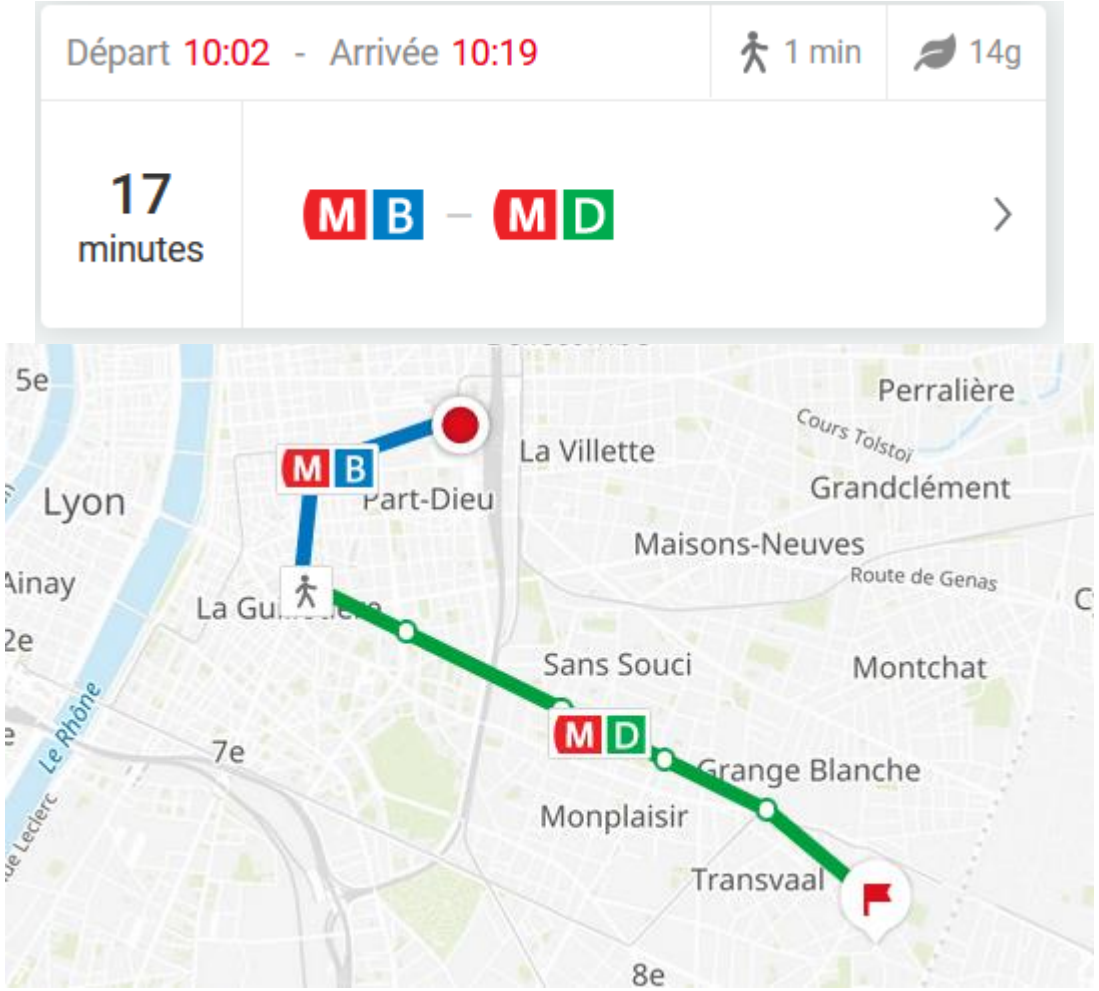
Introduction
Pseudoxanthoma elasticum (PXE) is an intractable Mendelian disease characterized by ectopic calcification of skin, eyes and blood vessels. Recently, increased activation of the DNA damage response (DDR) was shown to be involved in PXE pathogenesis, while the DDR/PARP1 inhibitor minocycline was found to attenuate aberrant mineralization in PXE cells and zebrafish.
Material and Methods
In this proof-of-concept study, we evaluated the anticalcifying properties of minocycline in Abcc6−/− mice, an established mammalian PXE model. Abcc6−/− mice received oral minocycline supplementation (40 mg/kg/day) from 12 to 36 weeks of age and were compared to untreated Abcc6−/− and Abcc6+/+ siblings. Ectopic calcification was evaluated using X-ray microtomography with three-dimensional reconstruction of calcium deposits in muzzle skin and Yasue's calcium staining. Immunohistochemistry for the key DDR marker H2AX was also performed.
Results
Following minocycline treatment, ectopic calcification in Abcc6−/− mice was significantly reduced (−43.4%, $p < 0.0001$) compared to untreated Abcc6−/− littermates. H2AX immunostaining revealed activation of the DDR at sites of aberrant mineralization in untreated Abcc6−/− animals.
Discussion/Conclusion
In conclusion, we validated the anticalcifying effect of minocycline in Abcc6−/− mice for the first time. Considering its favorable safety profile in humans and low cost as a generic drug, minocycline may be a promising therapeutic compound against vascular calcifications.

Se rendre au congrès de la Gare Part-Dieu à la Faculté Laennec



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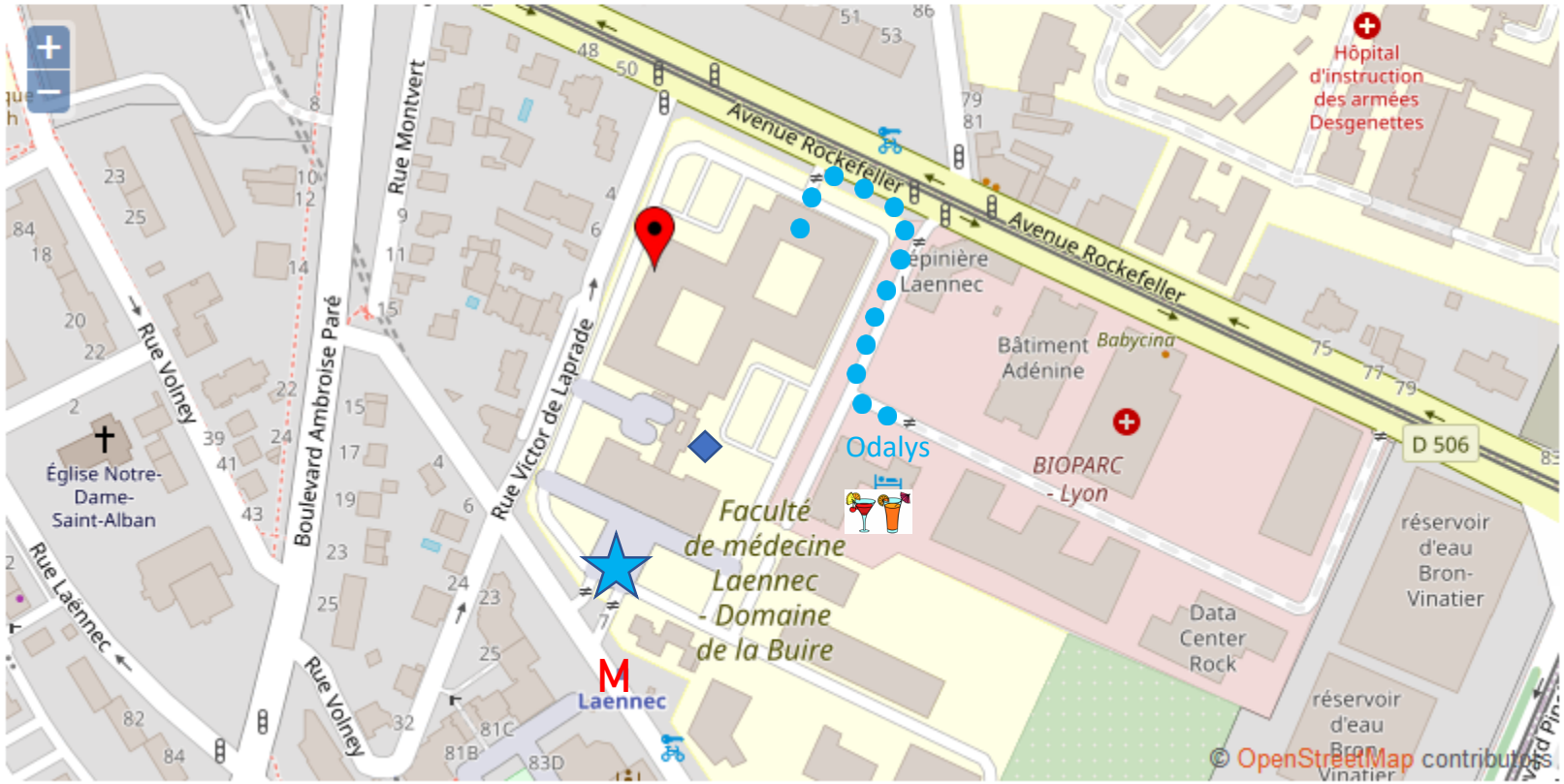
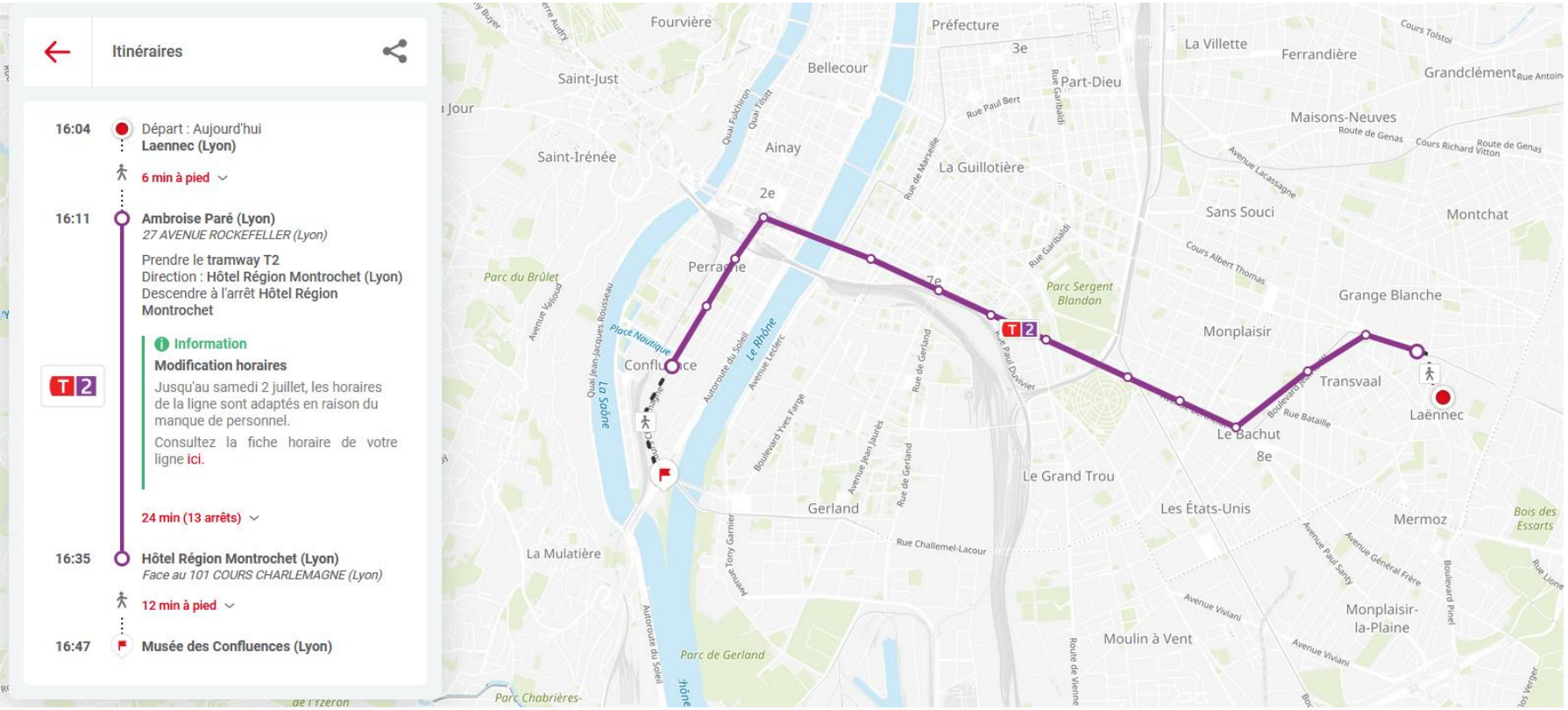
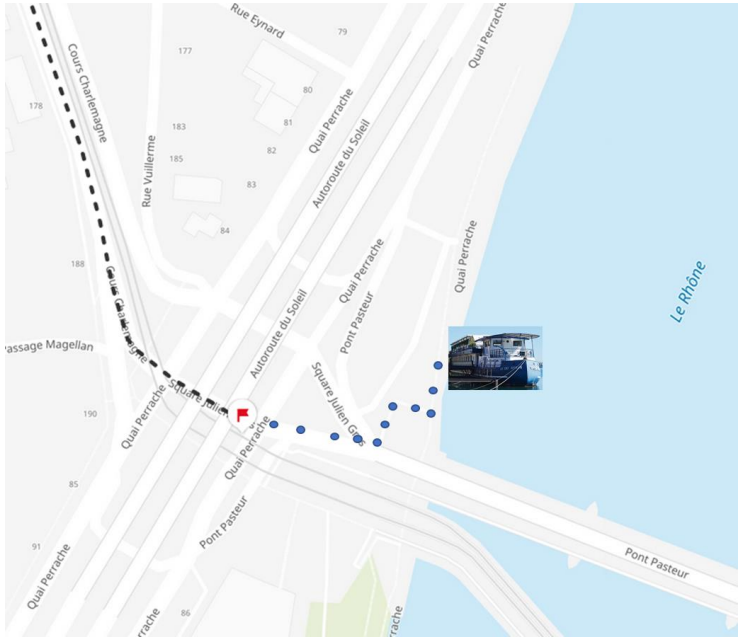
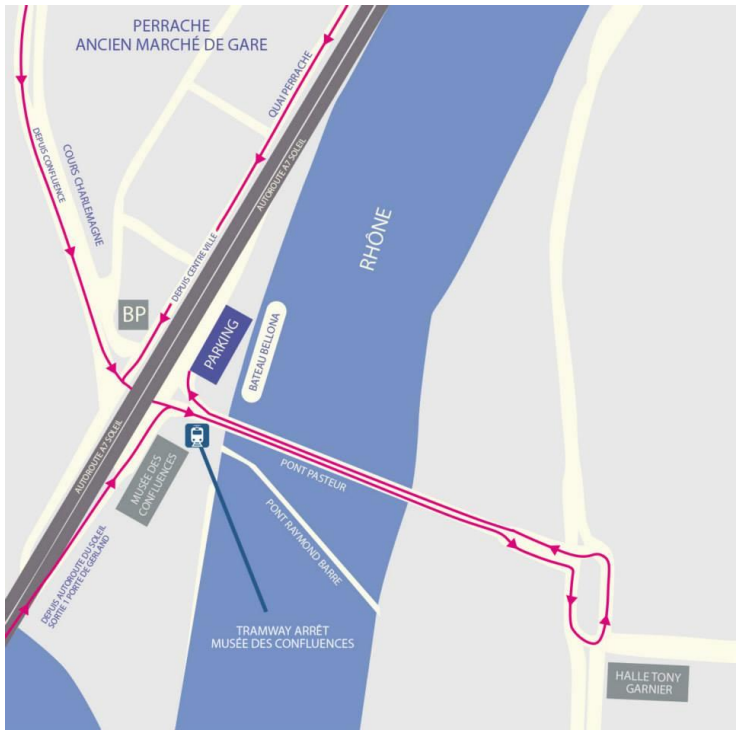


Se rendre au Gala diner depuis la Faculté Laennec: Péniche Bellona
84 quai Perrache 69002 Lyon







SYTRAL MOBILITÉS

Et le retour de la Péniche Bellona

T2 — Perrache → St-Priest Bel Air

H. REGION MONTROCHET.	21.17	21.32	21.48	22.03	22.18	22.33	22.49	23.04	23.19	23.35	23.50	0.06	0.21	0.37	0.52
PERRACHE.	21.22	21.38	21.53	22.08	22.23	22.39	22.54	23.09	23.25	23.40	23.56	0.11	0.27	0.42	0.58
CENTRE BERTHELOT	21.25	21.40	21.56	22.11	22.26	22.41	22.57	23.12	23.27	23.43	23.58	0.14	0.29	0.45	1.00
JET D'EAU - M. FRANCE	21.31	21.46	22.02	22.17	22.32	22.47	23.03	23.18	23.33	23.49	0.04	0.20	0.35	0.51	1.06
VILLON	21.33	21.48	22.03	22.18	22.34	22.49	23.04	23.19	23.35	23.50	0.06	0.21	0.37	0.52	1.08
GRANGE BLANCHE	21.38	21.53	22.09	22.24	22.39	22.54	23.09	23.24	23.40	23.55	0.11	0.26	0.42	0.57	1.13
ESSARTS - IRIS	21.43	21.58	22.13	22.28	22.44	22.59	23.14	23.29	23.44	0.00	0.15	0.31	0.46	1.02	1.17
HOTEL DE VILLE - BRON	21.45	22.01	22.16	22.31	22.46	23.02	23.16	23.31	23.47	0.02	0.18	0.33	0.49	1.04	1.20
EUROPE - UNIVERSITE	21.52	22.08	22.23	22.38	22.53	23.08	23.23	23.38	23.53	0.09	0.24	0.40	0.55	1.11	1.26
PORTE DES ALPES..	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1.28
PORTE DES ALPES	21.54	22.10	22.25	22.40	22.55	23.10	23.25	23.40	23.55	0.11	0.26	0.42	0.57	1.13	-
SAINT-PRIEST BEL AIR	22.09	22.24	22.40	22.54	23.09	23.23	23.38	23.53	0.09	0.24	0.40	0.55	1.11	1.26	-

T1 — Debourg → IUT Feyssine

DEBOURG	20.44	20.51	21.00	21.15	21.18	21.31	21.46	22.02	22.17	22.33	22.48	23.04	23.19	23.35	23.50	0.06	0.20	0.35
H. REGION MONTROCHET.	20.52	20.58	21.07	21.23	21.25	21.38	21.54	22.09	22.25	22.40	22.56	23.11	23.27	23.42	23.58	0.13	0.28	0.42
PERRACHE.	20.57	21.04	21.13	21.28	21.31	21.44	21.59	22.15	22.30	22.46	23.01	23.17	23.32	23.48	0.03	0.19	0.33	0.48
LIBERTE	21.06	-	21.21	21.37	-	21.52	22.08	22.23	22.39	22.54	23.10	23.26	23.41	23.57	0.12	0.28	-	-
GARE PART-DIEU	21.12	-	21.28	21.43	-	21.59	22.14	22.30	22.45	23.00	23.16	23.31	23.47	0.02	0.18	0.33	-	-
CHARPENNES CHARLES HERNU	21.18	-	21.33	21.49	-	22.04	22.20	22.35	22.50	23.06	23.22	23.37	23.53	0.08	0.24	0.39	-	-
LA DOUA - G.BERGER	21.24	-	21.40	21.55	-	22.11	22.26	22.42	22.57	23.12	23.28	23.44	23.59	0.15	0.30	0.46	-	-
IUT - FEYSSINE	21.29	-	21.44	22.00	-	22.15	22.31	22.46	23.01	23.17	23.32	23.48	0.03	0.19	0.34	0.50	-	-