Journée des Sciences de la Vie et de la Santé de Créteil
Maison du Handball de Créteil

Jeudi 10 octobre 2024

Programme scientifique élaboré par le
Comité d'Animation Scientifique de l'IMRB (COMASCI) et de l'Ecole Doctorale SVS

Jeudi 10 octobre 2024 – 8h45 à 18h
Maison du Handball de Créteil, 1 rue Daniel Costantini
94000 Créteil

Programme

08h45-09h00 : Accueil

9h00-9h15 : Ouverture par **Pascale Fanen** *et* **Jorge Boczkowski,** suivie d'une allocution de **Pierre Wolkenstein**, *Doyen de la faculté de santé* et de **Christophe Combadière**, *directeur de l'IMRB*

Session communications orales 1 : 9h15-10h00
Modérateurs : Céline Colnot – Patrice Bruscella

9h15-9h30. Ghislain BANOS: Engineering of 3D muscle constructs to model Duchenne Muscular Dystrophy (DMD) (Eq.Relaix – Dir. thèse : Nathalie Didier)

9h30-9h45. Saskia ECKERT: Endothelialization techniques for complex 3D-printed carotid artery structures (Eq. Pirenne – Dir. thèse : Pablo Bartolucci)

9h45-10h00. Laura FERTITTA: Standardizing the analysis of cutaneous neurofibromas in Nf1-KO mice and exploring drugs targeting tumor cells and their microenvironment in this model (Eq. Ortonne - Dir. thèse : Piotr Topilko)

Pause-café
Session posters 1 (Impairs) : 10h00-11h15

Session Communications orales 2 : 11h15–12h00
Modérateurs : Ophélia Godin – Yasmine Hachemi

11h15-11h30. Charline JEAN: Predicting frailty domain impairments and mortality with the Hospital Frailty Risk Score among older adults with cancer: the ELCAPA-EDS cohort study (Eq. Canoui Poitrine – Dir. thèse : Etienne Audureau)

11h30- 11h45. Joseph MATTAR: Efficacy of EXOPULSE MOLLII SUIT, a new multisite transcutaneous electrical stimulation technique, on several fibromyalgia associated symptoms (UR ENT-EA 4391 - Dir. thèse : Jean-Pascal Lefaucheur)

11h45-12h00. Kalthoum BELGHITH: Effects of eccentric training on the structural and mechanical properties of plantar flexors in subacute stroke survivors: a randomized controlled trial (UR BIOTN - Dir. thèse : Mustapha Zidi)

Déjeuner *
Session posters 2 (Pairs) : 12h15-13h15

*Avec la participation de **Valérie Langlois**, *assesseure aux affaires doctorales de l'UPEC*

Session Communications orales 3 : 13h15–14h00 :
Modérateurs : Ilaria Cascone – Leeyah Issop-Merlen

13h15-13h30. Marwa El HAJJ: Delivering SARS-CoV-2 mutated RBD antigens to the CD40 receptor: A strategy for inducing long-term antibody responses (Eq. Lévy – Dir. thèse : Véronique Godot)

13h30-13h45. Daphné CORBOZ: Angiopoietin-like 4 improves left ventricular function and coronary endothelial function during heart failure with preserved ejection fraction: a proof-of-concept study in pigs (Eq. Ghaleh – Dir. thèse : Bijan Ghaleh)

13h45-14h00. Virgina ZOGLIO: PAX3 drives functional muscle stem cell heterogeneity during muscle regeneration (Eq. Relaix - Dir. thèse : Frédéric Relaix)

14h00-15h00. **Conférence** de **Ghislaine Filliatreau** : Actualité de l'intégrité scientifique

Pause-café : 15h00-15h30

Session Communications orales 4 : 15h30–16h15 :
Modérateurs : Valérie Urbach – Aurélie Dupuy

15H30- 15H45. Maria ETHEL: Spatial distribution and role of PDGFRα+ skeletal stem/progenitor cells in bone regeneration (Eq. Relaix– Dir. thèse : Céline Colnot)

15H45-16h00. Khadeeja SY: Impact of specialized pro-resolving lipid mediators on the colonization of CF respiratory epithelia by Aspergillus fumigatus (Eq. Lanone – Dir. thèse : Valérie Urbach)

16h00-16h15. Céline SAKR: Sing next-generation sequencing to study cross-transmission: the case of Stenotrophomonas maltophilia (UR DYNAMIC – Dir. thèse : Jean-Winoc Decousser)

Réunion du jury d'attribution des prix / AG Codopodo : 16h30-17h00

17h00-17h30 : Conclusions et remise des Prix par **Pascale Fanen,** *Directrice de l'Ecole Doctorale Science de la Vie et de la Santé*

Prix de la meilleure communication orale

1- Engineering of 3D muscle constructs to model Duchenne Muscular Dystrophy (DMD)

Ghislain Banos[1], Anais Bleuzen[1], Teoman Ozturk[1], Julien Mignot1, Thomas Boudou[4], Olivier Stephan[4], Frédéric Relaix[1,2,3], Hélène Rouard[1,3], Nathalie Didier[1]

[1]Univ Paris Est Créteil, INSERM, EFS, IMRB, F-94010 Créteil, France, [2]EnVA, IMRB, F-94700 Maisons-Alfort, France, [3]AP-HP, Hôpital Mondor, Service d'histologie, F-94010 Créteil, France, [4]Laboratory of Interdisciplinary Physics (LIPhy), University of Grenoble Alpes, CNRS, F-38000, Grenoble, France.

01/10/2021

With the rapid advances in gene therapy and the constant need to rapidly test new drug candidates, the development of reliable *in vitro* skeletal muscle models reproducing the main features of muscular disorders has become essential and is therefore an active area of research in tissue engineering.

We have developed innovative biomimetic hydrogels (Hd-7KP) favoring the differentiation and the fusion of muscle stem cells (MuSC), as well as the formation of unidirectionally aligned and mature myofibers *in vitro*. Taking advantage of the properties of these hydrogels, we developed 2 approaches to engineer skeletal muscle tissue *in vitro:* (1) a 3D-Monolayer Model in which MuSC-derived myofibers are generated between 2 layers of hydrogel, and (2) a 3D-Muscle Model based on PDMS-micropillar technology that enables longer cultures, and functional testing (contractile force measurement and calcium transient imaging). Using these 2 approaches, we aim to model Duchenne Muscular Dystrophy (DMD), a X-linked neuromuscular disorder caused by mutations in the *DMD* gene encoding Dystrophin protein, for which therapeutic options are still missing. We purified MuSC from WT or *R-DMDdel52* (exon 52 deletion) rat muscles as source of cells.

Using our 3D-Monolayer Model, we observed that WT rat MuSC (rMuSC) differentiated on our hydrogels formed perfectly aligned and mature myofibers expressing adult *Myh* genes (*Myh 1, 2, 4* and *7*), surrounded by a basal lamina, and exhibiting regular striations of sarcomeric a-Actinin, peripheral myonuclei and AChR clusters. We noticed that DMD myofibers exhibited a reduced size, an increased number of branchings and diffuse AChR clusters compared to WT myofibers. By RT-qPCR, we observed a decreased expression of *Ttn*, *Ryr1* and *Myh* genes, and more markedly of the fast *Myh2* gene in DMD myofibers compared to WT myofibers.

Using our 3D-Muscle Model, we showed that 3D-DMD muscles have impaired spontaneous contractile activity with tetanic phases. Upon electrical stimulation, 3D-DMD muscles exhibit reduced amplitude of contraction and decreased specific force compared to 3D-WT muscles. To gain further insights into the mechanisms underlying these contraction defects, we are now seeking to study the calcium transients by live imaging. In agreement with the literature, our preliminary results suggest that 3D-DMD muscles exhibit elevated cytosolic calcium levels and spontaneous calcium pulses. Additionally, upon stimulation, 3D-DMD muscles show marked excitation-contraction coupling defects. Overall, we have developed a 3D muscle model reproducing key features of DMD that will be a powerful tool to study the molecular mechanisms of this pathology and to test new therapeutic approaches.

2- **Endothelialization techniques for complex 3D-printed carotid artery structures**

Auteurs: Saskia Eckert[1,2], Christian Kassasseya[1], Frédéric Segonds[2], Smaine Kouidri[2], Kim-Anh Nguyen-Peyre[3,4], Pablo Bartolucci[1,3,5]

[1]Université Paris-Est Créteil, France, [2] Arts et Metiers Institute of Technology, HESAM Université, Paris, France, [3]INSERM-U955, Equipe 2, Laboratoire D'Excellence, GRex, Institut Mondor, Créteil, France, [4]Etablissement Français Du Sang, Île-de-France Mondor, Créteil, France, [5]Centre De Référence Des Syndromes Drépanocytaires Majeurs, Hôpital Henri-Mondor, Assistance Publique-Hôpitaux De Paris (AP-HP), Créteil, France

Personalized factors in vascular geometry and hemodynamics, such as viscosity and flow rate, can in combination lead to significant flow anomalies in large arteries, detectable by advanced computer simulations. Linking these disturbed flow patterns to endothelial cell responses and signaling pathways remains challenging due to the flow complexity involved.

Our preliminary results suggest that the physiopathology of sickle cell disease-related cerebral vasculopathies is highly dependent on the patient-specific geometry of the carotid area with the bifurcation area being critical for disturbed flow patterns and stenosis development.

Using stereolithography 3D-Printing, we create detailed and highly accurate models of patient-specific carotid arteries as a support for endothelial cell culture. In order to minimize the amount of endothelial cells and the risk of contamination as well as time and cost factors, we focus on endothelialisation of the critical zone (the bifurcation area) and a control zone (in the pre-siphon). These two zones are removable segments in the printed artery. Surface plasma treatment changes the surface characteristics of the 3D-printed prototype so that a 0.5% gelatine coating can be applied.

For endothelialization of the carotid wall, a suspension of 10_6/mL Human Umbilical Vein Endothelial Cells (HUVECs) (passage 10) is seeded. The cells are guided to the artery wall either by gravity or by magnetic forces with HUVEC linked to CD31-dynabeads.

In the gravitational approach, the parts to be endothelialized are manually rotated at angles of 90° at 1.5-hour intervals or automatically rotated at a continuous speed (rpm=0,64/d[mm]) for 12 hours. In the magnetic approach, a quadruple magnet creates a radial magnetic gradient that attracts the cells from the suspension to the arterial wall. After guidance, the cells recognize the gelatin coating as an extracellular matrix and attach themselves.

The manual gravity approach stands out for its simplicity, as it requires no additional support or machinery, making it the most straightforward method to implement. However, it requires a higher cell quantity (4-8 times more than other approaches) due to the need for reinjecting cells through every 90° rotation.

The magnetic approach is the fastest method among the three, achieving full confluence in a cylindrical form within just 20 minutes post cellular suspension injection. However, the creation of a magnetic gradient field limits this approach primarily to radial magnetic fields (as required in the areas described).

The automated gravity approach is preferred for seeding cells in more complex forms. While not as rapid as the magnetic approach, it provides greater freedom in handling difficult geometries.

The cells are then exposed to an anemic conditions, as observed in patients with sickle cell disease (flow rate: 600ml/min; viscosity: 4cp). To reproduce the viscosity of blood, 5.1% high-density dextran (average mol wt 150,000) is added to cell culture medium. A protocol is currently under development to gradually increase shear stress to high levels, allowing the cells to develop their actin network and become more resistant to the high flow.

We aim to develop a cell-based personalized model that will allow us to test different biological hypotheses by modifying one biological or fluid mechanic factor at a time using the same 3D-printed carotid artery geometry. This 3D printed model incorporating a cellular approach will enable individualized patient follow-up and the evaluation of new therapies on the 3D printed models.

3- **Standardizing the analysis of cutaneous neurofibromas in *Nf1-KO* mice and exploring drugs targeting tumor cells and their microenvironment in this model**

Laura Fertitta, MD, PhD Student1,2,3, Fanny Coulpier2, Layna Oubrou2, Pierre Wolkenstein1,2,3, Piotr Topilko1,2,3
1. Dept. of Dermatology, National Referral Center for Neurofibromatoses; 2. Institut Mondor Recherche Biomédical, Henri Mondor Hospital, Assistance Publique – Hôpitaux de Paris (AP-HP), 94010 Créteil, France; 3. Université Paris Est Créteil

Neurofibromatosis type 1 (NF1) is a genetic autosomal dominant disorder caused by a mutation in the tumor suppressor gene *NF1*. The inactivation of *NF1* results in a hyperactivation of the RAS superfamily pathway. Cutaneous neurofibromas (cNF) affect almost all individuals with NF1. While benign, they are disfiguring, itchy, and sometimes painful, thus significantly affect quality of life. To date, no medical treatment exists. Our team has developed a new genetically engineered mouse model (*Nf1-KO*) that recapitulates various aspects of NF1 including cNF. In *Nf1-KO* mice, simultaneous *Nf1* loss and activation of fluorescent reporter Tomato (Tom) were induced in boundary cap cells and their derivatives including Schwann cells (SC). cNF present a spontaneous fluorescence (Tomato) in the *Nf1* mutant SC. In this model, skin injury enhances the development of cNF. This finding has enabled the development of 2 protocols of treatment suitable to perform *in vivo* assays aiming to prevent or shrink the cNF. The goal of this project was to: i) develop and validate a standardized procedure to assess the cNF in preclinical studies including robust endpoints of effectiveness of drugs to prevent or to shrink cNF, and ii) test the efficacy of different drugs using this procedure.

The project included 2 parts. 1/ The first was dedicated to the validations of the automated image-processing and analysis of macroscopic 2D and immunohistochemistry (IHC) images of cNF . Material from previous experiments was gathered to constitute a panel of macroscopic and IHC images of cNF and adjacent healthy-looking skin from *Nf1-KO* mice. A script was developed for both types of pictures (Fiji ®) and was validated by comparing their results to those manually generated. 2/ The second was focused on applying this standardized procedure to test the efficacy of 2 drugs on shrinking the cNF by simultaneously targeting Rac1/PAK/MRCKα/LIMK1/cofilin and Rho/ROCK/MRCK/ LIMK2/Cofilin pathways.

1/ The automated method of both macroscopic and IHC pictures was perfectly reproducible (intra-class correlations were of 1). The automated results were correlated to the manual results: Spearman coefficients of 0.93 or greater for the macroscopic pictures and of 0.94 or greater for the IHC pictures. The Bland-Altman plots showed no bias and minimal averages of differences between the measurements generated through the manual vs the automated methods (between 0.5% for the outcome “Tom+ area” on IHC pictures, and 1% for the outcome “total area” on macroscopic pictures). The mean durations of the automated method were significantly faster ($p=0.0006419$ for macroscopic pictures, and $p=1.159\times10^{-5}$ for IHC pictures).
2/ Two drugs were tested (M1 N=10, and M2 N=13) and compared to a placebo (N=12). The dosages of the drugs were established based on PK/PD studies. Systemic treatments lasted for 1 month. Macroscopic pictures analysis showed an increased surface area of cNF in M1 and placebo groups, while the M2 group exhibited a tendency towards reduction ($p=0.0596$). IHC pictures of cNF using 6 different panels demonstrated a significant reduction in the Tom+ area in M2 ($p=0.0127$) which correlated with a decrease in P-cofilin expression ($p=0.0055$), indicating the drug’s effectiveness on inhibiting these pathways and potentially reducing the tumor burden. In addition, the expression of periostin (pro-fibrotic marker) in tumor cells was significantly reduced in the M2 group ($p=0.0449$), suggesting a potential effect on fibrosis, as well as the expression CD45+ indicating immune cells ($p=0.0332$), suggesting an effect on inflammation.

The automated method was reliable, reproducible and very well correlated with the values generated manually. Its execution was significantly faster, resulting in a major time saver. These results allow the use of the two developed scripts to automatize and standardize the evaluation of the macroscopic and IHC pictures of the *Nf1-KO* mice, in preclinical trials targeting cNF. This method has been applied in a trial testing 2 drugs targeting the Rac1/PAK and Rho/ROCK/MRCK/ LIMK pathways showing for M2 a decrease in macroscopic pictures and significant decrease in tumor cells area in IHC pictures. Moreover, we also demonstrated an overactivation of this pathway in human cNF. Taken together, these results suggest that M2 is a promising compound for shrinking cNF in NF1.

Overall, we developed and validated a standardized and automated method for evaluating cNF in preclinical trials using our *Nf1-KO* mouse model. With this method, we demonstrated the efficacy of M2 in reducing the size of these tumors. To confirm these results, we plan to conduct a second trial with M2 in a larger cohort of animals and extend the treatment duration. If its efficacy is confirmed, the results should be translated to human studies, and M2 could be tested in NF1-related cNF.

4- **Predicting frailty domain impairments and mortality with the Hospital Frailty Risk Score among older adults with cancer: the ELCAPA-EDS cohort study**

Auteurs : Charline Jean[*1,2,3], Elena Paillaud[1,4], Pascaline Boudou-Rouquette[5], Claudia Martinez-Tapia[1,2], Frédéric Pamoukdjian[6], Meoïn Hagège[1], Stéphane Bréant[7], Claire Hassen-Khodja[8], Pierre-André Natella[2], Tristan Cudennec[9], Marie Laurent[1,10], Philippe Caillet[1,4], Florence Canouï-Poitrine**[1,2], Etienne Audureau**[1,2,3]*

[1]Université Paris-Est Créteil, Inserm, IMRB U955, Créteil, France

[2]Assistance Publique – Hôpitaux de Paris (AP-HP), Hôpital Henri-Mondor, Service Santé Publique & Unité de Recherche clinique, Créteil, France

[3]AP-HP, Chaire AI-RACLES, Paris, France

[4]AP-HP, Hôpital Européen Georges Pompidou, Service de Gériatrie, Paris, France

[5]AP-HP, Hôpital Cochin, Service d'Oncologie Médicale, Ariane program, Paris, France

[6]AP-HP, Hôpital Avicenne, Service de Gériatrie, Bobigny, France

[7]AP-HP, Pôle Innovation et Données, DSN, Paris, France

[8]AP-HP, Direction de la Recherche Clinique et de l'Innovation, Paris, France

[9]AP-HP, Hôpital Ambroise-Paré, Service de Gériatrie, Boulogne-Billancourt, France

[10]AP-HP, Hôpital Henri-Mondor, Service de Gériatrie et Médecine Interne, Créteil, France

**Corresponding author: Charline Jean, charline.jean@aphp.fr, ORCID: 0000-0002-6166-149X*

*** These authors contributed equally to this work*

Introduction. Automated frailty screening tools such as the Hospital Frailty Risk Score (HFRS) are primarily validated for care consumption outcomes. We assessed the predictive ability of the HFRS regarding care consumption outcomes and frailty domain impairments among older adults with cancer.

Methods. This retrospective study was based on the linkage between the ELCAPA multicenter cohort study and the Greater Paris University Hospitals' clinical data warehouse. Patients were ≥70 years old, had a solid tumor, were included in ELCAPA between 2016 and 2020 and were hospitalized in acute care. HFRS scores were calculated using data from the index admission and the preceding 6 months. A multidomain geriatric assessment (GA), including cognition, nutrition, mood, functional status, mobility, comorbidities, polypharmacy, incontinence, and social environment, was conducted at inclusion in ELCAPA, with computation of the G8 score. Logistic and Cox regressions measured associations between the G8, HFRS, and altered GA domains, prolonged length of stay, 30-day readmission, and 30-day mortality.

Results. Among 587 patients included (median age 82 years, metastatic cancer 47.0%), 237 (40.4%) were at increased frailty risk by the HFRS (HFRS >5) and 261 (47.5%) by the G8 (G8 score ≤10). The HFRS and G8 score were significantly associated with cognitive and functional impairments, incontinence, comorbidities, prolonged length of stay, and 30-day mortality. The G8 score was associated with polypharmacy, nutritional and mood impairment.

Conclusion. Although showing significant associations with short-term care consumption, the HFRS could not identify polypharmacy, nutritional, or mood impairments and showed low discriminatory ability across all GA domains.

5- **Efficacy of EXOPULSE MOLLII SUIT, a new multisite transcutaneous electrical stimulation technique, on several fibromyalgia associated symptoms.**

Joseph G. Mattar [1, 2], Moussa A. Chalah [1, 2, 3], Jean-Pascal Lefaucheur [2, 4], Samar S. Ayache [1, 2, 3, 4]
[1]Institut De La Colonne Vértébrale Et Des Neurosciences (icvns), 23 Rue Georges Bizet, 75116 - Paris (France)
[2]EA4391 Excitabilité Nerveuse & Thérapeutique, Université Paris Est Créteil, 94010 - Créteil (France)
[3]Department Of Neurology, Gilbert And Rose-Marie Chagoury School Of Medicine, 4504 - Byblos (Liban)
[4]Unité De Neurophysiologie Clinique, Dmu Fixit, Hôpital Henri Mondor, Assistance Publique-Hôpitaux De Paris (aphp), 94000 - Créteil (France)

Backgroud
Fibromyalgia is a frequent and underdiagnosed condition, characterized by diffuse and chronic musculoskeletal pain associated with several debilitating symptoms such as fatigue, insomnia, cognitive and mood disorders. These symptoms significantly alter quality of life and generate serious issues in managing daily activities. Different pharmacological approaches can be proposed but with a minimal beneficial effect compared to the induced side effects. Therefore, non-pharmacological treatments are being evaluated actually and electrotherapy is becoming of great interest.

Objectives
We aimed during this monocentric study, conducted at Henri Mondor Hospital – Créteil – France, to evaluate the effects of a new multisite stimulation technique – the Exopulse Mollii suit - on fibromyalgia associated symptoms.

Methods
33 patients were included in the study and randomly received, in a crossover manner, two blocks (active and sham) of fourteen daily stimulation sessions, separated by a two-week washout interval. Once this phase was completed, participants entered a phase 2 (an open label phase) during which they wore the suit on a daily basis for four consecutive weeks. We used the following stimulation parameters: frequency of 20 Hz, voltage of 20 V, and session duration of 60 min. Effects were assessed by the visual analog scale for pain (VASpain , primary outcome), and fatigue (VASfatigue) the pain catastrophizing scale (PCS), the Brief Pain Inventory (BPI), the Short Form 36 Health Survey (SF-36), the Fibromyalgia Impact Questionnaire (FIQ), and the Hospital Anxiety and Depression Scale (HADS). Data were analyzed using Friedmann test (for phase 1, with Dunn test for post hoc analysis) and Wilcoxon test (for phase 2). P value less than 0.05 was considered significant.

Results
Compared to sham, two weeks of active stimulation led to significant changes in VASpain, BPIinterference, several FIQ sub-scores, and some SF-36 dimensions. After four weeks of active stimulation (open label phase), further improvement was observed and concerned PCS, HADS and additional FIQ and SF- 36 aspects.

Discussion
Two weeks of active stimulation permitted promising analgesic, anti-fatigue effects and an improvement in quality of life. Affective symptoms and catastrophic pain-related thoughts improved also but after a longer stimulation period.
The underlying mechanisms appear to be complex and involve the ''gate control theory'' and possibly other central mechanisms. In other words, stimulation of large- diameter non-nociceptive fibers would induce an inhibitory effect on the transmission of the painful messages along small-diameter nociceptive fibers. In addition, transcutaneous electrical nerve stimulation may have resulted in several metabolic changes (Involving glutamate, aspartate, enkephalins, and endorphins levels, among others) and would have modulated the functioning of neural networks involved in pain perception / integration.

Conclusion
This new multisite stimulation method – the Exopulse Mollii suit - has offered promising pain-relieving and antifatigue effects in the context of a debilitating and difficult-to-manage disease such as fibromyalgia.
Further studies are needed before recommending this intervention in such a challenging condition.

6- **Effects of eccentric training on the structural and mechanical properties of plantar flexors in subacute stroke survivors: a randomized controlled trial**

Kalthoum Belghith, Mustapha Zidi, Wael Maktouf
Bioengineering, Tissues and Neuroplasticity, UR 7377, University of Paris-Est Créteil, Faculty of Health, 8 rue du Général Sarrail, 94010 Créteil, France

Stroke remains a leading cause of adult disability, often resulting in impairments such as weakened lower limb muscles, affecting most stroke survivors. Spastic paresis, a common consequence of stroke, involves both neurological and muscular changes, leading to decreased muscle contraction and stiffness. Current rehabilitation approaches focus on spasticity reduction but often overlook spastic myopathy, contributing to limited motor improvement. Eccentric Training (ET) has emerged as a potential solution due to its ability to enhance muscle strength and extensibility. However, its effectiveness in addressing post-stroke neuromuscular impairments remains underexplored. This study aims to investigate the impact of ET on gait speed and neuromuscular parameters in sub-acute stroke patients compared to conventional therapy.

This randomized controlled trial investigates the impact of eccentric training (ET) on the mechanical and structural properties of plantar flexor muscles in subacute stroke survivors. Thirty participants, recruited from a neurological rehabilitation clinic, were randomly assigned to either the Eccentric Training Group (ETG, n=15, age: 60.3 ± 8.03 years; BMI: 24.04 ± 3.68 kg/m²; male: 7, female: 8) or the Conventional Therapy Group (CTG, n=15, age: 63.2 ± 9.63 years; BMI: 23.16 ± 2.96 kg/m²; male: 10, female: 5). The ET protocol, designed to target muscle lengthening under tension, spanned 12 weeks with sessions twice a week. Both groups underwent a series of assessments before and after the intervention, evaluating parameters such as muscle stiffness, fascicle length, muscle thickness, pennation angle, gait speed, and range of motion (ROM).

The study revealed significant improvements in the ETG compared to the CTG. Specifically, the ETG exhibited a marked increase in ROM ($p<0.001$) and gait speed ($p<0.001$) post-intervention. Additionally, passive stiffness of the gastrocnemius medialis (GM) muscle significantly decreased at 10° and 20° of dorsiflexion in the ETG ($p<0.001$), indicating enhanced muscle flexibility and reduced rigidity. Structural measurements showed a significant increase in fascicle length and muscle thickness in the ETG, suggesting beneficial adaptations in muscle architecture.

A correlation analysis revealed strong associations between the decrease in muscle stiffness and improvements in both gait speed and ROM ($p<0.01$). These correlations indicate that reductions in muscle stiffness may play a key role in enhancing functional mobility outcomes following eccentric training.

These findings highlight the superior efficacy of eccentric training over conventional therapy in improving both functional and structural outcomes in stroke rehabilitation. By addressing muscle stiffness and enhancing mobility, ET presents a promising adjunctive therapy for stroke survivors, potentially leading to improved quality of life and greater independence. This study underscores the importance of incorporating targeted muscle training protocols in rehabilitation programs for optimal recovery post-stroke.

7- **Delivering SARS-CoV-2 mutated RBD antigens to the CD40 receptor: A strategy for inducing long-term antibody responses**

Marwa El Hajj1*, Mathieu Surénaud1, Florence Picard1, Guillaume Hypolite1, Amandine Sansoni2, Manon Fabregue2, Sarah Sharkaui2, Camille Pierrini2, Sylvain Cardinaud1, Mireille Centlivre1, Bernard Malissen2, Gerard Zurawski1, 3, Ana Zarubica2, Sandra Zurawski1, 3, Yves Lévy1, Véronique Godot1*

1 VRI / INSERM-U955 / UPEC, Créteil, France, 2 Centre d'Immunophénomique (CIPHE) / Aix Marseille Université / INSERM, Marseille, France, 3 Baylor Scott and White Research Institute, Dallas TX, United States

Purpose: The rapid availability of SARS-CoV-2 vaccines was pivotal during the COVID-19 pandemic. However, the emergence of variants (VOCs/VOIs) evading antibody (Ab) neutralization has reduced vaccine efficacy. Urgent needs are to develop new vaccines/strategies: i) targeting VOCs/VOIs; ii) inducing long-lasting Ab responses.

Methods: CD40.Pan.CoV is a Dendritic Cell (DC) targeting vaccine consisting of a mAb specific to human (h)CD40 fused with RBD harbouring K417N, L452R, T478K, E484Q, N501Y mutations common to VOCs and a Nucleocapsid sequence, (>95% conserved across Sarbecoviruses). Immunogenicity and viral protection were tested in hCD40 and hCD40/K18-hACE2 transgenic mice, respectively. Animals were immunized at days 0/21 with the CD40.Pan.CoV vaccine (10µg) plus poly-ICLC (50µg, i.p.) or the mRNA BNT162b2 vaccine (1µg, i.m.) and either sacrificed (n=5-10/Group) 14 days post-boost or infected (Wuhan strain; n=6-11/Group) 7 days post-boost. Control mice received poly-ICLC or PBS. In another set of experiments, mice primed with two doses of BNT162b2 were boosted at month (M) 8 with either BNT162b2 or CD40.Pan.CoV+ poly-ICLC (n=4-5/Group) and serum was collected monthly till M16. The levels of binding and neutralizing RBD-IgG were assessed with MSD tests. Splenic B cells were analysed by flow cytometry.

Results: The rate of protection reached 100% in CD40.Pan.CoV and BNT162b2 vaccine groups with no animals exhibiting clinical symptoms or viral replication in the lungs unlike mock animals. CD40.Pan.CoV induced IgG-specific RBD responses as potent as the BNT162b2 vaccine but with a broader range of cross-reactivity and neutralization against □□□/□/□VOC and higher frequency of germinal centre B cells. In BNT162b2-pre-immunized animals, BNT162b2 or CD40.Pan.CoV boost (M8) increased IgG-specific RBD responses. However, post-boost dynamics revealed different decreasing slopes of binding and neutralizing Ab responses with CD40.Pan.CoV maintaining long-lasting responses.

Conclusion: Our study presents the proof of concept of the efficacy and immunogenicity of a vaccine targeting a mutated-RBD and a conserved nucleocapsid region (Npep) to the CD40 receptor. The CD40.Pan.CoV vaccine induced humoral and B cell responses against VOC/VOIs, complete protection against SARS-CoV-2 with potentially superior immune outcomes than BNT162b2, and specifically antibody longevity when used as a boost. CD40.Pan.Cov vaccine will be moved to a phase I/II clinical trial in 2024.

8- **Angiopoietin-like 4 improves left ventricular function and coronary endothelial function during heart failure with preserved ejection fraction: a proof of concept study in pigs.**

Daphné CORBOZ[1], Gaëtan PALLOT[2], Jin Bo SU[1], Paul-Matthieu CHIARONI[1,3], Pierre BOUCHER[1,2], Alain BIZE[1], Jianping DAI[1,] Lucien SAMBIN[1], Romain GALLET[1,3], Stéphane GERMAIN[2], Bijan GHALEH[1,3*]*

[1]Inserm U955-IMRB, Equipe 3, Faculté de Santé – UPEC, Ecole Nationale Vétérinaire d'Alfort, Créteil, France

[2]Inserm U1050, Collège de France, Paris, France

[3]Service de Cardiologie, Hôpital Henri-Mondor AP-HP, Créteil, France

**authors equally contributed*

Heart failure with preserved ejection fraction (HFpEF) is a form of heart failure in which the left ventricular ejection fraction is above 50%, as opposed to heart failure with reduced ejection fraction (<50%). It represents more than half of heart failure cases worldwide and is associated with high morbidity and mortality. The pathophysiology of HFpEF is characterized by diastolic dysfunction and involves cardiac fibrosis, hypertrophy, inflammation, and coronary microvascular alterations. Inflammation is largely responsible for the endothelial dysfunction that is targeted in our study. To do so, we used a protein, angiopoietin-like 4 (ANGPTL4), capable of maintaining vascular integrity. Our objective was to evaluate whether ANGPTL4 improves left ventricular function and coronary vasodilation in a hypertensive-induced HFpEF pig model.

Sixteen chronically instrumented pigs received a continuous infusion of the potent vasoconstrictor, angiotensin II (IV, 30 ng/kg/min), for 38 days. After 35 days, the pigs were randomly treated with an intracoronary injection of placebo (n=9) or ANGPTL4 (n=7, 75 □g/kg). Left ventricular function and coronary vasomotion were investigated through hemodynamic measurements, echocardiography, and coronary functional tests before the start of angiotensin II infusion (Day 0), before treatment (~ Day 30), and one (Day 36) and three days (Day 38) after treatment. Samples were then collected for biological and histological analyses of cardiomyocyte cross sectional area, fibrosis, hypertrophy, intracellular calcium handling, oxidative stress, and vascular density.

Mean arterial pressure significantly and similarly increased in both groups, accompanied by left ventricular hypertrophy. Left ventricular systolic function was preserved while diastolic function was impaired (increases in left ventricular end diastolic pressure, E/A ratio, E/e' septal ratio, and E/e' lateral ratio) similarly in the two groups after several weeks of angiotensin II infusion. Concomitantly, coronary blood flow responses to reactive hyperemia (30 s) and administration of both acetylcholine (IV, 3 □g/kg) and nitroglycerin (30 □g/kg) were significantly reduced. Administration of ANGPTL4 significantly improved diastolic function and endothelium-dependent response to acetylcholine but had no effect on mean arterial pressure, hypertrophy, and endothelium-independent response to nitroglycerin.

In conclusion, intracoronary administration of ANGPTL4 improves left ventricular diastolic function and coronary endothelial function in a hypertensive, animal model of HFpEF.

9- **PAX3 drives functional muscle stem cell heterogeneity during muscle regeneration**

Virginia Zoglio[1], Sarah Chebouti[1], Fayez Issa[1], Sylvie Manin[1], Frédéric Relaix1[#] and Joana Esteves de Lima[1#]
[1] Univ Paris Est Creteil, INSERM, EnvA, EFS, AP-HP, IMRB, F- 94010 Creteil, France ([#] co-lead authors)

Abstract: Adult muscle stem cells, the satellite cells (SCs), play a pivotal role in skeletal muscle maintenance and repair and are characterized by the expression of the paired-homeobox transcription factors PAX3 and PAX7. In homeostasis, the SCs are in a quiescent state (G0) and highly express PAX7, which controls muscle post-natal growth and regeneration in the adult. A subset of SCs also expresses PAX3, which initiates the embryonic myogenesis and controls the specification, migration and proliferation of muscle progenitor cells to ensure normal skeletal muscle development in the embryo. Interestingly, SCs exhibit heterogeneity in terms of PAX3 expression in quiescence. Whereas only a low amount of SCs express PAX3 in hindlimb muscles (15%), 60% of SCs from the trunk and the forelimb muscles are positive for PAX3. Moreover, a distinct cellular function in the context of environmental stress was associated with the expression of PAX3 in SCs. Despite PAX3 established roles in driving myogenic specification in embryogenesis and in the response to environmental stress in SCs, its function in the context of regeneration remains under investigation.

To explore the role of PAX3 in the context of tissue damage we performed regeneration studies and cell cultures of FACS-isolated SCs. Our results unveiled a functional heterogeneity depending on PAX3 expression, as indicated by the distinct contribution to the self-renewal and differentiation of these cells, suggesting that PAX3 expression confers a faster response to injury with a higher commitment towards the myogenic program. Consistently, scRNA-seq data confirmed a distinct transcriptomic signature between the PAX3-positive and PAX3-negative SCs, shedding light on putative target genes that could potentially play a role in the establishment of the functional heterogeneity occurring within SCs sub-populations. Strikingly, our data unveiled a genetic crosstalk between PAX3 and SIX2 transcription factor, which is part of the homeoprotein family that is known to initiate the myogenic program in the embryo through the activation of *Myf5/Myod1* cascade. Furthermore, histological analysis on *Pax3* cKO mouse model in the context of tissue damage, revealed a key role of PAX3 in the maintenance of SCs and in tissue repair in muscles with high percentage of PAX3-expressing SCs.

Together these data disclose a novel aspect of SCs functions in the context of muscle regeneration, which depends on the expression of PAX3. We propose a model through which PAX3-expressing SCs display a faster activation and differentiation, exerting an adaptive response that positions them to respond rapidly under conditions of injury and stress.

10- **Spatial distribution and role of PDGFRα+ skeletal stem/progenitor cells in bone regeneration**

Maria Ethel, Cassandre Goachet, Simon Perrin, Fanny Coulpier and Céline Colnot
INSERM U955, IMRB, Team Biology of the neuromuscular system, Universite Paris Est Creteil

Bone regeneration relies on the activation and recruitment of skeletal stem/progenitor cells (SSPCs) forming bone and cartilage after injury. SSPCs represent a diversity of cell populations residing in bone (i.e., periosteum and bone marrow) and adjacent skeletal muscle[2,3,4]. Depending on their tissue origin, these SSPCs contribute differently to bone repair, bone marrow SSPCs contributing mostly to bone, SSPCs from skeletal muscle contributing mostly to cartilage, and periosteal SSPCs forming both cartilage and bone[2,3,4]. How the identity and tissue origins of these various SSPC populations relates to their functions in bone regeneration remains unknown.
The aim of this PhD project is to characterize the heterogeneity of SSPC populations and their role during bone repair, using transcriptomic analyses, genetic lineage tracing and in vivo functional analyses based on specific SSPC markers and the universal marker of SSPCs, Platelet-derived growth factor receptor alpha (PDGFRα).

To capture all SSPC populations within bone and adjacent skeletal muscle, we generated a musculoskeletal stromal cell atlas by integrating single-cell RNA-seq datasets from all bone compartments and skeletal muscle. We identified 2 main SSPC populations, CAR cells (Cxcl12-abundant reticular cells, expressing Adipoq, LepR, and Pdgfra) found exclusively in the bone marrow and endosteum, and PαS cells (PDGFRα+Sca1+ cells) found in all bone compartments, but predominantly the periosteum and skeletal muscle. Using tamoxifen-inducible Pdgfra^{CreERT2}/+;Rosa$^{tdTom/+}$ and Adipoq$^{CreERT2/+}$;Rosa$^{tdTom/+}$ mice, we performed flow cytometry and in vivo lineage tracing to confirm the spatial distribution of PαS and CAR within periosteum/skeletal muscle and bone marrow/endosteum respectively.

To functionally assess the distinct contribution and requirement of PαS and CAR cells in bone regeneration, we performed tibial fracture in Pdgfra$^{CreERT2/+}$;Rosa$^{tdTom/+}$ that were induced with tamoxifen locally in periosteum and skeletal muscle and in Adipoq$^{CreERT2/+}$;Rosa$^{tdTom/+}$ mice that were induced with systemic tamoxifen injection.
Lineage tracing and quantification of tdTom+ cells during fracture healing showed that PαS cells form most of the cartilage and bone within the fracture callus. We then induced the genetic depletion of PαS cells by local tamoxifen delivery in Pdgfra$^{CreERT2/+}$;Rosa$^{tdTom/DTA}$ (DTA mice) and Pdgfra$^{CreERT2/+}$;Rosa$^{tdTom/+}$ (control mice). Histomorphometric and micro-CT (X-ray microtomography) analyses showed impaired bone healing in DTA mice compared to control mice, indicating that PαS cells within periosteum and muscle are required for bone healing. Inactivation of Sox9, a key regulator of chondrogenesis, prevented callus formation and bone bridging in Pdgfra$^{CreERT2/+;}$Rosa$^{tdTom/+;}$Sox9$^{fl/fl}$ mice but not in Adipoq$^{CreERT2/+;}$Rosa$^{tdTom/+;}$Sox9$^{fl/fl}$ mice. These results define PαS cells as the main contributor to bone healing via endochondral ossification (involving cartilage-to-bone transformation) while CAR cells exhibit a minor contribution to healing via intramembranous ossification (direct bone formation).

Next, we explored the epigenetic regulation of cell fate decisions in response to bone fracture, as PαS in periosteum and skeletal muscle have a chondrogenic potential while only PαS in periosteum have osteogenic potential. Single nuclei multiome analyses of PαS from periosteum and skeletal muscle showed that periosteal PαS exhibit changes in chromatin accessibility associated with multiple osteogenic transcription factors, which are not present in the skeletal muscle SSPCs. These results reveal that periosteal SSPCs are osteoprimed for osteogenesis. Altogether, these results elucidate the heterogeneity of SSPC populations at the transcriptomic and epigenetic levels, and uncover their spatial distribution and requirement for healing, establishing periosteal SSPCs as the most essential population during bone repair.

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11- **Impact of specialized pro-resolving lipid mediators on the colonization of CF respiratory epithelia by Aspergillus fumigatus**

Khadeeja Adam Sy [1,2], Maëlle Briottet [1], Isabel Valsecchi [2], Marie Vaudin [1], Sephora John [1] , Ellie-flore Barny [1], Meyssa Ben Alaya [1], Mohamed El moustaphaoui [1,] Mapathé Faye [1], Yael Lellouche-Jacob [1], Ilakkiya Satkunarasa [1], Françoise Botterel [2] and Valérie Urbach [1]

[1]. IMRB, INSERM U955, UPEC, Créteil

[2]. Dynamyc, UPEC, EnvA, USC ANSES, Créteil

Inflammation is normally self-regulated by an active resolution phase, orchestrated by specialized pro-resolving mediators (SPMs) such as lipoxins (LX), resolvins (Rv), protectins (PD) and maresins. We recently showed that SPMs biosynthesis by airway epithelial cells is altered in cystic fibrosis (CF). CF is a genetic disease mainly characterized by airway chronic infection and excessive inflammation. *Aspergillus fumigatus*, a predominant filamentous fungus in CF is associated with lung injury and function decline. The consequences of the dysregulated SPMs biosynthesis on the colonization of the CF respiratory track by the filamentous fungi, *A. fumigatus* has not been investigated before this study.

Therefore, we studied the role of SPMs in the interactions between *A. fumigatus* and its host using a model of human CF airway reconstituted epithelium.

We used human nasal epithelial primary cultures (hNEC) from CF and non-CF patients and the bronchial epithelial cell line (CFBE). We inoculated *A. fumigatus* (*Af* Dsred) conidia (MOI 1:6, 24h) on epithelial cells grown on plastic or at air-liquid interface, treated or not with SPMs (10nM). SPM receptors expression was studied by RTqPCR and immunofluorescence. Fungal load was quantified by optical density using a microplate reader, by qPCR of gDNA, and using a galactomannan assay on the culture medium. Tight junctions were visualized using ZO-1 protein immunostaining. Antimicrobial peptides were explored using RTqPCR. The role of SPM receptors was evaluated using selective agonists and/or antagonists.

On one hand, exposure to the clinical strain of *A. fumigatus* for 24h disrupted most of the airway epithelial tight junctions. When cells were treated with SPMs (LXA4, LXB4, RvE1, RvD5 and PD1) simultaneously with *A. fumigatus*, the epithelial tight junction integrity was significantly protected. The SPMs' protecting effect on tight junctions was observed up to 12h after *A. fumigatus* exposure. The SPM protecting effect on tight junctions involved the G-protein coupled receptors, FPR2 (LXA4 and LXB4), GPR32 (RvD5 and LXB4), ChemR23 (RvE1) and GPR37 (PD1) that we found to be expressed in our CF and non-CF airway epithelial models. On the other hand, airway epithelium reduced *A. fumigatus* growth and secretion of one of its virulence factor galactomannan. The treatment of the airway epithelial cells with SPMs (LXA4, LXB4, RvE1, RvD2, RvD5, PD1) enhanced this latter effect with a further decrease of *A. fumigatus* galactomannan. Some SPMs as LXA4 and RvE1 stimulated the transcription of HBD2 and LL-37 antimicrobial peptides.

Our results show that several SPMs stimulate the protecting role of epithelial cells in enhancing its barrier function. SPMs also reduce the secretion of galactomannan, which is an *A. fumigatus* virulence factor playing a critical role in biofilm formation. This suggests that the anomaly of SPMs biosynthesis in CF could significantly contribute to the reduced capacity of respiratory epithelial cells to protect themselves and to fight *A. fumigatus*. This study opens new therapeutic perspectives.

12- **Sing next-generation sequencing to study cross-transmission : the case of Stenotrophomonas maltophilia**

Céline SAKR [1,2], Mélanie DARTY-MERCIER[4], Florence CIZEAU[1], David DUCELLIER[1], Maxime DANJEAN[1,2], Jean-Winoc DECOUSSER [1,2]
[1]-Infection control team, Henri Mondor University Hospital, Assistance Publique-Hôpitaux de Paris, Créteil, France
[2]- DYNAMYC EA 7380 - Université Paris Est Créteil, Faculty of health, Créteil, France
[4]- GenobioMICS platform, Henri Mondor University Hospital, Assistance Publique-Hôpitaux de Paris, Créteil, France

Introduction Stenotrophomonas maltophilia (Sm) is an opportunistic environmental pathogen responsible for infections in immunocompromised/mechanically ventilated intensive care patients. The respective roles of endogenous selection and cross-transmission in its acquisition in healthcare settings remain to be elucidated. The role of environmental reservoirs as secondary sources/reservoirs is also debated. The aim of this study is to investigate the epidemiology of Sm infection and colonisation in hospitals using a systematic genetic approach.

Material and Methods A prospective study was performed at Henri Mondor University hospital. Between January 2023 and April 2024, 200 deduplicated Sm strains of clinical and environmental origin were systematically collected without a priori selection. Their complete genomes were sequenced by Illumina NovaSeq 6000® next-generation sequencing (NGS) and compared using the core-genome Multi Locus Sequence Typing (cgMLST) method with RidomSeq Sphere® software to identify potential cross-transmission. An allelic distance < 10 was used as a marker of genetic relatedness.

Results Analysis of the core genomes identified 196 analysable genomes grouped into 28 genomic clusters (19 environmental clusters, 15 patient clusters and 4 combined clusters) that grouped genetically similar strains. Of these clusters, 11 included patients who had been in the same hospital ward at the same time, while 4 others included patients who had been in hospital at the same time but in different wards. In addition, 2 clusters included patients who had been admitted to the same ward at different times and, surprisingly, 2 clusters included patients who had never crossed paths in time or space.

Conclusion Unbiased NGS sequencing is a highly effective method for investigating the transmission of Sm strains between patients and within the environment. It enables the quantification of these transmission events, which are typically missed by conventional epidemiological surveillance due to the lack of distinctive phenotypic features (such as specific antibiotic resistance profiles) that would alert bacteriologists and hygienists. These findings highlight the importance of implementing measures to prevent cross-transmission and ensure effective environmental disinfection for Sm, a species generally considered to have low epidemiogenic potential and more commonly associated with endogenous infections. This approach may also be useful for the study of other microorganisms.

Prix du meilleur poster

Session matin

ALTTERSITZ Claire, équipe Leboyer (Dir. thèse : Stéphane Jamain) : *Gene expression analysis in the prefrontal cortex of mice with genetic vulnerability to mild stress.*

BERGE Gwladys, équipe Relaix (Dir. thèse : Marianne Gervais-Taurel) : *Long-term dioxin exposure aggravates endothelial damage and left ventricular diastolic dysfunction, only in male obese mice*

BOUCHER Pierre, équipe Ghaleh (Dir. thèse : Stéphane Germain et Bijan Ghaleh) : *Quantification of endothelial cell adherens junction morphotypes using artificial intelligence*

BOURRIER Kenza, UR BIPAR/PARANEM (Dir. thèse : Grégory Karadjian) : *Assessment of the infection level of young equids by Parascaris spp. in Normandy*

BUISSOT Clément, équipe Lanone (Dir. thèse : Sophie Lanone et Patrice Coll) : *Role of the exposome on the development of chronic obstructive pulmonary*

CHEBOUTI Sarah, équipe Relaix (Dir. thèse : Frédéric Relaix et Joana Esteves de Lima) : *PAX3 Orchestrates Developmental Trajectories During Early Mouse Organogenesis*

COJOCARU Andreea, équipe Relaix (Dir. thèse : Frédéric Relaix) : *Comparative analysis of FAPs behavior and ECM composition in extraocular and tibialis anterior muscles: implications for Duchenne Muscular Dystrophy*

DELMONT, ThaIs, équipe Derumeaux (Dir. thèse : Geneviève Derumeaux et Laurianne Bonnet) : *Cardiotoxicity of Doxorubicin in mice: Role of senescence and protective potential of senolytic treatment*

EL FEGHALY Sarah, équipe Bachoud-Lévi (Dir. thèse : Hassan Hosseini) : *Knowledge and effects of sociodemographic, socioeconomic and dental factors on strokes in Lebanon and France.*

GROS Vincent, équipe Derumeaux (Dir. thèse : Serge Adnot) *: Chronic and intermittent hypoxia: clock genes disruption and implication for lung cell senescence*

IRAWAN Tabitha, équipe Relaix (Dir. thèse : Nathalie Chevallier et Nicolas Espagnolle) : *Development of Pre-vascularized Bone Spheroids from a Single Tissue Source*

JACQUET Juliette, équipe Derumeaux (Dir. thèse : Laurent Boyer et Serge Adnot) : *Counteracting pulmonary vascular endothelial cell senescence to combat age-related lung dysfunction and pulmonary hypertension*

LECLERC Alexane, équipe Leboyer (Dir. thèse : Josselin Houenou) *: Influence of mood and prior affective cues on emotions perception: behavioral investigations on healthy and psychiatric populations*

MATAR Rola, équipe Pawlotsky (Dir. thèse : Stéphane Chevaliez et Daniel Candotti) : *No Amino Acid Substitution in HBV Pres1 or HDAg Associated With Suboptimal Response to Bulevirtide Treatment in Participants With Chronic Hepatitis Delta*

MIENANZAMBI Stecy, équipe Lanone (Dir. thèse : Bénédicte Duriez) : *An iPSC-derived bronchial epithelial model to study nonsense mutations in Cystic Fibrosis*

OUMESLAKHT Loubna, équipe Ortonne (Dir. thèse : Nicolas Ortonne) : *Identification of novel ICOSL isoforms recurrently expressed in Sezary Syndrome*

SADEGHI Mohammad, UR EC2M3 (Dir. thèse : Iradj Sobhani et Denis Mestivier) : *Role of the Gut Microbiota in Digestive Tumors: A Comparison between Lynch Syndrome, Sporadic Colorectal Cancer, and Gastrointestinal Neuroendocrine Tumor*

SESSA Anna, équipe Pawlotsky (Dir. thèse : Vincent Leroy) : *What are the predictive factors of hepatic events in patients with autoimmune hepatitis?*

SMAIL Oussama, équipe Relaix (Dir. thèse : Philippos Mourikis) : The Role of Notch signalling pathway in Fibro-adipogenic progenitors (FAPs) Life cycle and the consequences on Extracellular matrix proteins

THIBAUDEAU Sarah, ThAI UMR Virologie ANSES-INRAE_ENVA (Dir. thèse : Jennifer Richardson) : *Modeling Hazara and Dugbe virus infection in ticks to study survival and spread of Crimean-Congo hemorrhagic fever virus in* the environment.

VINCENT Lhéo, UR BIOTN (Dir. thèse : Mustapha Zidi, Pierre Portero, Waël Maktouf) *: Influence of fatigue on the active and passive components of the plantar flexor muscles using shear wave elastography*

WEIZMAN Orianne, équipe DERUMEAUX/HEGP (Dir. thèse : Nicolas Lellouche et Eloi Marijon) : *Sudden Cardiac Arrest in Women*

Session après-midi

BARISEEL Romane, équipe Cohen (Dir : José Cohen) : *A Murine Model Mirroring Human Hematopoietic Stem-Cell Transplantation Outcomes to Unravel T Lymphocyte-Mediated Complications*

BELLIL Tanina, équipe Lanone (Dir : Sophie Lanone et Yuli Watanabe) : *Impact of perinatal exposure to nanoparticles on lung development and function*

BLEUZEN Anaïs, équipe Relaix (Dir : Nathalie Didier et Frédéric Relaix) : *Human engineered skeletal and cardiac muscles derived from iPSC for the modeling of neuromuscular disorders and the development of screening platforms*

BOUKHOBZA Amina, Laboratoire GLY-CRRET (Dir : Patricia Albanese et Benjamin Even) : *Structure/Function characterization of matrix heparan sulfate and associated proteoglycans in senescent synoviocytes during Osteoarthritis.*

BRUNON Eva, équipe Pawlotsky (Dir : Jean-Michel Pawlotsky et Patrice Bruscella) : *Role of human respiratory small extracellular vesicles during RSV infection*

CARLIER Andréa, équipe Relaix (Dir : Stéphane Blot et Isabel Punzon) : *Pan-therapy, CRISPR/Cas13-mediated, for Centronuclear myopathies by targeting DYNAMIN 2*

CHRETIEN Alexandra, équipe Relaix (Dir : Guillemette Crépeaux et Marika Nosten-Bertrand) : *Autophagy and neurodevelopmental disorders: Anatomical, histological and behavioral characterization from preweaning up to adulthood Irgm1-KO mice*

COURCOUX Raphaël, équipe Relaix (Dir : Marianne Gervais-Taurel) : *Impact of dioxin and AHR signaling on the cardiorenal syndrome*

DUMONT Félix, équipe Relaix (Dir : Olivier Stettler) : *Analysing the role of 3-0 sulfated heparans at the neuromuscular junction and the consequences of their reduction in DMD animals*

GAILLET Antoine, équipe Derumeaux (Dir : Nicolas De Prost et Armand Mekontso-Dessap) : *Clinical phenotypes and outcomes associated with respiratory syncytial virus infection in critically ill patients: a retrospective multicentre cohort study in Great Paris area hospitals, 2017-2023*

GOACHET Cassandre, équipe Relaix (Dir : Céline Colnot) : *Role of Schwann cells and their interactions with skeletal stem progenitor cells in bone regeneration*

HAJJAR Joelle, équipe Relaix (Dir : Frédéric Relaix et Valentina Taglietti) : *Molecular mechanisms regulating TSHR signaling pathway*

ISSA Fayez, équipe Relaix (Dir : Joana Esteves de Lima) : *Cell identity is regulated by HIRA-H3.3 in distinct cell lineages*

KOVACI Franceska, équipe Relaix (Dir : Céline Colnot) : *Combined MEK/SHP2 inhibition alleviates spine deformity in mice lacking Nf1 gene in boundary cap cells*

MAGNAN Jeanne, équipe Cohen (Dir : Ilaria Cascone et José Cohen) : *Role of CDKN2A in the regulation of the immune tumor microenvironment in mouse models of Pancreatic Ductal Adenocarcinoma*

MELLUL-ALTABE Rakel, équipe Relaix (Dir : Frédéric Relaix et Peggy Lafuste) : *Impact of SARS-CoV-2 on skeletal muscle: Modeling SARS-CoV-2 infection in vitro by using human myotubes*

MIGNOT Julien, équipe Relaix (Dir : Nathalie Didier) : *Development of therapeutic strategies for Volumetric Muscle Loss (VML) repair based on innovative hydrogels associated with human MuSC*

ROUZET Julie, UR BIPAR (Dir : Delphine Le Roux) *: Feline intestinal explant model to study interactions of Toxoplasma gondii with mucosal immune responses of its definitive host*

SEVERA Gianmarco, équipe Relaix (Dir : Edoardo Malfatti et Isabelle Richard) : *Digital Myopathology and Myo MRI correlation In Limb Girdle Muscular Dystrophy R1 (LGMDR1)*

SOOCHETA Sri Kamini, équipe Pawlotsky (Dir : Fatima Clerc) *: Impact of environmental pollution and the AhR signaling pathway on hepatic carcinogenesis*

THOMSON Taylor, équipe Pawlotsky (Dir : Christophe Rodriguez) : *MetagenomIA : Artificial Intelligence for Emerging Pathogen Surveillance*

WATANABE Naoto, équipe Ghaleh (Dir : Renaud Tissier) : *Total liquid ventilation improved short-term outcome during life-threatening Acute Respiratory Distress Syndrome in large animals*