UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Master 2

Parcours / Track

Nutrition Health and Mobility

Propositions de stages

Internship proposals

Année / Year
2025-2026

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Tableau récapitulatif des propositions de stages (2 pages) / Summary table of internship proposals (2 pages)

En rouge, les stages proposés également sur le parcours BIP/ In red, internships also offered in the BIP Track

*** : fléché pour un étudiant Profession de Santé / *targeted for a medical student**

	Responsable/ Tutor	Laboratoire / Research Unit	Sujet de stage / Intenship's subject
1	**Averous Julien**	UNH	Plant protein and health prevention: role of an intermittent amino acid restriction
2	**Blanquet Stéphanie**	MEDIS	Interactions of plant extracts containing polyphenols designed to reduce hypertension with human gut microbiota in an *in vitro* model of the human gut
3	**Bonnet Mathilde**	M2ISH	Role of L-serine on the pro-carcinogenic effect of Colibactin-positive *E.coli*
4	**Bruhat Alain**	UNH	Decipher the role of the GCN2-ATF4 pathway in pancreatic adaptation to sulfur amino acid restriction.
5	**Carvalho Frédéric**	Neuro Dol	Pathophysiological study of the enteric nervous system in the colonic hypersensitivity associated with chronic abdominal pain in IBS patients and related comorbidities.
6	**Cia David**	Neuro Dol	Establishment of a preclinical model for ocular rosacea: investigation of pathophysiological mechanisms and exploration of novel therapeutic approaches.
7	**Combaret Lydie**	UNH	Search for Effectors Modulating TGFβ/BMP Signalling to Preserve Muscle Mass
8	**Delort Laëtitia**	UNH	Breast cancer and obesity: Development of tumour-derived organoids for personalized treatment
9	**Ennequin Gaël**	AME2P	Impact of a multidisciplinary (Physical activity and nutrition) weight loss intervention on metabolic dysfunction-associated steatotic liver disease (MASLD) in adolescents with obesity.
10	**Evrard Bertrand**	UNH	Effect of Innovative Probiotics on Dendritic Cell Maturation and T Cell Polarisation: Implications for Food Allergies
11	**Fauchon Camille**	Neuro Dol	Transcranial low-intensity ultrasound stimulation for treating chronic neuropathic pain.
12	**Guillot Charlène N°1**	iGreD	Investigating the emergence of muscle type diversification in vertebrates
13	**Guillot Charlène N°2**	iGreD	Perivitelline albumen as novel model to study amniotic fluid's influence in epithelial-to-mesenchymal transition during body axis elongation
14	**Guillot Charlène N°3**	iGreD	Exploring How Folate Drives Embryonic Development—From cell fate regulation to Morphogenesis
15	**Le Bacquer Olivier**	UNH	Impact of cannabidiol on muscle atrophy induced by tumor secretions and chemotherapy in a co-cultured myotube model.
16	**Rouzaire Paul**	Chelter	Development of a Murine Model to Study Interactions Between CAR-T Cells and Respiratory Pathogens
17	**Talvas Jérémie**	UNH	INSPORTED, co-supplementation with insect proteins and vitamin D in the context of return to physical activity
18	**Thivel David**	AME2P	Energetic and metabolic adaptations to simulated weight loss during a graded walking exercise in adolescents with obesity.
19	**Vareille-Delarbre Marjolaine**	LMGE	Interactions between *Klebsiella pneumoniae* and inflammasomes in intestinal epithelial cells
20	**Zbili Mickaël**	Neuro Dol	In vivo and in vitro characterization of cortical plasticity development in facial ne uropathic pain.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

*	***Pinel Alexandre Stage FLECHE***	*UNH*	*Cancer-associated cachexia and chemotherapy during esophageal carcinoma : impact on adipose tissue metabolism*
*	***Gueugneau Marine Stage FLECHE***	*UNH*	*: Involvement of the patient and caregivers in optimizing the nutritional management of malnourished patients after hospital discharge*

Laboratoires / Research Units :

AME2P	Metabolic Adaptations to Exercise under Physiological and Pathological Conditions
CHELTER	Role of intra-Clonal HEterogeneity and Leukemic environment in ThErapy Resistance of chronic leukemias
iGReD	institut de Génétique Reproduction et Développement
LMGE	LMGE Laboratoire Microorganismes: Génome Environne
M2iSH	Microbes Intestin Inflammation et Susceptibilité de l'Hôte
MEDIS	Microbiologie Environnement Digestif Santé
Neuro DoI	Neurosciences et Douleur
UNH	Unité de Nutrition Humaine

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : **Plant protein and health prevention: role of an intermittent amino acid restriction**

Laboratory : UNH UMR1019 INRAE/UCA
Laboratory director : Didier Remond
Address : Centre de Recherche INRAE, 63122 Saint Genès Champanelle

Internship tutor : Julien Averous
Tel : 04 73 62 42 04
e-mail : julien.averous@inrae.fr

Summary :

In rodents, it has been established that a chronic dietary restriction in methionine is effective to prevent the onset of obesity and its related metabolic diseases such type 2 diabetes (T2D). Methionine is one of the nine essential amino acids (EAA) that share two important characteristics: (i) they cannot be synthetized de novo by the organism and (ii) they have no dedicated storage. Therefore, if dietary EAA supply is low, the organism engages an adaptive response. The signaling pathway involving the kinase GCN2 and the transcription factor ATF4 plays a major role in this adaptive response. In the context of a chronic dietary restriction in methionine, there is not a clear consensus concerning the role of the GNC2/ATF4 pathway in the effects of this nutritional strategy on obesity/T2D. However, the expression of the FGF21 is increased by ATF4, this hormone has been described as major actor in the beneficial effects of methionine restriction. In human, the permanent consumption of a synthetic diet (containing free amino acids) restricted in methionine as performed in rodent's studies is not conceivable. Moreover, long-term consumption of such a diet leads to undesirable effects such as a decrease of muscle mass. In the objective to transfer the restriction of methionine to human nutrition, we have set-up in mice an intermittent methionine restriction using specific plant proteins, whose methionine contents are low, instead of using free amino acid diet. Our initial results indicate a protective effect of this strategy on weight gain and glucose tolerance in the context of a high-fat diet. A more detailed analysis of how methionine restriction influences cellular functions and metabolism will be conducted in different organs, with particular focus on the liver. The underlying mechanisms of these effects will be explored, including investigation of the GCN2/ATF4 pathway using a transgenic mouse model.

Methodologies (key words) : Animal experimentation, RT-qPCR, Western Blot, Elisa.

Publications of the research group on the proposed topic (3 max.)

Decreased ATF4 expression as a mechanism of acquired resistance to long-term amino acid limitation in cancer cells. Mesclon F, et al Oncotarget. 2017 Apr

GCN2 contributes to mTORC1 inhibition by leucine deprivation through an ATF4 independent mechanism. Averous J et al. Sci Rep. 2016 Jun

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title: Interactions of plant extracts containing polyphenols designed to reduce hypertension with human gut microbiota in an *in vitro* model of the human gut

Laboratory: UMR454 MEDIS
Laboratory director: Mickael DESVAUX
Address: Faculté de Pharmacie - Bâtiment CBRV 5ème étage-28, Place Henri Dunant - BP38-63001 Clermont-Ferrand Cedex 1

Internship tutor: Stéphanie BLANQUET-DIOT
Tel: +33 (0)4 73 17 83 90
e-mail: stephanie.blanquet@uca.fr

Summary:
High blood pressure is a multifactorial disease leading to the increase risk of heart attack, stroke and metabolic syndrome, associated to gut microbiota perturbations. Totum-854 is a unique combination of polyphenol rich plant extracts, developed as an innovative nutritional solution for the overall management of hypertension. The preclinical evaluation of active compounds can be carried out *in vivo* using rodents, yet this approach remains limited by significant differences between animal and human digestive physiology, as well as increasing regulatory and societal constraints. A relevant alternative is the use of complex and dynamic *in vitro* models of the human digestive environment, such as the M-SHIME (Mucosal-Simulator of Human Intestinal Microbial Ecosystem. This model has been recently adapted to simulate both the lumen and mucus-associated microbes from the ileal and colon compartments.
In this context, the objective of the internship will be to evaluate the bilateral interactions of Totum-854 with human and colon microbiota in the M-SHIME, i.e., the effects of vegetal extracts on microbiota composition and metabolic activities, but also their metabolization by gut microbes. The first part of the internship will be dedicated to a literature review on the role of human gut microbiota in the etiology of hypertension. Then, *in vitro* experiments will be performed in the M-SHIME inoculated with stools from different healthy donors to assess the effects of Totum-854 on microbiota composition (qPCR and 16S metabarcoding) and gas/short chain fatty acids production. Plant metabolites will also be followed by UPLC-UV-MS.
This training will be performed in partnership with Valbiotis company and CMET laboratory from Ghent University in Belgium, in the frame of the international associated laboratory HOMIGUT.

Methodologies (key words): M-SHIME, *in vitro* fermentation, flow cytometry, molecular biology (qPCR, sequencing), chromatography analysis, bioinformatics

Publications of the research group on the proposed topic (3 max.)

- Delbaere K, Roegiers I, Bron A, Durif C, Van de Wiele T, Blanquet-Diot S, Marinelli L. The small intestine: dining table of host-microbiota meetings. FEMS Microbiol Rev. 2023 19;47(3).
- Langhi C, Vallier M, Bron A, Otero Y, Maura M, Le Joubioux F, Blomberg N, Giera M, Guigas B, Maugard T, Chassaing B, Peltier S, Blanquet-Diot S, Bard JM, Sirvent P. A polyphenol-rich plant extract prevents hypercholesterolemia and modulates gut microbiota in western diet-fed mice. Frontiers in Cardiovascular Medicine. 2024 11:1342388.
- Esmail GA, Uriot O, Mottawea W, Denis S, Sultan S, Njoku EN, Chiba M, Tosh S, Blanquet-Diot S*, Hammami R* (*co-senior authors). Western diet-based NutriCol medium: A high-pectin, low-inulin culture medium promoted gut microbiota stability and diversity in PolyFermS and M-ARCOL continuous in vitro models. Food Res Int. 2025 206:115993.

Please send this sheet **jointly** to the following addresses:
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Role of L-serine on the pro-carcinogenic effect of Colibactin-positive *E.coli*

Laboratory : M2iSH
Laboratory director : Mathilde Bonnet
Address : Faculté de médecine. CBRV 3ème étage. 28 place H.Dunant. 63000 Clermont Ferrand.

Internship tutor : Mathilde Bonnet
Tel : 04-73-17-83-81
e-mail : mathilde.bonnet@uca.fr

Summary :
Colonic tissues in colorectal cancer (CRC) patients are colonized by colibactin-producing *Escherichia coli* (CoPEC). Colibactin is a genotoxin synthesized by the *pks* genomic island. Metabolomic studies have revealed that CoPEC infection leads to a reprogramming of intestinal epithelial cell metabolism, resulting in a decrease in L-serine. In a previous study, we showed that L-serine contributes to CoPEC persistence in the gastrointestinal tract and enhances its pro-carcinogenic functions.
The objective of this internship is to understand how L-serine influences the pro-carcinogenic effects of CoPECs, with a focus on the tumor microenvironment and oxidative stress. The first aim will be to study the impact of an L-serine-depleted (SD) diet on immune cell populations in the intestinal mucosa and tumors of CoPEC-infected animals, using immunostaining or flow cytometry. These studies will focus specifically on neutrophils, T lymphocytes (CD8+), and ILC3s. The modulation of these cell populations will be correlated with tissue and serum cytokine levels, measured by multiplex cytometry (KC, IL-10, IL-4, IL-22, IL17A), as well as with tumor development. Moreover, induction of oxidative stress and inflammation during the infection was evaluated using optical *in vivo* imaging (IVIS spectrum- IMOST IVIA platform), and MPO and lipocalin-2 levels determination by ELISA. Same experiment will be performed using a CoPEC mutant unable to metabolize L-serine.
This work will allow to better understand the impact of nutrition factor on pro-carcinogenic properties of CoPEC in colorectal cancer.

Methodologies (key words) : Immunohistochemistry (fluorescent microscopy)***, imaging,*** molecular biology (RNA extraction, cDNA synthesis, qRT-PCR); biochemistry (ELISA), preclinical model of infection

Publications of the research group on the proposed topic (3 max.)

1- Devaux et al. L-serine promotes pro-carcinogenic effects of colibactin-producing E. coli. *In revision*
2-Lopès A et al. Colibactin-positive Escherichia coli induce a procarcinogenic immune environment leading to immunotherapy resistance in colorectal cancer. Int J Cancer. 2020 Feb 9.
3- Gagnière J et al. Interactions between microsatellite instability and human gut colonization by Escherichia coli in colorectal cancer. Clin Sci (Lond). 2017 Mar 1;131(6):471-485.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Decipher the role of the GCN2-ATF4 pathway in pancreatic adaptation to sulfur amino acid restriction.

Laboratory : Team PROTEOSTASIS, UMR1019 INRAE/UCA, Human Nutrition Unit
Laboratory director : Didier REMOND
Address : INRAE Research center of Theix – 63122 Saint-Genès-Champanelle, FRANCE

Internship tutor : Alain Bruhat, PhD
Tel : +33 4 73 62 41 50
e-mail : alain.bruhat@inrae.fr

Summary :
The literature indicates that, in rodents, restriction of sulfur amino acids (SAA—methionine and cysteine) extends lifespan, limits body weight gain, and provides protection against metabolic diseases. This dietary restriction activates the eIF2α-ATF4 signaling pathway. However, the specific role of the GCN2 eIF2α kinase, an amino acid sensor responsive to essential amino acid deprivation, remains poorly understood. This signaling pathway can promote survival through autophagy or lead to apoptosis under prolonged or severe stress conditions.
Our preliminary results in mice show that the eIF2α-ATF4 pathway is early induced in the pancreas with a diet devoid of SAA. The aim of this internship is to decipher the role of the GCN2-ATF4 signaling pathway in maintaining proteostasis within the pancreas, a process essential to the proper functioning of this organ. More specifically, the aim will be to determine how this pathway contributes to the adaptation of pancreatic cells to SAA restriction. Two complementary approaches will be implemented: (i) an *in vivo* approach, using a mouse line genetically invalidated for GCN2 (GCN2-KO), to assess the tissue consequences of the absence of this pathway during SAA restriction. (2) an *in vitro* approach, using a pancreatic cell line treated with a specific pharmacological inhibitor of GCN2, to study the cellular and molecular effects in a controlled environment. In both models, activation of the GCN2-ATF4 pathway will be analyzed using transcriptomic (RT-qPCR) and protein (Western blot) approaches to identify the functions and metabolic pathways regulated in response to SAA restriction. In parallel, the potential crosstalk between the GCN2-ATF4 pathway and the mTOR pathway, central to the regulation of metabolism and cell growth, will also be investigated.

Methodologies (key words) : nutritional experiment in mice, cell culture, analysis of gene expression by RT-qPCR and protein expression by western-blot.

Publications of the research group on the proposed topic (3 max.)

Carraro *et al.* (2022). Activation of the eIF2α-ATF4 Pathway by Chronic Paracetamol Treatment Is Prevented by Dietary Supplementation with Cysteine. *Int J Mol Sci*. 2022;23(13):7196.

Chaveroux *et al.* (2015). In vivo imaging of the spatiotemporal activity of the eIF2α-ATF4 signaling pathway: insight into stress and related disorders. *Science Signaling*, 28;8 (374):rs5.

B'chir W, et al. (2013). The eIF2α-ATF4 pathway is essential for stress-induced autophagy gene expression. *Nucleic Acids Res*earch, 41(16):7683-99.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title :
Pathophysiological study of the enteric nervous system in the colonic hypersensitivity associated with chronic abdominal pain in IBS patients and related comorbidities.

Laboratory : U1107 INSERM/UCA NeuroDOL – Laboratoire de Pharmacologie Fondamentale et Clinique de la Douleur
Laboratory director : Pr Radhouane Dallel
Address : Faculté de Médecine et de Pharmacie, 28 place Henri Dunant 63000 Clermont-Ferrand

Internship tutor : Dr Frédéric CARVALHO
Tel : 04 73 17 81 03
e-mail : frederic.carvalho@inserm.fr ou frederic.carvalho@uca.fr

Summary :
Irritable Bowel Syndrome (IBS) is a common and complex gastrointestinal disorder characterized by chronic abdominal pain and altered bowel habits, often accompanied by comorbidities such as anxiety and depression. One of the hallmark features of IBS is colonic hypersensitivity (CHS), a heightened perception of visceral pain whose pathophysiological mechanisms remain poorly understood. Increasing evidence suggests that dysfunctions of the enteric nervous system (ENS) play a critical role in mediating these symptoms, acting at the interface between the immune system, gut microbiota, and central nervous system. This **M2 internship project** will aim to explore the pathophysiological role of the ENS in relation to CHS and its associated comorbidities using preclinical models that reflect three complementary IBS-related etiologies. Depending on the outcome of ongoing ANR funding evaluations, the student will focus on one of the following topics: (1) the role of the AhR/IL-22/Reg3γ signaling pathway in either maintaining or alleviating CHS; (2) the long-term impact of early-life cross-feeding alterations between microbial communities on visceral pain sensitivity; or (3) the effects of chronic exposure to a chemical mixture mimicking the dietary inorganic exposome on gut physiology and CHS.
The project will integrate multidisciplinary techniques including behavioral pain assays, immunohistochemistry, molecular biology, and microbiota analysis, and will contribute to a better understanding of how environmental, microbial, and immunological factors interact with the ENS to promote chronic abdominal pain. This internship offers the opportunity to work within a collaborative and translational research environment and may serve as a foundation for doctoral training in neurogastroenterology.

Methodologies (key words) : Behavioral assessment in mice (colonic sensitivity, anxiety, depression,…), Calcium imaging, ELISA, Histological studies, Immunostaining, RT-qPCR

Publications of the research group on the proposed topic (3 max.)
1. Meynier M., *et al.*, 2024. Pasteurized *Akkermansia muciniphila* improves irritable bowel syndrome-like symptoms and related behavioral disorders in mice. *Gut microbes*, 16(1), 2298026. PMID: 38170633.
2. Gervason S, *et al.*, 2023. Antihyperalgesic properties of gut microbiota: Parabacteroides distasonis as a new probiotic strategy to alleviate chronic abdominal pain. *Pain*, PMID: 37756665.
3. Meynier M., *et al.*, 2022. AhR/IL-22 pathway as new target for the treatment of post-infectious irritable bowel syndrome symptoms. *Gut microbes*, 14(1):2022997. PMID: 35090380.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Establishment of a preclinical model for ocular rosacea: investigation of pathophysiological mechanisms and exploration of novel therapeutic approaches.

Laboratory : NeuroDol UMR 1107 Inserm UCA - team 1 « Pharmacologie Fondamentale et Clinique de la Douleur » (PFCD)
Laboratory director : Pr Radhouane Dallel
Address : Faculté de Médecine et de Pharmacie, 28 place Henri Dunant 63000 Clermont-Ferrand

Internship tutor : Dr David CIA
Tel : 04 73 17 79 83
e-mail : david.cia@uca.fr

Summary :

Ocular rosacea is a chronic inflammatory disease characterized by inflammation of ocular surface tissues, including the eyelid margin and cornea. In the most severe cases, corneal inflammation can lead to ulceration and infection which, if left untreated, may perforate the eye and result in vision loss. Currently, available treatments are mainly symptomatic and often ineffective, based on the use of antibiotics, corticoids and artificial tears. Despite these treatments, the frequency of relapses remains high. The intestinal and/or ocular surface microbiota may be a promising therapeutic target, as it could contribute to inflammation and corneal sensitization in ocular rosacea patients. **This internship** is part of a research project aimed at deepening the understanding of the pathophysiological mechanisms involved in inflammation and corneal hypersensitivity associated with ocular rosacea, with the goal of identifying novel therapeutic approaches. Preliminary work has been initiated to develop a preclinical animal model of the disease. Two murine models are currently under development: one based on ocular surface exposure to ultraviolet B (UVB) radiation, and the other on ocular instillation of the antimicrobial peptide LL-37. **Initial data** obtained through ELISA and histological analyses indicate corneal inflammation in both models. This inflammation appears to be accompanied by hypersensitivity of the ocular surface, as evidenced by the behavioral “eye wiping” test. Furthermore, gene expression analyses by quantitative RT-PCR show an overexpression of several genes linked to innate immunity and ocular microbiota regulation. **The main objective of the internship** will be to confirm these preliminary findings and to further characterize the two models. Particular attention will be given to the study of the gut and ocular surface microbiota, with the aim of identifying a microbial signature specific to the pathology and evaluating innovative microbiota-based therapeutic strategies.

Methodologies (key words) : Behavioral assessment of ocular sensitivity in mice (eye-wiping test, von-Frey test, …), ELISA, Histological studies, Immunostaining, RT-qPCR

Publications of the research group on the proposed topic (3 max.)

Jacquemot, N., Wersinger, E., Brabet, P., & Cia, D. (2023). Hydrogen Peroxide Affects the Electroretinogram of Isolated Perfused Rat Retina. *Current Eye Research*, *48*(12), 1179-1188.

Hassel, C., Couchet, M., Jacquemot, N., Blavignac, C., Loï, C., Moinard, C., & Cia, D. (2022). Citrulline protects human retinal pigment epithelium from hydrogen peroxide and iron/ascorbate induced damages. *Journal of Cellular and Molecular Medicine*, *26*(10), 2808-2818.

Meynier, M., Daugey, V., Mallaret, G., Gervason, S., Meleine, M., Barbier, J., ... & Carvalho, F. A. (2024). Pasteurized akkermansia muciniphila improves irritable bowel syndrome-like symptoms and related behavioral disorders in mice. *Gut microbes*, 16(1), 2298026.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Search for Effectors Modulating TGFβ/BMP Signalling to Preserve Muscle Mass

Laboratory : Unité de Nutrition Humaine, UMR1019, Equipe Proteostasis
Laboratory director : Didier Rémond
Address : INRAE Auvergne Rhone Alpes, Route de Theix, 63122 Saint Genes Champanelle

Internship tutor : Lydie Combaret
Tel : 04 73 62 48 24
e-mail : lydie.combaret@inrae.fr

Summary :

Skeletal muscle atrophy occurs in various physiological (e.g., aging) and pathological conditions (such as cancers and chronic diseases), as well as during physical inactivity. It has detrimental consequences for patients' autonomy, quality of life and treatment efficacy. Muscle atrophy is thus a major public health concern for which no effective treatments currently exist.

Using a comparative physiology approach with murine models of induced atrophy and a model of natural resistance to atrophy, the brown bear during hibernation, a prolonged state of fasting and physical inactivity, we have demonstrated the importance of modulating the balance between the TGFβ and BMP signalling pathways (Cussonneau et al. 2021, Cussonneau et al. 2022). Finally, our research has also suggested the presence of circulating compounds in the serum of hibernating brown bears that may have therapeutic potential against muscle atrophy (Chanon et al. 2018).

In that context, the Master 2 internship aims at further investigating mechanisms that enable the favourable modulation of TGFβ/BMP signalling in muscle cells. For that purpose, we will focus (i) on the possible cross-talk between the TGFβ and BMP signalling with other signalling pathways and (ii) on the role of circulating compound in the serum of brown bears on the regulation of the TGF/BMP signalling pathways.

Located in an attractive setting, our team of approximately 20 people offers a friendly and dynamic environment with strong collaboration between members. This internship is a great opportunity to expand your network, gain valuable experience, and explore the possibility of pursuing a Ph.D.

Methodologies (key words) :
Cell culture, isolated muscle fibers, siRNA, Western blots, RT-qPCR

Publications of the research group on the proposed topic (3 max.)

Cussonneau et al. 2021. Concurrent BMP Signaling Maintenance and TGF-β Signaling Inhibition Is a Hallmark of Natural Resistance to Muscle Atrophy in the Hibernating Bear. Cells 10, 1873.

Cussonneau et al. 2023. Induction of ATF4-Regulated Atrogenes Is Uncoupled from Muscle Atrophy during Disuse in Halofuginone-Treated Mice and in Hibernating Brown Bears. Int. J. Mol. Sci. 24, 621.

Chanon et al. 2018. Proteolysis inhibition by hibernating bear serum leads to increased protein content in human muscle cells. Sci Rep. 2018 Apr 3;8(1):5525.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Interactions between *Klebsiella pneumoniae* and inflammasomes in intestinal epithelial cells

Laboratory : UMR CNRS 6023 Laboratoire Microorganismes : Génome Environnement (LMGE), Equipe CMES : Communautés microbiennes : écotoxicologie-santé
Laboratory director : Didier DEBROAS
Address : UFR de Pharmacie, 28 place Henri Dunant, 63000 Clermont-Ferrand

Internship tutor : Marjolaine VAREILLE-DELARBRE
Tel : 04.73.17.81.22
e-mail : marjolaine.vareille-delarbre@uca.fr

Summary :

Klebsiella pneumoniae is a ubiquitous Gram-negative bacterium and a major cause of nosocomial infections. As commensal bacteria of the gut, *K. pneumoniae* colonizes the intestinal microbiota and interacts with immune cells in the intestinal mucosa without triggering a significant inflammatory response. This immune evasion may facilitate bacterial dissemination and the establishment of extra-intestinal infections. However, the mechanisms underlying this ability to avoid inflammation remain poorly understood and are crucial to uncovering how *K. pneumoniae* manipulates the host's intestinal immune responses.

The objective of this internship is to investigate the interactions between *K. pneumoniae* and the NLRP3, NLRP10, and NLRP12 inflammasomes—key components of the innate immune system and potent activators of inflammatory pathways—in human intestinal epithelial cells. The modulation of inflammasome gene and protein expression by *K. pneumoniae* will be assessed using RT-qPCR and western blotting in infected cells. Levels of the pro-inflammatory cytokines IL-1β and IL-18 will be measured by ELISA.

Additionally, the activation of inflammatory caspases, particularly caspase-1, will be analyzed through enzymatic assays, and the induction of pyroptosis, a form of highly inflammatory programmed cell death, will be evaluated via flow cytometry.

The roles of major bacterial factors—such as the capsule, lipopolysaccharide, and siderophores—in modulating host immune responses will be examined using various *K. pneumoniae* mutants available in the laboratory.

This project will contribute to a deeper understanding of the immune evasion strategies employed by *K. pneumoniae* within the intestinal environment and may lead to the identification of novel therapeutic targets.

Methodologies (key words) : cell culture, bacterial infections, RT-QPCR, ELISA, flow cytometry

Publications of the research group on the proposed topic (3 max.)

Vareille-Delarbre M, Miquel S, Garcin S, Bertran T, Balestrino D, Evrard B, Forestier C Immunomodulatory Effects of *Lactobacillus plantarum* on Inflammatory Response Induced by *Klebsiella pneumoniae*. Infect Immun. 2019 Oct 18;87(11):e00570-19.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Breast cancer and obesity: Development of tumour-derived organoids for personalized treatment

Laboratory : ECREIN Team, Human Nutrition Unit (Didier Rémond)
Laboratory director : Florence Caldefie-Chézet
Address : UFR Pharmacie, 28 place Henri Dunant, 63000 Clermont-Ferrand

Internship tutor : Laetitia DELORT
Tel : 04.73.17.79.70
e-mail : laetitia.delort@uca.fr

Summary :
Breast tumour organoids represent a major advance in breast cancer research. This three-dimensional model more realistically reproduces the heterogeneity of human tumours, enabling us to better understand the interactions between tumour cells and their microenvironment, and to test the effectiveness of treatments. They also offer a personalized approach for each patient, reducing the need for animal experiments and facilitating the identification of suitable therapies, particularly for overweight women, who are often less sensitive to standard treatments.
The project of this Master 2 internship will consist in the development of an organoid model based on cells derived from patient tumours.
Cancer cells will be isolated from fresh tumour tissue using a combination of mechanical disruption and enzymatic digestion and the cell pellet will be resuspended in a basement membrane matrix with reduced concentrations of growth factors, enabling the formation of three-dimensional structures. After approximately 2 to 3 weeks, the organoids will be dissociated and then seeded in fresh matrix for amplification. An in-depth characterization of the organoids will be carried out: organoid growth, cell death, histopathological markers (ER, PR, HER2 and KI67) by immunohistochemistry and genetics (DNA sequencing of the primary tumour and organoids).

Methodologies (key words) : 3D Cell culture, molecular biology, confocal microscopy, histochemistry

Publications of the research group on the proposed topic (3 max.)

1. Habanjar O, Nehme R, Goncalves-Mendes N, Cueff G, Blavignac C, Aoun J, Decombat C, Auxenfans C, Diab-Assaf M, Caldefie-Chezet F, Delort L. The obese inflammatory microenvironment may promote breast DCIS progression. Front Immunol. 2024 Jul 12;15:1384354
2. Habanjar O, Maurin AC, Vituret C, Vachias C, Longechamp L, Garnier C, Decombat C, Bourgne C, Diab-Assaf M, Caldefie-Chezet F, Delort L. A bicellular fluorescent ductal carcinoma in situ (DCIS)-like tumoroid to study the progression of carcinoma: practical approaches and optimization. Biomaterials Science, 2023, May 2;11(9):3308-3320
3. Delort L, Cholet J, Decombat C, Vermerie M, Dumontet C, Castelli F, Fenaille F, Auxenfans C, Rossary A, Caldefie-Chezet F. The adipose microenvironment dysregulates the mammary myoepithelial cells and could participate to the progression of breast cancer. Front Cell Dev Biol. 2021,8:571948

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Impact of a multidisciplinary (Physical activity and nutrition) weight loss intervention on metabolic dysfunction-associated steatotic liver disease (MASLD) in adolescents with obesity.

Laboratory : Metabolic Adaptations to Exercise under Physiological and Pathological Conditions (AME2P, UPR3533)
Laboratory director : David Thivel
Address : 3 rue de la Chebarde, 63170 Aubière

Internship tutor : Gael Ennequin
Tel : 0473407679
e-mail : gael.ennequin@uca.fr

Summary :

Long considered in adults only, liver alterations and particularly metabolic dysfunction-associated steatotic liver disease (MASLD) can be found in about 5 to 11% of the general pediatric population, reaching 30 to 50% among children and adolescents with obesity (Panganiban et al., 2025). While pediatric guidelines actually encourage lifestyle interventions (AASLD guidelines, Chalasani et al., 2018), their efficacy on metabolic and liver parameters remains to be further clarified and particularly the role of the degree of weight reduction induced (Reinehr & Andler, 2004). In line with its effective and now established collaboration with the University of Salzburg (Austria) (Pixner et al., 2022; Julian et al., 2022), the POWELL study has been launched tending to explore the overall nutritional, energetic and metabolic adaptations to weight loss, its degree, rate and variability, in adolescents with obesity (RBHP 2023 BOIRIE 2). Forty adolescents with obesity are enrolled in a multidisciplinary intervention and participate to a full clinical, metabolic, nutritional and energetic evaluation every 4 weeks. The aim of the present internship would be to take advantage of this POWELL study, contributing to its overall data collection and particularly handling the liver-related evaluations, treatment and analysis. The research question would focus on the effect of the degree of weight loss and its rate on the liver-related profile in this population.

Methodologies (key words) : Firboscan, DXA-scans, Blood sampling, indirect calorimetry

Publications of the research group on the proposed topic (3 max.)

Julian V, Bergsten P, **Ennequin G**, Forslund A, Ahlstrom H, Ciba I, Dahlbom M, Furthner D, Gomahr J, Kullberg J, Maruszczak K, Morwald K, Olsson R, Pixner T, Schneider A, Pereira B, Ring-Dimitriou S, **Thivel D**, Weghuber D. Association between alanine aminotransferase as surrogate of fatty liver disease and physical activity and sedentary time in adolescents with obesity. Eur J Pediatr. 2022 Aug;181(8):3119-3129

Couret A, King JA, Pereira B, **Courteix D**, Obert P, Vinet A, Walther G, Lesourd B, Chapier R, Zak M, Bagheri R, Ugbolue CU, Abergel A, **Thivel D**, Dutheil F, **Ennequin G**. Effect of different modalities of exercise on Fatty Liver Index in patients with metabolic syndrome: The RESOLVE randomized trial. Clin Res Hepatol Gastroenterol. 2024 Oct;48(8):102461.

Ennequin G, Buchard B, Pereira B, **Bonjean L**, **Courteix D**, Lesourd B, Chapier R, Obert P, Vinet A, Walther G, Zak M, Bagheri R, Ugbolue CU, Abergel A, Dutheil F, **Thivel D**. Noninvasive biomarkers of non-alcoholic fatty liver disease in patients with metabolic syndrome: insights from the RESOLVE Study. Minerva Gastroenterol (Torino). 2023 Dec;69(4):494-503

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title: Effect of Innovative Probiotics on Dendritic Cell Maturation and T Cell Polarisation: Implications for Food Allergies

Laboratory: Immunology laboratory, ECREIN Team, Unité de Nutrition Humaine (UMR 1019 INRAE/UCA)
Laboratory director: Pr. B. Evrard
Address: Clermont-Ferrand Faculty of Medicine and Paramedical Professions
28, Place Henri Dunant, 63001 Clermont-Ferrand

Internship tutor: Pr. B. Evrard
Tel: 04 73 75 06 62
e-mail: bevrard@chu-clermontferrand.fr

Summary:

This project investigates the immunomodulatory properties of next-generation probiotic candidates, with a particular focus on their potential role in the treatment of allergic diseases, especially food allergies. In allergic patients, a shift in immune balance is commonly observed, notably characterized by an increase in the Th2 T cell subset. Moreover, dysbiosis is frequently reported in these individuals, highlighting the crucial interplay between the immune system and gut microbiota, and suggesting the therapeutic potential of probiotics.

Building on previous findings that identified strict anaerobic gut bacteria capable of modulating human monocyte-derived dendritic cells (mo-DCs), this study aims to determine whether these interactions promote inflammatory or regulatory immune responses, specifically the induction of regulatory T cells (Tregs) and the suppression of Th2 responses. To investigate this, an autologous model will be employed in which mo-DCs matured with a probiotic strain will be co-cultured with naïve T cells, allowing for an analysis of the resulting T cell polarization.

Techniques such as spectral cytometry and cytokine quantification will be used to characterize T cell subsets (Th1, Th2, Th17, Tregs), while CFSE-based proliferation assays will assess T cell expansion. The expected outcomes include confirmation that selected probiotic strains can promote Treg development and stimulate anti-inflammatory cytokine production, therefore having the potential to effectively reduce allergic responses and restore immune tolerance, and so supporting their future application as novel therapeutic agents, notably in peanut or nuts gastro-intestinal oral immunotherapy.

Methodologies (key words): cell culture, monocyte-derived dendritic cells, proliferation assay, spectral cytometry, cytokine quantification

Publications of the research group on the proposed topic (3 max.)

B. Evrard et al., « Dose-dependent immunomodulation of human dendritic cells by the probiotic Lactobacillus rhamnosus Lcr35 », PLoS One, vol. 6, no 4, p. e18735, avr. 2011, doi: 10.1371/journal.pone.0018735.

T. Bertran et al., « Slight Pro-Inflammatory Immunomodulation Properties of Dendritic Cells by Gardnerella vaginalis: The "Invisible Man" of Bacterial Vaginosis? », J Immunol Res, vol. 2016, p. 9747480, 2016, doi: 10.1155/2016/9747480.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Transcranial low-intensity ultrasound stimulation for treating chronic neuropathic pain.

Laboratory : N**euro-Dol Inserm/UCA U1107**
Laboratory director : Prof. Radhouanne Dallel
Address : Faculté de Chirurgie Dentaire - 2, Rue de Braga, 63100 Clermont-Ferrand

Internship tutor : Camille Fauchon
Tel : 06 99 24 57 90
e-mail : camille.fauchon@uca.fr

Summary :
Low intensity focused transcranial ultrasound stimulation (LIFUS) is an emerging technique that will overcome current technological barriers[1] - i.e., stimulating deep brain structures non-invasively, without tissue damage but with high spatial precision that remains unattainable with other techniques. LIFUS uses mechanical energy through the intact skull to reversibly modulate (excitation/inhibition) brain activity with adjustable depth of focus and without lasting neurological effects. LIFUS offers superior penetration and spatial resolution to modulate deep areas, compared to other non-invasive brain stimulation methods such as transcranial magnetic (TMS) or electrical stimulation (tDCS). Unlike TMS/tDCS, LIFUS is also compatible with fMRI, enabling real-time tracking, brain mapping, and quantification of its modulatory effect. The system is compatible with a recently acquired robotized arm for guiding neuromodulation coils, allowing for correction of patient movements during session and accurate neuronavigation targeting.

We are interested in developing cortical stimulation techniques for pain relief. **Therefore, we would like to investigate the safety, efficacy, and mechanism of action of LIFUS in humans.** Recent findings suggest that LIFUS targeting deep brain regions like the anterior cingulate cortex (ACC) can reduce heat pain sensation in healthy individuals. Hence, we will assess the effects of LIFUS on mechanical, heat and cold pain thresholds, temporal summation of pain, conditioned pain modulation, and pain associated with capsaicin sensitization in healthy participants. Clinical protocol including patients suffering from neuropathic pain will be planned in the ambition of a PhD thesis on this topic.

Methodologies (key words) : Clinical research; Neurosciences; non-invasive neuromodulation; low-intensity focus ultrasound; chronic neuropathic pain; quantitative

Publications of the research group on the proposed topic (3 max.)

Soliman N*, MOISSET X*, et al., Pharmacotherapy and non-invasive neuromodulation for neuropathic pain: a systematic review and meta-analysis. Lancet Neurol. (2025) *co-first

Thomas, J., FAUCHON, C., et al., Effects of multiple transcranial magnetic stimulation sessions on pain relief in patients with chronic neuropathic pain: A French cohort study in real-world clinical practice." European Journal of Pain(2025).

Moisset X, et al., Pharmacological treatments of neuropathic pain: real-life comparisons using propensity score matching. Pain. (2022)

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Investigating the emergence of muscle type diversification in vertebrates

Laboratory : iGRED
Laboratory director : Krzysztof Jagla
Address : 28 place Henri Dunant

Internship tutor : Prikshit
Tel :
e-mail : prikshit@uca.fr

Summary : This project investigates how a single pool of neuro-mesodermal progenitors (NMPs) generates diverse axial segments for distinct muscle types using chicken embryos. We performed lineage tracing identifying NMP contributions to cervical , thoracic , and lumbar axial segments. Previous work from our lab showed that NMPs possess a dynamic transcriptomic signature during these axial segment formation , with the CDX (caudal) gene family displaying notable temporal variation (Guillot et al., 2021). As chromatin remodelers, CDX genes are key in spinal cord fate (Metzis et al., 2018), suggesting a possible role in mesodermal regionalization and muscle diversification.

To test this, we analyzed CDX expression and chromatin accessibility in NMPs across developmental stages using HCR-FISH, and qPCR. We found out that CDX expression is dynamic and spatio-temporally heterogeneous within the NMPs. Based on this previously unreported heterogeneity of CDX expression and existing literature, we hypothesize that distinct combinations of CDX genes remodel chromatin to establish specific axial identities.

Using single nuclei Multiomics techniques, we are investigating how CDX heterogeneity influences NMP axial fate by identifying CDX target genes involved in axial specification. During the internship, we will focus on validating the axial specificity of these targets and test their functional roles using CRISPR-Cas9 knockout or targeted overexpression.

Methodologies (key words): CRISPR-Cas9, Sn-Multiomics, CDXs, NMPs, Morphometry, HCR, Imaging

Publications of the research group on the proposed topic (3 max.)

Guillot C, Djeffal Y, Michaut A, Rabe BA, Pourquie O: Dynamics of primitive streak regression controls the fate of neuro-mesodermal progenitors in the chicken embryo. eLife 2021;10:e64819

H. Jin, Z. Liu, J. Mou, M. Tang, X. Huang, K. Liu, Q. Zhang, K.O. Lui, & B. Zhou, Dual genetic tracing demonstrates the heterogeneous differentiation and function of neuromesodermal progenitors in vivo, Proc. Natl. Acad. Sci. U.S.A. 122 (14) e2402305122, https://doi.org/10.1073/pnas.2402305122 (2025).

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER
BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : **Perivitelline albumen as novel model to study amniotic fluid's influence in epithelial-to-mesenchymal transition during body axis elongation.**

Laboratory : iGReD
Laboratory director : Krzysztof Jagla
Address : 28 place Henri Dunant 63000 Clermont Ferrand

Internship tutor : Felipe Maurelia Gaete
Tel :
e-mail : felipe_alonso.maurelia_gaete@uca.fr

Summary :

During gastrulation, epiblast cells undergo epithelial-to-mesenchymal transition (EMT), forming the mesenchymal layer. This process continues during body axis extension, where epiblast stem cells (i.e., Neuro Mesodermal Progenitors, NMPs) give rise to neural and mesodermal tissues forming the trunk and tail in vertebrates. Despite growing knowledge of NMP regulation, the role of soluble factors within the amniotic environment, which directly contacts NMPs, remain unexplored, primarily due to accessibility challenges in mammals. This proposal uses *Gallus gallus* embryos as a model system to investigate the influence of amniotic fluid on NMP EMT during body axis elongation. Since amniogenesis occurs later in avian development, the proteome of the perivitelline albumen likely contributes to EMT by acting as a pre-amniotic fluid. By analysing the proteomic composition of the perivitelline albumen and introducing specific modulators into this environment, we aim to assess the responsiveness of NMPs to soluble factors. This approach seeks to uncover novel molecular mechanisms that promote EMT. This study will enhance our understanding of soluble molecules driving EMT during development and provide insights into putative therapeutic targets regulating stem cell differentiation and metastatic transition of cancer cells.

Methodologies (key words) :
Molecular Biology//Proteomic analysis (Western Blot and Mass Spectrometry)//Morphological analysis (Immunofluorescence, HCR, *in-vivo* tracing).

Publications of the research group on the proposed topic (3 max.)

1. Chau KF, Springel MW, Broadbelt KG, Park HY, Topal S, Lun MP, Mullan H, Maynard T, Steen H, LaMantia AS, Lehtinen MK. Progressive Differentiation and Instructive Capacities of Amniotic Fluid and Cerebrospinal Fluid Proteomes following Neural Tube Closure. Dev Cell. 2015 Dec 21;35(6):789-802. doi: 10.1016/j.devcel.2015.11.015. PMID: 26702835; PMCID: PMC4691285.
2. Garriock RJ, Chalamalasetty RB, Kennedy MW, Canizales LC, Lewandoski M, Yamaguchi TP. Lineage tracing of neuromesodermal progenitors reveals novel Wnt-dependent roles in trunk progenitor cell maintenance and differentiation. Development. 2015 May 1;142(9):1628-38. doi: 10.1242/dev.111922. PMID: 25922526; PMCID: PMC4419273.
3. Charlene Guillot, Yannis Djeffal, Arthur Michaut, Brian Rabe, Olivier Pourquié (2021) Dynamics of primitive streak regression controls the fate of neuromesodermal progenitors in the chicken embryo eLife 10:e64819.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title: Exploring How Folate Drives Embryonic Development—From cell fate regulation to Morphogenesis

Laboratory : iGReD
Laboratory director : Krzysztof Jagla
Address : 28 place Henri Dunant 63000 Clermont Ferrand

Internship tutor : Charlene Guillot
Tel :
e-mail : charlene.guillot@uca.fr

Summary :
The vertebrate trunk and tail form through coordinated contributions of mesodermal and neural cells from the tailbud. Disruptions in this process can cause neural tube defects (NTDs), like spina bifida, which are influenced by both genetic and environmental factors. While folic acid (FA) supplementation prevents many NTDs, its role in posterior body axis development remains unclear.
NeuroMesodermal Progenitors (NMPs)—bipotent cells generating both neural and mesodermal tissues—are particularly sensitive to environmental cues, including folate (vitamin B9). Our lab uses avian embryos to model folate deficiency and trace NMP lineages. We've shown that FA deficiency impairs axis elongation, resulting in NTD-like phenotypes marked by neural tube closure defects and mesodermal abnormalities.
Single-cell RNA sequencing revealed reduced NMP proliferation, altered metabolism, and nearly a 50% drop in NMP numbers. To further explore these effects, this internship will induce FA deficiency in NMPs using CRISPR knockout of MTHFD1, a key folate pathway enzyme. We'll investigate axis formation using live imaging, HCR FISH, immunofluorescence, and qPCR to map gene expression changes and cell fate. This project will uncover how folate shapes vertebrate development at the single-cell level, with implications for understanding and preventing NTDs.
If you're curious about how metabolism intersects with development, we invite you to join our research.

Methodologies (key words): Molecular Biology/Morphological analysis
Immunofluorescence, HCR-FISH, *in-vivo* live imaging, single-cell quantitative analysis.

Publications of the research group on the proposed topic (3 max.)

1. Guillot C, Djeffal Y, Michaut A, Rabe B, Pourquié O. Dynamics of primitive streak regression controls the fate of neuromesodermal progenitors in the chicken embryo. Elife. 2021 Jul 6;10:e64819. doi: 10.7554/eLife.64819. PMID: 34227938
2. Oginuma M, Moncuquet P, Xiong F, Karoly E, Chal J, Guevorkian K, Pourquié O. A Gradient of Glycolytic Activity Coordinates FGF and Wnt Signaling during Elongation of the Body Axis in Amniote Embryos. Dev Cell. 2017 Feb 27;40(4):342-353.e10. doi: 10.1016/j.devcel.2017.02.001. PMID: 28245921
3. Binagui-Casas A, Dias A, Guillot C, Metzis V, Saunders D. Building consensus in neuromesodermal research: Current advances and future biomedical perspectives. Curr Opin Cell Biol. 2021 Dec;73:133-140. doi: 10.1016/j.ceb.2021.08.003. Epub 2021 Oct 28. PMID: 34717142.

Please send this sheet **jointly** to the following addresses :
isabelle.vaillant@uca.fr **and** corinne.malpuech-brugere@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Impact of cannabidiol on muscle atrophy induced by tumor secretions and chemotherapy in a co-cultured myotube model.

Laboratory : Equipe "Alimentation, Santé Musculaire et Sarcopénie". Unité de Nutrition Humaine UMR1019.
Laboratory director : Pr Yves Boirie
Address : UFR de Médecine et des Professions Paramédicales. UNH - UMR1019 Equipe ASMS - 5ème étage R3.28 place Henri Dunant. 63001 Clermont-Ferrand

Internship tutor : Dr Olivier LE BACQUER, HDR
Tel : 04.73.17.82.48
e-mail : olivier.le-bacquer@inrae.fr

Summary : Cachexia is a multifactorial wasting syndrome characterized by severe involuntary loss of body weight, loss of skeletal muscle mass (with or without loss of fat mass), anorexia, and dysregulated energy and protein metabolism. It is often associated with cancer development and has a negative impact on cancer treatment and patient survival. Maintaining skeletal muscle mass in cancer patients is therefore crucial. Cancer treatment itself, like chemotherapy, can also contribute to cachexia. Cannabidiol is a phytocannabinoid derived from *Cannabis sativa,* that can modulate the endocannabinoid system activity. Recent studies have demonstrated its antineoplastic properties in in vitro and preclinical models. In addition, several studies have shown that it may have beneficial effects on the maintenance of skeletal muscle mass and function in various physiopathological conditions.
The aim of this Master 2 project is to investigate whether cannabidiol can influence the development of cachexia in vitro in a model of myotubes in culture. To this end, C2C12 myotubes will be co-cultured with MLM3 cancer cells (model of head and neck cancer) and treated with chemotherapy (cisplatin) to reproduce what is observed in the clinic, and the effect of cannabidiol on atrophy , protein homeostasis and mitochondrial dysfunctions will be characterized.

Methodologies (key words) : Cell co-culture (muscle and cancer cells), spheroids, western-blot, RT-qPCR, Immunohistology.

Publications of the research group on the proposed topic (3 max.)

1. Le Bacquer O, Sanchez P, Patrac V, Rivoirard C, Saroul N, Giraudet C, Kocer A, Walrand S. Am J Physiol Cell Physiol. 2024 Apr 1;326(4):C1226-C1236. Cannabidiol protects C2C12 myotubes against cisplatin-induced atrophy by regulating oxidative stress.
2. Fajardo L, Sanchez P, Salles J, Rigaudière JP, Patrac V, Caspar-Bauguil S, Bergoglgio C, Moro C, Walrand S, Le Bacquer O**.** Am J Physiol Endocrinol Metab. 2023 Feb 1;324(2):E176-E184. Inhibition of the endocannabinoid system reverses obese phenotype in aged mice and partly restores skeletal muscle function.
3. Le Bacquer O, Salles J, Piscitelli F, Sanchez P, Martin V, Montaurier C, Di Marzo V, Walrand S. J Cachexia Sarcopenia Muscle. 2022 Feb;13(1):662-676. Alterations of the endocannabinoid system and circulating and peripheral tissue levels of endocannabinoids in sarcopenic rats

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title: Development of a Murine Model to Study Interactions Between CAR-T Cells and Respiratory Pathogens

Laboratory: EA (UR) CHELTER 7453
Laboratory director: Prof. Marc Berger
Address: UFR de Médecine & Pharmacie, 58 rue Montalembert, 63000 Clermont-Ferrand

Internship tutor: Prof. Paul Rouzaire
Tel: +33(0)4 751 983
e-mail: porouzaire@chu-clermontferrand.fr

Summary :

Treatment with genetically modified T cells (CAR-T cells) is revolutionizing the management of hematological malignancies. However, the development of respiratory infections is a major complication observed in patients undergoing CAR-T cell therapy, significantly impacting both treatment efficacy and patient prognosis. To date, no experimental studies have been conducted, and the underlying pathophysiological mechanisms remain poorly understood.

The aim of this project is to develop a murine model to study the interactions between CAR-T cells and respiratory pathogens. To achieve this, a lung infection model using *Klebsiella pneumoniae* will be established in mice treated with anti-CD19 CAR-T cells, which specifically target B lymphocytes.

The objectives are: (1) to investigate the impact of CAR-T cell therapy on bacterial colonization and the pulmonary microbiota, and (2) to assess how respiratory infections affect CAR-T cell efficacy.To address this question, animals will receive an injection of CAR-T cells followed by intranasal instillation of *K. pneumoniae* 24 hours later. Pulmonary colonization by the pathogen will be monitored over a 7-day period through bacterial load quantification. The expression of genes encoding key virulence factors of *K. pneumoniae* (capsule, pili, siderophores), as well as the potential emergence of antibiotic resistance genes, will be assessed by RT-qPCR in lung tissues.The in vivo efficacy of CAR-T cells will be evaluated using A20 cells (expressing luciferase). Bioluminescence of the A20 cells will be monitored weekly following inoculation. CAR-T cell proliferation will be assessed in serial blood samples based on EGFP expression.At the end of the experiment, mice will be sacrificed to assess CAR-T cell and A20 cell infiltration in the spleen and lungs.

The knowledge generated from this study will help improve the therapeutic management of patients receiving CAR-T cell treatment.

Methodologies (key words): *in vivo* experimentation (mouse), cell culture, flow cytometry, RT-QPCR

Publications of the research group on the proposed topic (3 max.)

- Dougé A, El Ghazzi N, Lemal R, Rouzaire P. Adoptive T Cell Therapy in Solid Tumors: State-of-the Art, Current Challenges, and Upcoming Improvements. Mol Cancer Ther. 2024
- Vareille-Delarbre M, Miquel S, Garcin S, Bertran T, Balestrino D, Evrard B, Forestier C Immunomodulatory Effects of Lactobacillus plantarum on Inflammatory Response Induced by Klebsiella pneumoniae. Infect Immun. 2019

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : INSPORTED, co-supplementation with insect proteins and vitamin D in the context of return to physical activity

Laboratory : Human Nutrition Unit, UMR1019 INRAE/UCA
Laboratory director : Didier Rémond
Address : 28, place Henri Dunant, 63000 Clermont-Ferrand

Internship tutor : Talvas Jérémie
Tel : 04 73 17 82 80
e-mail : jeremie.talvas@uca.fr

Summary :
Our project aims to test the impact of a multimodal approach combining nutritional supplementation with insect protein and vitamin D with an adaptated physical activity program in a preclinical model of elderly C57BL/6 mice. The goal is to simulate a return to activity after a period of sedentary lifestyle associated to weight gain by optimizing post-exercise muscle regeneration and limiting the onset of muscle pain.
To mimic the weight gain frequently observed in humans with aging, 50-week-old mice (middle-aged adults) will all be subjected to a high-calorie, high-fat diet for 8 weeks with the aim of increasing their weight, particularly visceral and subcutaneous fat. This increase in fat mass is expected to have deleterious metabolic consequences (inflammation, lipotoxicity, insulin resistance, oxidative stress, etc.) but are nevertheless reversible. To reverse this phenotype, the mice thus prepared will be subjected for 16 weeks to a physical activity protocol combining predominantly aerobic exercises by imposed running on a treadmill, resistance exercises and balance exercises. During the training period, diets of mice will be supplemented with insect proteins (Tenebrion) and/or Vitamin D. The objective is to obtain a loss of weight/fat mass and a gain and/or maintenance of muscle mass as well as an improvement in the physical capacities of the animals. We will evaluate the locomotor performance of the mice and their body composition through longitudinal monitoring. As a final point, we will measure the rate of muscle protein synthesis and myokines/exerkines production.

Methodologies (key words) : treadmill running, rotarod, handgrip test, echoMRI, ELISA, Western Blot, Q-PCR

Publications of the research group on the proposed topic (3 max.)
-Vitamin D deficiency contributes to overtraining syndrome in excessive trained C57BL/6 mice. Talvas J et al. Scand J Med Sci Sports. 2023 Nov;33(11):2149-2165.
-Vitamin D status modulates mitochondrial oxidative capacities in skeletal muscle: role in sarcopenia. Salles J et al. Commun Biol. 2022 Nov 24;5(1):1288.
-Vitamin D supplementation associated with physical exercise promotes a tolerogenic immune environment without effect on mammary tumour growth in C57BL/6 mice. Aldekwer S et al J. Eur J Nutr. 2021 Aug;60(5):2521-2535.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : Energetic and metabolic adaptations to simulated weight loss during a graded walking exercise in adolescents with obesity.

Laboratory : Metabolic Adaptations to Exercise under Physiological and Pathological Conditions (AME2P, UPR3533)
Laboratory director : David Thivel
Address : 3 rue de la Chebarde, 63170 Aubière

Internship tutor : David Thivel
Tel : 0473407679
e-mail : david.thivel@uca.fr

Summary :
According to Jansson et al., the regulation of energy balance might be leptin-independent but rather under the control of a gravitostatic regulation at the upper extremity of the weight status spectrum (Jansson et al., 2023). Both preclinical and clinical studies obtained reduced body weight after few weeks of mechanical overload (simulating weight gain) through adaptations of food intake and energy metabolism (Ohlsson et al., 2020; Jansson et al., 2021), which we suggested to be particularly due to FFM adaptations (Thivel & Boirie, 2020). However, some preliminary results of our group observed specific post-WL energetic adaptations to such a simulated weight regain in adolescents with obesity. Indeed, after an effective multidisciplinary weight loss (MDWL), the energy metabolism during locomotion has been explored with and without a simulated weight regain and interestingly EE did not rise back to pre-weight loss values, as a potential way to preserve the regained weight (Thivel et al., 2023). More recent evidences also show that in weight-stable adolescents with obesity, a mechanical simulation of 5 and 10% of weight gain is not accompanied by an equivalent rise of their energy cost and metabolism during locomotion (Thivel et al., 2024). Altogether, these results tend to suggest the absence of energy metabolism adaptations to counteract weight gain and regain in this population. This internship will be intergraded in the DELOAD project (RIPH-2-BOIRIE-2025) that explores the impact of simulated weight loss on the energy cost and metabolism during locomotion in adolescents with obesity. By taking advantage of an anti-gravity technology, the adolescent ill indeed be asked to performed a graded walking exercise with a simulated body weight placing them ad overweight and then normal weight.

Methodologies (key words) : AlterG, DXA-scans, indirect calorimetry

Publications of the research group on the proposed topic (3 max.)

Thivel D, **Ennequin G**, Siroux J, Couret A, Beraud D, Pereira B, Duclos M, Lazzer S, Boirie Y, **Isacco L**. Acute simulated weight gain might not increase the energy cost of walking in adolescents with obesity. Pediatr Obes. 2024 Dec 30:e13197.

Thivel D, **Ennequin G**, Lambert C, Siroux J, **Ratel S**, Boscaro A, Pelissier L, Julian V, Cardenoux C, Duclos M, Lazzer S, Pereira B, Boirie Y, **Isacco L**. Improved walking energy efficiency might persist in presence of simulated full weight regain after multidisciplinary weight loss in adolescents with obesity: the POWELL study. Int J Obes (Lond). 2024 Mar;48(3):384-393

Thivel D, Boirie Y. The Gravitostat theory: Body fat is lost but is fat-free mass preserved? EClinicalMedicine. 2020 Oct 3;27:100531.

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr

UNIVERSITÉ Clermont Auvergne

MASTER BIOLOGIE SANTE

Track « Nutrition, Health, Mobility »

Proposal for a Master 2 internship – 2025-2026

Title : In vivo and in vitro characterization of cortical plasticity development in facial neuropathic pain.

Laboratory : Neuro-Dol, Université Clermont-Auvergne, INSERM UMR 1107
Laboratory director : Radhouane Dallel
Address : Faculté de chirurgie dentaire - 2, Rue de Braga 63100 CLERMONT-FERRAND

Internship tutor : Mickael Zbili
Tel : 04 73 17 73 17
e-mail : mickael.zbili@uca.fr

Summary :
Neuropathic pain is a major public health problem affecting 7–10% of the general population. It often arises from a primary lesion in the nervous system, such as a nerve or spinal cord injury, but are characterized by a persistence of the pain sensation after the lesion disappearance. While, repetitive transcranial cortical stimulations display an analgesic effect on neuropathic pain, the mechanism of neuropathic pain emergence is still poorly understood. It has been proposed that neuropathic pain originated from maladaptative neuronal plasticity in cortical sensory networks inducing hyperexcitability of somatosensory cortex. Following this hypothesis, the hyperexcitability of the primary somatosensory cortex (S1) causes a persistent pain sensation.
To explore this hypothesis, we used a rodent model of facial neuropathic pain: the infraorbital nerve ligature (IONL). We showed that IONL induced both a pain development in the vibrissae region an increase of neuronal excitability in the S1BF cortex (primary somatosensory cortex barrel field, the cortex corresponding to vibrissae region). However, to fully understand the link between facial pain and cortical hyperexcitability, we need to know the exact temporal relationship between these modifications. The purpose of this internship will be to combine in vivo calcium imaging (fiber photometry), behavioral measurements (Von Frey pain test) and immunohistochemistry of neuronal axon initial segment (AIS) to decipher the kinectics of pain and cortical hyperexcitability in neuropathic facial pain. This preliminary study will pave the way to the unraveling of new molecular targets for neuropathic pain treatment. In addition, the aim of this internship is to continue the study as part of a three-year PhD program.

Methodologies (key words): Fiber photometry, Calcium imaging, Von Frey pain test, immunohistochemistry

Publications of the research group on the proposed topic (3 max.)

1. Moisset X, Lefaucheur J.P (2018) Non pharmacological treatment for neuropathic pain : Invasive and non-invasive cortical stimulation. *Revue Neurologique*. doi: 10.1016/j.neurol.2018.09.014.

2. Zbili M, Rama S, Benitez MJ, Fronzaroli-Molinieres L, Bialowas A, Boumedine-Guignon N, Garrido JJ, Debanne D (2021) Homeostatic regulation of axonal Kv1.1 channels accounts for both synaptic and intrinsic modifications in CA3 circuit. *PNAS*. doi: 10.1073/pnas.2110601118.

3. Moisset X, Bouhassira D, Attal N (2021) French guidelines for neuropathic pain: An update and

Please send this sheet **jointly** to the following addresses :
corinne.malpuech-brugere@uca.fr **and** isabelle.vaillant@uca.fr