Call for PhD application

General information

Title of the offer: Thesis offer (F/M) - Human ImmunoMetabolism and healthy AGing: lifelong Exercise Signature (HIMAGES)
Place of work: Nice - Université Côte d'Azur
Release date: 06/09/2023
Name of scientific responsible: Pr. Serge Colson and Pr. Anne-Sophie Rousseau
Type of contract: CDD PhD student/doctoral contract
Contract duration: 36 months
Start date of the position: Mid - October 2023
Work shift: Full time

Project funded by the "Graduate School and Research Health Science Ecoystems" and the "Academy of Excellence 4: "Complexity and Diversity of Living Systems" - Université Côte d'Azur

Doctoral school of registration: Sciences du Mouvement Humain (ED463; https://ecole-doctorale-463.univ-amu.fr/fr)

Location: Nice – Université Côte d'Azur
Directors: Pr. Serge Colson (LAMHESS – UPR6312) and Pr. Anne-Sophie Rousseau (iBV CNRS UMR 7277, INSERM U1091)

Project description

Most people are exposed to multiple factors that increase oxidative stress and are deficient in skeletal muscle (SKM)-induced body movement that requires energy. The metabolic status is altered, and this may impact metabolic routes, inflammatory mediators, but also differentiation and function of immune cells. It is known that a compromised immune system has the potential to influence functional decline throughout the body. The reduction of intrinsic capacity with physical inactivity can lead to a state of susceptibility to factors (e.g. sedentarity, obesity, aging) increasing the risk of lifestyle-related diseases. Vitality capacity is considered the underlying physiological determinant of intrinsic capacity, a crucial concept in healthy aging. It characterizes an individual's intrinsic physiological capacities resulting from the interaction of metabolism, neuromuscular function, immune functions and stress response. This concept is vague but highlights the newly interest in the field of healthy aging and exercise for immunometabolism.

Alteration of molecular signaling pathways, metabolic reprogramming, increased lipid metabolism, peroxisomal activity, and oxidative stress contribute to the decline in function and survival of T lymphocytes (LT) with age. Regulatory CD4+ T cells (Tregs) represent the main regulatory component of the adaptive immune system that fine-tunes inflammatory responses, keeps them in check and prevents long-lasting autoimmunity. The maintenance and function of these cells including their regulatory functions in tissues (e.g. adipose tissue (AT), SKM) are compromised with physical inactivity and aging and may be involved in intrinsic capacity maintenance. Globally proinflammatory T cells use mainly glycolysis for their metabolism whereas anti-inflammatory Tregs cells mainly use fatty acid oxidation (FAO). Some metabolic modulators could increase FAO of both mice and human CD4+T cells and increase their polarization toward the anti-inflammatory Tregs. We have performed mice experiments to verify the relevance *in vivo* of these metabolic and phenotypic changes observed in *vitro* in a context of obesity, aging and exercise. Our published data link modification of T cells to body composition and aerobic exercise performance leading to novel hypotheses for reducing age-related changes in tissues by manipulating fatty acid metabolism of T cells. If increasing fatty acid used in CD4+ T cells

could be beneficial in an obesity treatment context, this may not be the case in older adults. We found in mice that by specifically deleting a fatty acid metabolism modulator in T cells prevent changes related to aging-induced increase susceptibility to chronic diseases: (1) Tregs sequestration in lymph nodes, (2) body composition and (3) loss of physical capacities.

Our results raised important questions for the field of exercise sciences by suggesting that the main target of exercise with the goal to improve health would be T cell metabolism. However, how to transpose those findings to humans? It is still not clear whether neuromuscular adaptations due to long-term regular aerobic physical activity are linked to immune cell functions and body functions or vice-versa. It is well known that aging is associated with a loss of motor neurons number as well as with an increased coactivation between muscles during locomotor tasks. However, motor neurons loss is preserved in highly trained older master athletes and investigating spinal motor neurons synergies with high-density surface electromyography techniques would participate to the identification of age-related decline biomarkers in neuromuscular control and locomotor function. In other word, how to characterize vitality capacity or the transition towards a healthier phenotype through an interdisciplinary approach? Determining the physiological phenotype of human vitality is a challenging prospect. Immunometabolism is closely linked to vitality, so is neuromuscular function.

Studies are critically required to better understand specific metabolic processes in immune cells as well as motor neurons synergies with age in both physiological and pathological conditions that alter whole-body metabolism and to achieve clinical translation. The innovative approach will be to include in a cross-sectional study "healthy" older adults to discriminate the effects associated with physical inactivity that exacerbate the aging process, multiple exposures, oxidative stress, inflammation and susceptibility to cardiovascular pathologies. We will characterize and compare the immunometabolic and neuromuscular profiles of lifelong physically active individuals to lifelong physically inactive individuals. Moreover, we will correlate these newly identified markers with indicators of metabolism, neuromuscular function, immunity, and stress response. What if immune cell metabolism determined neuromuscular function?

GENERAL HYPOTHESIS:

T cell metabolism determine vitality and age-related protection/susceptibility to chronic diseases that could be characterized by circulating, neuromuscular and functional biomarkers.

Context of work environment

Université Côte d'Azur is ideally located between the coast and the mountains in a region known for its quality of life. At the heart of Europe, with easy access to the Nice Côte d'Azur International Airport, it is an open door to the academic and scientific world.

Université Côte d'Azur is a public institution with a scientific, cultural and professional purpose under the Ministry of Higher Education, Research and Innovation. In 2016, it received the "Initiative of Excellence" award in recognition of its scientific and educational excellence | more information.

The university's different campuses are located mainly in Nice, Sophia Antipolis and Cannes but they extend as far as La Seyne-sur-Mer and Menton. The university employs more than 3,000 staff members who are spearheading efforts in RESEARCH, INNOVATION AND EDUCATION and inventing a model university for the 21st century.

During the doctoral contract, the student will conduct her/his work in the Laboratory of "Motricité Humaine, Expertise, Sport, Santé" UPR6312 (see, for more information: https://lamhess.univ-cotedazur.fr/) and in the "Institut de Biologie de Valrose" CNRS UMR 7277, INSERM U1091 (see, for more information: http://ibv.unice.fr/), both located in Nice, under the supervision of Pr. Serge Colson and Pr. Anne-Sophie Rousseau.

Desired qualifications:

Applicants should have a background in one or several of the following research fields: neuromuscular physiology, muscle physiology, integrated physiology, exercise physiology, molecular biology.
Data analysis and treatment skills, although not mandatory, will be valued.

Essential requirements for this PhD position are: excellent grades, the ability to learn, understand and apply new physiological concepts and experimental methodologies from different disciplines, a strong motivation as well as the willingness to work in a team.
Fluency in French is not mandatory. An intermediate level in English (or higher) is expected.

Further information

Applicants should contact Anne-Sophie.ROUSSEAU@univ-cotedazur.fr and/or serge.colson@univ-cotedazur.fr as soon as possible to prepare their application.
Please send your file to Anne-Sophie.ROUSSEAU@univ-cotedazur.fr and serge.colson@univ-cotedazur.fr in a **single PDF file** with the name of candidate including the documents below. The file can be either in French or in English.

- Detailed CV
- Letter specifying the motivations for this doctoral project (max. 1 page)
- A detailed research project related to the project description above (max. 5 pages)
- Transcripts of previous undergraduate and graduate education
- Contact details of one or two referents (optional)

Calendar

Opening date: 06/09/2023 12:00

Closing date: 27/09/2023 12:00 Noon CET

Estimated date of publication of results of the preselection: 28/09/2023

Auditions for selected applicants: 04/10/2023 – 14h-17h (French Time)