**Master 2 internship project**

**Year 2023-2024**

**Laboratory/Institute:** HP2 **Director:** Pr. Jean-Louis PEPIN

**Team:** **Head of the team:**

**Name and status of the scientist in charge of the project:** Pr. Gilles FAURY

**HDR: yes X no ☐**

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**Program of the Master’s degree in Biology:**

**☐** Microbiology, Infectious Diseases and Immunology **☐** Structural Biology of Pathogens

**X** Physiology, Epigenetics, Differentiation, Cancer **☐** Neurosciences and Neurobiology

**Title of the project:** Sleep apnea-induced intermittent hypoxia: impact on the function and structure of arteries and elastic fibres during ageing and in genetic disease, and pharmacotherapy.

Objectives (up to 3 lines):

**1)** uncovering the specific signaling and molecular mechanisms triggered by obstructive sleep apnea syndrome in mice, young, old or affected by genetic diseases altering arterial structure/function and elastic fibers (Williams or Marfan syndromes), **2)** repairing/replacing damaged arterial elastic fibers and improving arterial function.

Abstract (up to 10 lines):

Obstructive sleep apnea syndrome (OSAS), featuring temporary breathing interruptions during sleep, is an important public health problem (prevalence up to 20% in adults, more in the elderly). OSAS generates intermittent hypoxia (IH) which leads to cardiovascular conditions, such as hypertension, cardiac infarct and insufficiency, vascular remodeling and arterial stiffening, involving the hypoxia-induced factor (HIF) and endothelin pathways. Therefore, the investigation of the processes leading to arterial stiffening and subsequent dysfunctions is of major importance in the understanding of OSAS-induced pathologies. Arterial stiffening, i.e. elasticity reduction, is due to the disruption of the wall elastic fibers which crucially contribute to normal hemodynamics. IH-induced alterations of arterial function and elastic fibers and their major components, elastin and microfibrils/fibrillin-1, therefore needs deep investigations. Pharmacological treatments (minoxidil, dill extract, synthetic elastic protein) already proven as correcting arterial structure/function in other pathologies will be assessed for their efficiencies in IH-exposed mice.

Methods (up to 3 lines):

A murine model of intermittent hypoxia (IH) will be used: special cages impose to the mice alternating periods of normoxia/hypoxia for 8h/day, mimicking IH present in OSAS. The consequences (hypertension, arterial thickening and mechanics, elastic fiber production and disruptions, gene dys-expression) will be studied.

Up to 3 relevant publications of the team:

- Coquand-Gandit M, Jacob MP, Fhayli W, Romero B, Georgieva M, Bouillot S, Estève E, Andrieu JP, Brasseur S, Bouyon S, Garcia-Honduvilla N, Huber P, Bujan J, Atanasova M, Faury G. Chronic treatment with minoxidil induces elastic fiber neosynthesis and functional improvement in the aorta of aged mice. Rejuvenation Res. 2017;20:218-230.

- Fhayli W, Boëté Q, Kihal N, Cenizo V, Sommer P, Boyle WA, Jacob MP, Faury G. Dill Extract Induces Elastic Fiber Neosynthesis and Functional Improvement in the Ascending Aorta of Aged Mice with Reversal of Age-Dependent Cardiac Hypertrophy and Involvement of Lysyl Oxidase-Like-1. Biomolecules. 2020 ; 10(2):173. doi: 10.3390/biom10020173.

- Boëté Q, LoM, LiuKL, VialG, LemariéE, RougelotM, Steuckardt I, Harki O, Couturier A, Gaucher J, Bouyon S, Demory A, Boutin-Paradis A, El Kholti N, Berthier A, Pépin JL, Briançon-Marjollet A, Lambert E, Debret R and Faury G. Physiological impact of a synthetic elastic protein in arterial diseases related to alterations of elastic fibers: effect on the aorta of elastin-haploinsufficient male and female mice. Int J Mol Sci. 2022 ; 23:13464. https://doi.org/10.3390/ijms232113464.

Requested domains of expertise (up to 5 keywords):

- physiology, experimentation in animals, arterial elasticity / elastic fibers, ageing / genetic diseases, pharmacotherapy.