



Proposal for a 2nd year Master internship (2020-2021)

Supervisors: Guillaume Walther (assistant prof., principal investigator); Sylvain Battault (postdoctoral research fellow)

e-mail: guillaume.walther@univ-avignon.fr

Phone number: 04 90 16 29 45

Laboratory location:

Laboratoire de Pharm-Ecologie Cardiovasculaire, Avignon Université. 74 Rue Louis Pasteur
84000 AVIGNON

Project title:

Effects of intense artificial sweetener consumption on cardiovascular function and glucose metabolism in diet-induced obese mice.

Internship proposal :

Recent observational studies (1) report an increase in cardiovascular morbidity and mortality in regular consumers of diet soda drinks with an increased risk in people with obesity (3). Our laboratory is currently leading an experimental project that seeks to establish the existence or absence of a causal link between these two events. In our team, a first study in healthy rats, showed an accumulation of visceral adipose tissue accompanied by impaired endothelial function after 10 weeks of consumption of a cocktail of sweeteners (4). However, the mechanisms explaining the specific increase in cardiovascular risk and the specific impact of each sweetener molecule remain to be elucidated. In this regard, we will first study the effect of intense artificial sweeteners (Sucralose, Acesulfam K and Saccharin). In a future study, we will address the question whether natural sweeteners (Stevia, Stevioside, Rebaudioside A) and artificial sweeteners induce different biological responses.

To answer these questions, our laboratory has developed a large number of laboratory techniques ranging from *in vivo* physiology to molecular biology and cell culture.

Main methods considered:

- Animal monitoring (body mass, preparation of food and drink rations, food consumption record).

- In vivo glucose tolerance (OGTT) and insulin (ITT) tests. Blood sampling throughout the protocol.
- Measurement of in vivo arterial blood pressure.
- Evaluation of morphology and cardiovascular function, both in vivo (ultrasound echocardiography) and ex vivo (isolated organ stations).
- Post-mortem tissue sampling.
- Test of angiogenic capacities of budding (Sprouting assay) on aorta rings in matrigel.
- Isolation and cultivation of vascular smooth muscle cells.

References:

1. Malik VS, Li Y, Pan A, De Koning L, Schernhammer E, Willett WC, et al. Long-Term Consumption of Sugar-Sweetened and Artificially Sweetened Beverages and Risk of Mortality in US Adults. *Circulation* [Internet]. 2019 Mar 18 [cited 2019 Mar 21]; Available from: <https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.118.037401>
2. Yin K-J, Xie D-Y, Zhao L, Fan G, Ren J-N, Zhang L-L, et al. Effects of different sweeteners on behavior and neurotransmitters release in mice. *J Food Sci Technol*. 2020 Jan 1;57(1):113–21.
3. Mullee A, Romaguera D, Pearson-Stuttard J, Viallon V, Stepien M, Freisling H, et al. Association Between Soft Drink Consumption and Mortality in 10 European Countries. *JAMA Intern Med* [Internet]. 2019 Sep 3 [cited 2019 Oct 31]; Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2749350>
4. Risdon S, Meyer G, Marziou A, Riva C, Roustit M, Walther G. Artificial Sweeteners Impair Endothelial Vascular Reactivity: Preliminary Results In Rodents. *Nutrition, Metabolism and Cardiovascular Diseases* [Internet]. 2020 Feb 12 [cited 2020 Feb 14]; Available from: <http://www.sciencedirect.com/science/article/pii/S0939475320300478>

Additional information of interest:

This project, called SOSweet, is funded by ANR (National Agency of Research) and FFRD (French Federation for Diabetes Research).