Master 1 or Master 2 position for an internship in medicinal chemistry

Developing (semi-)synthetic strategies
towards multi-target anti-inflammatory agents starting from natural scaffolds

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Location: SONAS (Campus du Végétal) 42 rue Georges MOREL, 49070 BEAUCOUZE (France)

Details: 4 to 6 months position (from January 2026 / ca 550€ paid monthly)

Project objectives and research plan:

While acute inflammation is a short-term adaptive response to harmful stimuli, chronic inflammation is prolonged, dysregulated and deleterious, and is implicated in the pathogenesis of many diseases including asthma, arthritis, inflammatory bowel disease and cancer, as well as in neurodegenerative and cardiovascular diseases. Multiple pro-inflammatory, immunomodulatory and pro-resolving signaling cascades orchestrate inflammation. Targeting cyclooxygenases by non-steroidal anti-inflammatory drugs (NSAIDs) is one strategy to relieve inflammation, though long-term use of NSAIDs is afflicted with severe side effects. Hence, the social and economic burden of inflammation-associated pathologies emphasizes the high need for new efficient and safe anti-inflammatory drugs. Single-target inhibitors block key nodes within the complex lipid mediator networks but fail in adjusting homeostasis. To circumvent the resulting side effects, drug candidates should selectively interfere with pro-inflammatory lipid mediator biosynthesis through multiple targets without suppressing the resolution of inflammation. Our consortium found that human endogenous vitamin E metabolites (LCMs) - and a broad spectrum of semisynthetic analogues – limit inflammation by targeting 5-LO while increasing the systemic levels of the pro-resolving lipid mediator resolvin E3.[1] LCMs are orally available, relieve inflammation in animal models of peritonitis and asthma, and promote wound healing.[2]

While limiting the onset of inflammation has been the main goal of many anti-inflammatory drug development projects, many recent studies have highlighted the importance of promoting the resolution to restore homeostasis more efficiently. Various enzymatic targets involved in the synthesis of lipid specialized pro-resolving mediators (SPM) stemming from polyunsaturated fatty acids, such as arachidonic acid, have been described as validated therapeutic targets.

The current project aims at developing, through semi- or total synthesis,[3] multi-target ligands that would both limit the production of pro-inflammatory lipid mediators and enhance the synthesis of SPM.

1- H. Pein, et al. "Endogenous metabolites of vitamin E limit inflammation by targeting 5-lipoxygenase". Nature Communications, 2018, 9, 3834.
2- K. Neukirch, et al. "Exploration of long-chain vitamin E metabolites for the discovery of a highly potent, orally effective, and metabolically stable 5-LOX inhibitor that limits inflammation." J. Med. Chem., 2021, 64, 11496-11526.
3- A. Ville, et al. "Efficient semi-synthesis of natural delta-(R)-tocotrienols from a renewable vegetal source". J. Nat. Prod., 2019, 82, 51-58.

Steps of the project (enzymatic assays will be run by our partners in Jena and Graz)

- Extraction and purification of plant specialized metabolites
- Semi-synthesis or total synthesis, purification and structural characterization of analogues
- *in vitro* evaluation of the inhibitory activity of the corresponding ligands
- Development of problem-solving skills
- Oral and written dissemination of the results
- Communication about the project during lab seminars

Alignment of the current project with SDGs:
No Poverty (SDG #1): Through the production of innovative and cost-effective treatments for chronic inflammatory diseases, this medicinal chemistry project should give the opportunity to disrupt the cycle linking illness and socioeconomic disadvantage—ultimately helping to reduce poverty.
Good Health and Well-being (SDG #3): This SDG centers on advancing drug discovery and development to fight disease and improve human health, aligning closely with the fundamental mission of a medicinal chemistry project.
Quality Education (SDG #4): Such a hands-on project in medicinal chemistry can foster global education and skill development in the field of drug discovery.
Gender Equality (SDG #5): Gender dimensions and inequalities have been highlighted for many inflammatory troubles (endometriosis, inflammatory bowel disease). The final aim of this medicinal chemistry project can definitely address these issues and participate to gender equality.

Profile of the candidate: Master 1 or Master 2 student with a background in organic/medicinal chemistry. B1 English level is mandatory.

SONAS Laboratory: SONAS is located in a recently built institute (July 2015), offering large space for both laboratories and offices. SONAS has all the contemporary and state-of-the-art equipment necessary to run extraction of natural ressources (ultrasound assisted extractor) and efficient organic synthesis, with, among them, a Anton Paar microwave reactor. The technical platform, run by SONAS, dedicated to purification and structural analysis, equipped with a 400 MHz JEOL spectrometer, will be freely accessible. This guarantees fast analytical feedbacks to monitor the efficacy of organic synthesis reactions and purification of the corresponding crude mixtures.