

## Development of vitamin E analogues as anti-inflammatory agents through semisynthesis or total synthesis

Project supervisor: Dr Jean-Jacques HELESBEUX (jj.helesbeux@univ-angers.fr)

Location: SONAS (Campus du V g tal) 42 rue Georges MOREL, 49070 BEAUCOUZE

Details: 6 months position (January to June 2022 / ca 550  paid monthly)

### Project objectives and research plan:

We recently identified an endogenous metabolite of vitamin E, which is produced in humans as hormone-like signaling molecule, limits inflammation by targeting 5-lipoxygenase. Remarkably, the vitamin E metabolite accumulates in immune cells at sites of inflammation. The translation of the endogenous vitamin E metabolite into a drug-like molecule was hampered by the questionable oral availability and poor metabolic stability against side-chain truncation. Thus, we aimed at developing a new series of analogues that would answer these issues.

SONAS has a long term expertise in natural products chemistry starting with sourcing of strategic plant materials. Over the years, our laboratory managed to gather plants from different places in the world and possessing a high content in T3 analogues. Besides that preliminary step, researchers at SONAS develop methods to extract and purify secondary metabolites. SONAS has also set up different methodologies to selectively modify every part of vitamin E analogues backbones, opening doors to the semisynthesis of numerous structurally diverse libraries.

The project closely involves other **European partners** from **Austria** (expertise in molecular modeling, biological assays) and **Germany** (biological assays).

Our laboratory is equipped with all facilities related to the extraction, purification, analysis, characterization and (semi-)synthesis of natural products such as: accelerated solvent extraction (ASE) system, ultrasonic extractor, flash chromatography, analytical, semi-prep and prep HPLC (DEDL, UV-DAD, fluorescence), UPLC-MS, GC-MS, 400MHz NMR spectrometer and microwave reactor.

### Steps of the project (to be shared with other team members)

- Extraction and purification of  $\delta$ -garcinoic acid
- Semi-synthesis, purification of  $\alpha$ -CEHC
- Synthesis of oxidized vitamin E analogues
- Development of a total synthesis strategy towards racemic  $\delta$ -CEHC.
- Resolution, separation, purification of (*R*)- $\delta$ -CEHC

### Skills and experience

- Strong background in organic chemistry.
- Previous experience in the field of medicinal chemistry
- Ability to work in a multidisciplinary team. Scientific rigour and creativity
- French is a plus, **English is compulsory** (level B2)

### Recent publications by our consortium:

Pein, H., *et al. Nat Commun*, 9, 3834 (2018).

Dinh, C. P., *et al. Eur J Med Chem*, 202, 112518 (2020).

Neukirch, K., *et al. J Med Chem*, 64, 11496-11526 (2021).