**Title of the PhD project**

Targeting the brain with AceDoPC® and protective metabolites: an innovative therapeutic strategy for neurological diseases

**Disciplines:** Biochemistry

**Laboratory:** CarMeN laboratory (Cardio-Metabolism, Diabetes and Nutrition) - Director: Hubert Vidal - Team: Lipo

**Doctoral school:** Interdisciplinary Doctoral program in health-sciences (EDISS) - ED 205

**Description**

Neurological diseases constitute a challenge for both the health system and research policy in France and abroad. Because of the limitations of current therapies and considering the significant medical, personal, social and economic costs of these pathologies, the need for novel therapeutic and new strategies are becoming urgent. We propose a new therapeutic approach by specifically targeting the brain with new neuroprotective lipid vectors. Docosahexaenoic acid (DHA) is the main omega-3 fatty acid accumulating in the brain and is essential for cerebral functions. While DHA deficiency in the brain has been shown to be linked to the emergence of cerebral diseases, studies showed that a dietary intake of DHA could prevent or attenuate neurologic disturbances linked with ageing or neurodegenerative diseases. In this context, targeting the brain with DHA or its protective metabolites might offer great promise in developing new therapeutics for neurodegenerative diseases. We have synthesized a specific vector of DHA transportation to the brain patented and named AceDoPC®. AceDoPC® has already been characterized by its neuroprotective action in stroke induced in rats or in an *in vitro* model of cell cultures mimicking ischemic conditions. One therapeutic approach to cerebral diseases is to promote neurogenesis to counteract neuronal loss (i.e. in stroke or Alzheimer’s disease among others). We showed that AceDoPC® also increases neurogenesis in an *in vitro* model of cerebral ischemia. Preliminary studies of the potential mechanisms involved in neuroprotection pointed out that AceDoPC® neuroprotective and regenerative effects might be due in part to its anti-oxidative and anti-inflammatory effects. In addition, AceDoPC® may be a direct precursor of acetylcholine, being considered as the missing neurotransmitter in AD, in providing both the acetyl and choline residues (patent deposit N° 1751880).

The major objective of the PhD project is to better understand the therapeutic potentials of AceDoPC® and metabolites in *in vitro* models and pre-clinical models of neurological diseases in animals.

**Description of the project methodology:** We will identify the mechanisms involved and the targets affected by the neuroprotective effects observed with AceDoPC® and metabolites using different models reflecting the pathophysiological situations of interest: Study of the effects on: neurogenesis, oxidative stress and metabolic inflammation, histone acetylation (epigenetic effects), cell biology status (morphology, differentiation...). The ability of AceDoPC® and metabolites to prevent or correct behavior disorders (learning, memory …) will also be analyzed.

**Collaborations:**
- LipTher® (Lipids for Therapeutics): a start-up that produce AceDoPC® at a large scale.
- We also recently started a collaborative study with URAFPA laboratory (Nancy, Dr. C. Malaplate-Armand and Pr. T. Oster), expert in neurobiochemistry (model of Alzheimer’s disease) and nutrition.
- Creatis (Pr. N. Nighoghossian, Pr. Y. Berthezène): collaboration with the stroke group. The objectives of this team are to study the pathophysiology of cerebral ischemia and to evaluate new neuroprotective strategies. Expertise in this field is also present in CarMeN laboratory (Dr Marlène Wiart and Pr. E. Canet-Soulas).

**Expected results:** Our preliminary data and the experiments envisioned assure us to obtain answers on the mechanisms of action and targets of AceDoPC® and metabolites.

**Perspectives:** This project has a high potential for socio-economic development and for clinical development. The industrial sector concerned is the food industry, lipid engineering and pharmaceutical industry (therapeutics).

**Skills required:**

Techniques to be used during the PhD project: Cell cultures, lipid analyses (use of the IBiSA Functional Lipidomics platform), western and dot blots, immunohistochemistry.

**Bibliography:**


**Key-words:** Innovation in Health - Neuroprotection - Therapeutics - Lipids –Bioengineering – Biochemistry

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Application should include: CV, application letter, Names and addresses of two references.

The application file should be sent before May 14, 2017 to: (email of the supervisor).

The open competitive recruitment process is in two steps: 1. Internal laboratory procedure. 2. Interdisciplinary jury of EDISS.