



CBH Graduate School  
Université Grenoble Alpes



### PhD Thesis Offer

#### Anticancer Agents through Development of antibody-Drug conjugates targeting ferroptosis

**Funding:** CBH-Graduate School

**Hosting Laboratories:** LRB, UMR Inserm U1039 (Faculté de Médecine)/IAB, UMR CNRS 5309

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**Start Date for thesis:** September 2024

**Key Words:** Cancer ; Anticancer agents; Ferroptosis; Ferroptosis inducers; Antibodies; ADC, Synthesis; Biological Evaluation

*The thesis will be carried out between two laboratories: the LRB Bioclinical Radiopharmaceuticals laboratory (UMR U1039) located at the Grenoble Faculty of Medicine, and the Institute for Advanced Biosciences IAB (UMR 5309). The two laboratories are 500 m apart. The first develops part of its research on the medicinal chemistry of anticancer drugs. The second has strong expertise in the biology of cancer and anticancer drugs.*

#### Project Context:

Non-apoptotic, iron-dependent cell death, known as ferroptosis, is a very recent and emerging strategy for anticancer drug design and development. In this context, ferroptosis inducers present growing interest as anticancer drugs. Furthermore, antibody-drug conjugates (ADCs) which are products combining cytotoxic agents (small molecules) and antibodies for their targeting property are relevant for developing anticancer agents in order to specifically kill cancer cells. . Very recently (2022) we reported for the first time in the literature, the design and synthesis of the first ADC combining a ferroptosis inducer and a monoclonal antibody, trastuzumab. The first biological evaluation tests resulted in particularly promising results.

The ADC project submitted to the EUR is part of this strategy and consists of developing new conjugates combining new ferroptosis-inducing molecules with monoclonal antibodies. Led by a chemist active in the field of medicinal chemistry of anticancer drugs and a biologist specializing in the biology of cancer, the ADC project presents great therapeutic prospects in oncology. It will bring to the fore a new topical theme around ferroptosis. Ultimately, the achievements of the ADC project will open interesting perspectives towards a related theme, "cuproptosis", a new copper-dependent cell death.

#### Objectives of the project:

The ultimate objective is to develop an ADC drug candidate combining a ferroptosis inducer and an antibody as an anticancer agent in the context of targeted chemotherapy.

#### Candidate Profil:

The desired training for candidates is a master 2 in the field of medicinal chemistry with an interest in bioactive molecules. Experience in the field of multistep organic synthesis is strongly desired. A B1 level in language English is strongly desired.

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