



CBH Graduate School
Université Grenoble Alpes

Pathophysiology of Exertional Heat Stroke

PhD Program

Exertional Heat stroke (EHS) manifests a specific form of hyperthermia crisis in young and otherwise healthy individuals during strenuous physical activities, and is defined by an abnormal elevation of body temperature involving a hypermetabolic state of skeletal muscle. It is lethal if untreated due to a risk of multi-organ failure, and ranks third among the cause of athlete's death. EHS share numerous symptoms with Malignant Hyperthermia (MH), a pharmacogenetic disease triggered by exposure to halogenated anesthetics, and due to mutations in genes regulating calcium homeostasis during skeletal muscle contraction. However, EHS is so far not genetically characterized, and its pathophysiology still unclear. Thanks to genetic investigations on a cohort of soldiers having experienced EHS, the molecular genetic unit of Grenoble Hospital and the Cellular Myology and Pathology team (GIN) have discovered mutations in two genes encoding calcium channels that could be responsible for EHS susceptibility. **Knock-in mice models were produced for these mutations and the goal of the project is to decipher the consequences at the molecular and metabolic level of these mutations. The PhD program will be conducted with molecular studies on primary muscle cells cultures in the GIN and metabolic investigations on whole animal and muscles in the LBFA laboratory.** The project aims at a better understanding of EHS physiopathology, leading to a rational to design potential therapeutic targets. It is based on the first genetic mice models of EHS, and the complementary expertise of the two laboratories.

Candidate profile

Candidate should hold a Master Degree in Biology (ideally in Physiology, Molecular or Cell Biology) and have a strong interest in muscle physiology using animal models. Good communication skills are required, as well as adaptability, to work in two different laboratories.

Language : French level B1 and/or English level B2 .