RESEARCH TRAINING PROGRAM

I. General Information

Title of the research project:
Identification of potential biomarkers for the progression from episodic to chronic migraine: evaluation in human and animal models of migraine

Name and address of the department:
Laboratorio di Neurofisiologia dei Sistemi Autonomici Integrativi, IRCCS Fondazione Mondino, Pavia

Student's supervisor:
Dr. Rosaria Greco

II. Description of the project

(max 1500 characters, spaces included)
Background
Migraine is a neurological disorder of great clinical importance and its pathophysiology is only partly known. The available treatments are associated with a poor to moderate effectiveness and limited tolerability, thus there is a real need for new specific treatments. Clinical studies suggest that biological origin of migraine is multifactorial, including abnormal nociceptive processing, altered neuronal activity and changes in cerebrovascular and immune functions. Accessible animal models do not fully replicate the multiple components of the disease, however, with the model based on nitroglycerin (NTG) administration or induction of dural inflammation, it is possible to evaluate multiple components related to the migraine attack and to identify new potential therapeutic targets.

What is the aim of the project?
The aim of the project is to investigate the impact of cannabidiol and endocannabinoids in preclinical rodent models of migraine (NTG model, dural inflammation model) and trigeminal hyperalgesia stratified by site of action (peripheral vs central); to evaluate the potential targets of CGRP antagonism in the abovementioned animal models and in migraneurs' samples (peripheral blood).

What techniques and methods are used?
To achieve the proposed aims, the following methods will be used: animal models specific for migraine pain and trigeminal hyperalgesia; behavioral tests; rt-PCR, western blotting, ELISA, immunohistochemistry, Flow Cytometry.

When did the department start working on this project? (year)
2020

Type of research project:

x Basic science ☐ Clinical research without lab work ☐ Clinical research with lab work

III. Student's involvement

The student will mainly observe	☐ YES	☐ NO
The student will observe the experiments but will be involved in data analysis	x YES	☐ NO
The student will take active part in experiments ("lab work")	x YES	☐ NO
The student will take active part in clinical examination (clinical research)	☐ YES	☐ NO
The student will be allowed to work with patients	☐ YES	☐ NO

What are the tasks expected to be accomplished by the student?
(max 500 characters, spaces included)
The student will learn basic laboratory techniques: Immunohistochemistry, DNA and RNA extraction from rat's peripheral blood and tissues, in real time PCR. In addition, he/she will also perform evaluation of nociceptive behavior in animal models.

What is expected from/what will be the general outcome of the student?
☐ To prepare a poster / presentation / scientific report / abstract
☐ The student's name will be mentioned in a future publication
☐ Opportunity to present together with the supervisor the results on a conference
x No specific outcome is expected

IV. Requirements

What skills are required from the student?
(max 500 characters, spaces included)
Pharmacology (required), Neurology (preferred)

Is there any special knowledge or a certain level of studies needed?
☐ Subjects passed:
_____

☐ Previous experience with:
_____

x Certificate of:
_____Safety certificate in biological laboratories
☐ None

Are there any legal limitatons in the student's involvement in the project? x YES ☐ NO
If yes, what are the limitations?
If the student wants to participate to the evaluation of nociceptive tests in animal models, he/she should be inserted in the experimental protocol to be allowed to enter in the animal house.

For the use of students considering participating in the project, further information can be found from the following references:
(please add specific references, max 3)

Greco R, Demartini C, Zanaboni AM, Tassorelli C. Chronic and intermittent administration of systemic nitroglycerin in the rat induces an increase in the gene expression of CGRP in central areas: potential contribution to pain processing. J Headache Pain. 2018 Jul 13;19(1):51. doi: 10.1186/s10194-018-0879-6. PubMed PMID: 30003352; PubMed Central PMCID:PMC6043463.

Greco R, Demartini C, Zanaboni AM, Piomelli D, Tassorelli C. Endocannabinoid System and Migraine Pain: An Update. Front Neurosci. 2018 Mar 19;12:172. doi:10.3389/fnins.2018.00172. eCollection 2018. Review. PubMed PMID: 29615860; PubMed Central PMCID: PMC5867306.

Demartini C, Greco R, Zanaboni AM, Sances G, De Icco R, Borsook D, Tassorelli C. Nitroglycerin as a comparative experimental model of migraine pain: From animal to human and back. Prog Neurobiol. 2019 Jun;177:15-32. doi:10.1016/j.pneurobio.2019.02.002. Epub 2019 Feb 13. Review. PubMed PMID: 30771365.

V. Schedule

Duration of the project:
☐x 1 month ☐x 2 months ☐x 3 months

There are approximately _5_____ hours of work per day.

Available months:
☐x January X☐ February X☐ March ☐x April X☐ May ☐x June
x☐ July ☐ August X☐ September ☐x October ☐x November ☐x December

How many students can you accept to the project at the same time? ____1_____

Special remarks:
(e.g., students should bring a white coat, any vaccinations required, etc.)

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NOTE: a scientific report is required at the end of the program