RESEARCH TRAINING PROGRAM

I. General Information

Title of the research project:
Clinical efficacy of cariprazine and its relationship with polymorphisms of dopamine and serotonin receptors: a prospective study on schizophrenia.

Name and address of the department:
Centro di Ricerca in Farmacologia Medica, Polo di Ricerca Biomedica Monte Generoso, Via Monte Generoso n. 71, Varese

Student's supervisor:
Marco Ferrari

II. Description of the project

(max 1500 characters, spaces included)

Background
Schizophrenia is the most severe among the psychotic disorders, being a complex entity characterized by positive, negative and cognitive symptomatic dimension. Cariprazine (CAR) is a piprazine derivative approved by the FDA in 2015 for the treatment of schizophrenia. High affinity for D3 dopamine receptors and observed actions on 5HT1A, 5HT2A and alpha 1B receptors differentiate it pharmacologically from other antipsychotics.
Several genetic variants, in particular single nucleotide polymorphisms (SNPs, i.e. DNA sequence variations occurring when a single nucleotide in the genome differs between paired chromosomes), have been described in DR genes (DR) and 5HT genes (5HT). Actually the correlations between SNPs presence and biological activity in these genes is extensive studied but, little is known about the extent of impacting SNPs in dopamine and serotonin receptors genes on CAR clinical efficacy in schizophrenia treatment.

What is the aim of the project?
In this study we will investigate the relationship between efficacy and safety of CAR and SNPs in dopamine and serotonin receptor genes in a schizophrenic patients. Defining such relationships would represent the possibility to bring to the clinical practice genetic biomarkers useful in identifying target groups of patient.

What techniques and methods are used?
DNA extractions and genotyping by Real Time PCR using TaqMan probe-technique.

When did the department start working on this project? (year)
2019

Type of research project:
☐ 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	☐ YES ☑ NO
The student will take active part in experiments ("lab work")	☑ 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 for DNA extractions and SNPs identifications by Real Time genotyping technique. S/he will help in preparing and performing experiments, in data analysis and interpretation, and will collaborate in collecting and recording patients' clinical data.

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
☐ No specific outcome is expected

IV. Requirements
What skills are required from the student?
(max 500 characters, spaces included)
Ability to work in team, collaboration and communication skills, knowledge of Scientific English.

Is there any special knowledge or a certain level of studies needed?
☑ Subjects passed:
Pharmacology (required), Genetic (required).
_____

☐ Previous experience with:
_____

☐ Certificate of:
_____

☐ None

Are there any legal limitatons in the student's involvement in the project?   ☐ YES ☑ NO
If yes, what are the limitations?
_____

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)

Comi C, Ferrari M, Marino F, Magistrelli L, Cantello R, Riboldazzi G, Bianchi ML, Bono G, Cosentino M. **Polymorphisms of Dopamine Receptor Genes and Risk of L-Dopa-Induced Dyskinesia in Parkinson's Disease**. Int J Mol Sci. 2017 Jan 24;18(2). pii: E242. doi: 10.3390/ijms18020242. PubMed PMID: 28125015; PubMedCentral PMCID: PMC5343779.

Ferrari M, Bolla E, Bortolaso P, Callegari C, Poloni N, Lecchini S, Vender S, Marino F, Cosentino M. **Association between CYP1A2 polymorphisms and clozapine-induced adverse reactions in patients with schizophrenia**. Psychiatry Res. 2012 Dec 30;200(2-3):1014-7. doi: 10.1016/j.psychres.2012.07.002. Epub 2012 Aug 16. PubMed PMID: 22901441.

Bolla E, Bortolaso P, Ferrari M, Poloni N, Callegari C, Marino F, Lecchini S, Vender S, Cosentino M. **Are CYP1A2*1F and *1C associated with clozapine tolerability?: a preliminary investigation**. Psychiatry Res. 2011 Oct 30;189(3):483. doi: 10.1016/j.psychres.2011.03.011. Epub 2011 Apr 8. PubMed PMID: 21481946.

V. Schedule

Duration of the project:
☑ 1 month   ☑ 2 months   ☑ 3 months

There are approximately __5__ hours of work per day.

Available months:
☑ January	☑ February	☑ March	☑ April	☑ May	☑ June
☑ July	☑ August	☑ September	☑ October	☑ November	☑ December

How many students can you accept to the project at the same time? __1__

Special remarks:
Students should bring a white coat. Vaccination against tetanus and HCV are strongly recommended.

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