## Sujet N° (à remplir par l’ED) :
Identification of Novel Gene(s) in Arrhythmogenic right ventricular Dysplasia/Cardiomyopathy (ARVD/C) by Whole Exome Sequencing (WES) in Iranian population

## Titre de la thèse :
Identification of Novel Gene(s) in Arrhythmogenic right ventricular Dysplasia/Cardiomyopathy (ARVD/C) by Whole Exome Sequencing (WES) in Iranian population

## 3 mots-clés :
- Genetics
- Arrhythmias
- Exome sequencing

## Unité/equipe encadrante : EQUIPE I: Génétique Cardiovasculaire

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## Contexte socioéconomique et scientifique (env. 10 lignes) :
Arrhythmogenic right ventricular dysplasia or cardiomyopathy (ARVD/C) is an inherited heart disease, which usually occurs in adulthood and is characterized by replacement of the right ventricular myocardium by fibro-fatty tissue. ARVD/C patients are at increased the risk of cardiac arrhythmias, syncope and sudden cardiac death. ARVD/C is usually an autosomal dominant disease, pathogenic mutations are usually found in about 13 genes: the most common are Plakophilin 2 (PKP2) (found in 10 to 45% of patients), followed by Desmoplakin (DSP) (10 to 15%), Desmoglein 2 (DSG2) (7 to 10%), Desmocollin 2 (DSC2) (2%), Plakoglobin (JUP) (0.5-2%) and TMEM43 (rare). Though rare, ARVD/C causal mutations have also been reported in dilated cardiomyopathy (DCM) causal gene. Mutation in these genes altogether comprise 50% of ARVD/C cases, leaving 50% of all the ARVD/C patients still without a genetic cause.

## Hypothèses et questions posées (env. 8 lignes) :
We have identified 45 probands with ARVD/C with multiple patients in each family (total 45 families). Probands are negative for a PKP2 mutation. Patients in this study are of various ethnicities originating from different parts of Iran. Clinical part of the study is being conducted at Rajaei Cardiovascular, Medical & Research Center, Tehran. Taking advantage of these new, phenotypically well-characterized ARVD patients tested negative for major ARVD genes we aim to identify NEW ARVD disease-causing genes.

## Grandes étapes de la thèse (env. 12 lignes) :
Assuming autosomal dominant or recessive transmission of the disease we aim to perform Whole Exome Sequencing taking advantage of Schott’s laboratory expertise in gene identification. Whole Exome sequencing will be followed by pathologic variant identification, familial segregation, and clinical characterization in their carriers. In conclusion, this study aims to identify new genes/mutations in ARVD/C patients by Whole Exome Sequencing.

## Compétences scientifiques et techniques requises par le candidat (2 lignes) :
- Training / academic background in Human Genetic, Medical Genetic, Genetic Disorder semiology & Genetic Counseling.
- independent thinking, maturity and confidence

## 3 publications de l’équipe d’accueil relatives au domaine (5 dernières années) :


Collaborations nationales et internationales:

1- Prof. Connie Bezzina; University of Amsterdam’s Faculty of Medicine, Amsterdam, The Netherlands

2- Professeur Michel Haissaguerre; Director of Liryc Head of the Cardiology – Electrophysiology and Cardiac Pacing

   Department University Professor

3- Prof. Makita Naomasa; National Cerebral and Cardiovascular Center Osaka, Japan