AIX-MARSEILLE UNIVERSITE
ECOLE DOCTORALE DES SCIENCES DE LA VIE ET DE LA SANTE – ED62

PROPOSITION SUJET DE THESE

Concours d'attribution des Contrats Doctoraux 2019 – 2022
A renvoyer impérativement **avant le 2 mars 2019** par courriel au format **PDF** à edsvs-direction@univ-amu.fr

1. Choix du sous-jury (vous ne pouvez cocher qu'une seule case) :

☐ JURY 1 – Biologie Cellulaire (Développement – Immunologie – Biologie Végétale – Physiologie).

☐ JURY 2 – Microbiologie – Génomique (Bioinformatique – Biochimie Structurale – Biochimie).

☐ JURY 3 – Neurosciences (Neurobiologie cellulaire – Neurosciences Cognitives et Comportementales – Neuroimagerie – Neurosciences Computationnelles).

☒ JURY 4 – Biologie Santé (Oncologie – Cardiovasculaire – Santé Publique – Maladies Infectieuses – Génétique).

Laboratoire	
Nom et N°:	Marseille Medical Genetics Center
Adresse :	27 Bd Jean Moulin - 13385 Cedex 05 Marseille
Directeur :	Pr Nicolas Levy
Website :	https://www.marseille-medical-genetics.org/
Nom de l'équipe	
Responsable équipe :	Dr Stéphane Zaffran, DR INSERM
Nombre d'HDR dans l'équipe	4
Directeur de Thèse	
Nom :	Dr Zaffran
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HDR obtenue le :	05 mars 2005
Nom(s) du(es) doctorant(s) en cours d'encadrement :	Aucun
Nom et date de soutenance du précédent doctorant encadré :	Théron Alexis, 08-09-2017
Publication du Doctorant :	1: Rambeau P, et al. Int J Cardiol. 2017;249:340-343. PMID: 28986054. 2: Théron A, et al. Arch Cardiovasc Dis. 2016;109(3):188-98. PMID: 26711547. 3: Theron A, et al. Eur J Cardiothorac Surg. 2016;50(1):180-2. PMID: 26670804. 4: Odelin G, et al. Cardiovasc Res. 2014;104(3):443-55. PMID: 25344368.

Résumé du projet de thèse (**420 mots max**) :

- Rational

Congenital heart disease (CHD), defined as an abnormality of the heart, is the most common type of human birth defect, occurring in ~9 per 1000 live births and at a significantly greater incidence in miscarriage and still births. The complexity in understanding the etiology of CHDs is heightened by variability influenced by genetic, epigenetic and/or environmental modifiers. Well-recognized nongenetic causes of CHDs include environmental teratogens, such as excess maternal exposures to Vitamin A and its retinoid derivatives. Conversely, maternal Vitamin A/retinoic acid (RA) insufficiency can result in fetal death, or a broad range of abnormalities including cardiac malformations. Genetic alterations reducing retinol uptake or RA production have been implicated in human CHD. The molecular mechanisms underlying these lethal effects are not well understood.
Over the last decade, our team has been working on the role of Vitamin A during early cardiogenesis (Ryckebusch et al., 2008; Lin et al., 2010; Ryckebusch et al., 2010; Bertrand et al., 2011; El Robrini et al., 2016; Stefanovic & Zaffran, 2017; De Bono et al., 2018).

- Objectives

RA acts as a diffusible activator of nuclear receptors (RA receptors, RARs) and the basic mechanism for transcriptional regulation by RARs relies on DNA binding to specific sequence elements, the RA response elements (RAREs). The PhD candidate will study the roles of RA signaling and RARs in gene regulation during cardiogenesis, and the consequence of its deregulation in heart formation. She/he will, through a series of missions, provide a detailed map of RAREs involved in the development of the heart.

- Methods

The PhD candidate will use mouse models deficient in embryonic RA synthesis and mouse lines for lineage tracing. The PhD candidate will use wide-range of modern molecular techniques for distinguishing between direct, indirect, positive and negative regulatory effects of RA signals during cardiogenesis.

- Expected results

Interaction between genetic predisposition to heart defects and an environmental factor may cause heart defects and embryo loss in mice. Some cases of fetal death and/or CHD might arise by such an interaction in humans.

- PhD profile required

Candidates should have a Master degree in a life science subject, and preferably work experience with molecular biology, an excellent higher education track record and strong scientific curiosity. We seek a highly motivated scientist who is able to work independently but also as part of a team and has good communications skills.

Co-supervision - Dr Sonia Stefanovic (CRCN INSERM).

For more information contact Dr S. Zaffran (stephane.zaffran@univ-amu.fr) or Dr S. Stefanovic (sonia.stefanovic@univ-amu.fr)

Web site for additional details:
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http://www.zaffranlab.com/
https://twitter.com/zaffranlab