PROJECT 1

DoS: Simone Sala, MD

Title: Inflammation as a substrate for ventricular arrhythmias in primary cardiomyopathies

Curriculum: Experimental and Clinical Medicine

Link to OSR/UniSR personal page: https://www.hsr.it/clinica/specialita-cliniche/aritmologia-ed-elettrofisiologia-cardiaca/

Project description (*Number of characters, including spaces*: 2.000 - 3.000):

Among different clinical presentation of myocardial inflammation in primary or genetic cardiomyopathies, malignant ventricular arrhythmias, such as ventricular tachycardia and ventricular fibrillation, represent a significant cause of sudden cardiac death. Also, nonsustained ventricular tachycardia and frequent premature ventricular complexes are associated with an increased cardiovascular mortality. Recently, it was demonstrated that active inflammation is a predictor of arrhythmic events recurrence, even after ventricular tachycardia ablation, in autoimmune myocarditis. However, the arrhythmogenic role of inflammation in primary cardiomyopathies has still to be investigated.

To date, endomyocardial biopsy remains the gold standard for myocardial inflammation diagnosis and etiological classification. However, the research of active-phase inflammation is not part of the routine diagnostic assessment for primary cardiomyopathies. In this setting, advanced cardiac imaging may in turn allow early detection and more precise localization of inflammation.

Nowadays, molecular mechanisms underlying malignant ventricular arrhythmias are largely unknown in patients with primary cardiomyopathies and associated cardiac inflammation.

Thus, there is a great translational interest in the comprehensive characterization of immune cell population phenotype and transcriptional profile, pro-inflammatory cytokine pool, and cardiac autoantibodies. In order to identify specific molecular pathways and targets in different stages of inflammation and in different cardiomyopathies, myocardial samples will be evaluated via experimental pathology techniques (i.e., immunohistochemistry, immunofluorescence), before and after etiology-specific treatment. Arrhythmias will be extensively characterized to identify novel inflammation-specific patterns. Furthermore, genetic factors will be extensively explored to investigate the susceptibility to inflammation and arrhythmias.

The aim of the project is to explore the role of inflammation in the pathogenesis of ventricular arrhythmias in patients with endomyocardial biopsy-proven cardiac inflammation in the context of primary cardiomyopathies. Understanding these features will lead to the development of molecular-based therapeutic opportunities to target ventricular arrhythmias.

Skills to be acquired by the student:

1.   To investigate the molecular basis of arrhythmogenesis in patients with myocardial inflammation in primary cardiomyopathies.

2.   To describe type, entity, and mechanisms of innate and adaptive immunity in different cardiomyopathies.

3.   To correlate immunity and arrhythmogenesis based on a multiparameter model, including genetic, imaging, laboratory, and electrophysiological characteristics of patients with biopsy-proven inflammation and clinical documentation of ventricular arrhythmias in primary cardiomyopathies.

References (max. 3)

1.   Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, Fu M, Heliö T, Heymans S, Jahns R, Klingel K, Linhart A, Maisch B, McKenna W, Mogensen J, Pinto YM, Ristic A, Schultheiss HP, Seggewiss H, Tavazzi L, Thiene G, Yilmaz A, Charron P, Elliott PM; European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Disese. Eur Heart J. 2013;34:2636-2648.

2.   Peretto G, Sala S, Rizzo S, Palmisano A, Esposito A, De Cobelli F, Campochiaro C, De Luca G, Foppoli L, Dagna L, Thiene G, Basso C, Della Bella P. Ventricular Arrhythmias in Myocarditis: Characterization and Relationships With Myocardial Inflammation. J Am Coll Cardiol. 2020 Mar 10;75(9):1046-1057. doi: 10.1016/j.jacc.2020.01.036. PMID: 32138965.

3.   Eugene Braunwald. Cardiomyopathies: An Overview. 15 Sep 2017 doi.org/10.1161/CIRCRESAHA.117.311812Circulation Research. 2017;121:711–721

PROJECT 2 (optional)

DoS: _____

Title: _____

Curriculum: _____

Link to OSR/UniSR personal page:

Project description (*Number of characters, including spaces*: 2.000 - 3.000):

Skills to be acquired by the student:

References (max. 3)