Analysis of the snoRNA profile in ischemic and dilated cardiomyopathy

E. Tarazon 1, L. Perez Carrillo 1, I. Alvarez 2, I. Gimenez Escamilla 1, M. Delgado Arija 1, I. Gonzalez 2, M. Portoles 1, E. Rosello-Lleti 1

1Hospital Universitario y Politecnico La Fe, Health Research Institute of the Hospital La Fe (IIS La Fe) & CIBERCV (Institute Carlos III, Madrid), Valencia, Spain
2Health Research Institute La Fe, Valencia, Spain

Funding Acknowledgements: Type of funding sources: Public grant(s) – National budget only. Main funding source(s): National Institute of Health "Fondo de Investigaciones Sanitarias del Instituto de Salud Carlos III" co-funded by European Union

Introduction: In last decade, knowledge of how non-coding RNAs (ncRNAs) contribute to the pathogenesis of cardiovascular disease has increased exponentially. However, other than miRNAs, relatively little is known about how other small RNAs specifically contribute to heart failure. snoRNAs have been known for decades, mainly for their role in biogenesis and ribosomal modification. Moreover, recent studies have provided fundamental information on how snoRNA regulated non-coding RNA expression. However, the contribution of these non-coding RNAs to human disease is a relatively new area of research, with heart failure being relatively unknown and understudied.

Purpose: We aimed to investigate whether snoRNA expression is regulated during heart failure from dilated (DCM) and ischemic (ICM) origin, and how its biogenesis is affected by the pathophysiology of the disease.

Methods: Heart tissue samples from ICM (n=22) and DCM (n=20) patients and control (CNT, n=8) subjects were analyzed by non-coding RNA-Sequencing (ncRNA-Seq) to evaluate transcriptome changes in snoRNA/scaRNA. In addition, through mRNA sequencing we analyzed the biogenesis pathway of these ncRNA in ICM (n=13) and DCM (n=13) patients compared to CNT (n=10). Microarray analysis was used to validate the alterations found in the snoRNA/scaRNA expression (ICM, n=24; DCM, n=20; CNT, n=10).

Results: A generalized alteration of the snoRNA biogenesis pathway was not observed, we only found NOLC1 underexpression in ICM patients (FC=-1.42, p<0.05). NOLC1 encodes a nucleolar protein that acts as a regulator of RNA polymerase I and connects RNA polymerase I with enzymes responsible for ribosomal processing and modification. However, ncRNA-Seq data showed altered profiles of snoRNA/scaRNA in ICM and DCM patients. We identified 24 differentially expressed snoRNAs in ICM and 35 in DCM, while only 3 scaRNAs in DCM patients. We highlight SNORD14C that was upregulated in DCM patients (FC=2.37, p<0.01) and we confirmed in the microarray analysis (FC=1.10, p<0.05). Moreover, SNORD116-18 was related to ejection fraction in ICM patients (r=0.460, p<0.05).

Conclusion: Our data indicate that there are changes in the expression of snoRNA and scaRNA with a specific profile for each etiology, ICM and DCM. However, a marked alteration in its biogenesis is not observed. Taken together and given the relationship of SNORD116-18 to ventricular function, our results offer a novel and promising insight into the differential involvement of these molecules in the pathophysiology of ICM and DCM.