# *In Silico* Analysis of miRNA and mRNA Gene Expression profiles: Interaction Gene-Toxicity of Antiplatelet Therapy

Freitas, R.C.C.[1], Bortolin, R.H.[1], Lopes, M. B.[1], Hirata, M.H.[2], Hirata, R.D.C.[2], Silbiger, V.N.[1], Luchessi, A.D.[1]

[1]Department of Clinical and Toxicological Analysis, Federal University of Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil
[2]School of Pharmaceutical Sciences, University of Sao Paulo, São Paulo, Brazil

**INTRODUCTION**: Antiplatelet therapy is essential in the prevention of cardiovascular diseases. However, genetic, epigenetic and non-genetic variability may influence the efficacy and safety of antiplatelet drugs, especially clopidogrel, which is a standard treatment to prevent thrombotic events. **OBJECTIVES**: miRNAs and mRNAs interactions and drug toxicity were investigated in silico using available microarray data from acute coronary syndrome (ACS) patients with differential platelet and clopidogrel response. **MATERIAL AND METHODS**: Data of platelet miRNA expression (GSE59488) from ACS patients with high (HPR) and low platelet reactivity (LPR) and mRNA expression in peripheral blood cells (GSE32226) from coronary artery disease (CAD) patient responders and non-responders to clopidogrel were downloaded from Gene Expression Omnibus (GEO). miRNAs-target mRNAs interactions were analyzed using a miRNA database (http://microrna.org) and Ingenuity Pathways Analysis 6 software (IPA). **RESULTS AND DISCUSSION:** Six miRNAs and 20 mRNAs were differentially expressed in platelets and blood leukocytes, respectively. The miR-145-5p and miR-26a-5p were upregulated, while miR-107, miR-15b-5p, miR-4701-3p and miR-598 were downregulated in patients with HPR compared to LPR. Ten target mRNAs (*ADIPOR1, CYS1, FAM20B, GLMP, LGALS2, MKRN9P, NFXL1, SENP5, ST13 and UBE2F*) were more expressed and ten mRNAs were less expressed (*ABO, BTNL3, CFD, CHMP4B, GK3P, INSL3, PEX11A, SLC7A8, SPRR1A* and *SULT1A1*) in non-responders than responders to clopidogrel. The IPA interaction analysis software showed 17 miRNAs and 68 target mRNAs differentially expressed. *ST13* mRNA is regulated by miR-107; *SENP5* is regulated by miR-15b-5p, miR-26a-5p, miR-30c-5p and miR-106-5p; *SLC7A8* is regulated by miR-145-5p; *BTNL3* and *CFD* is regulates by miR-4701-3p. Drug toxicity IPA tool showed that these miRNAs/mRNAs are associated with clopidogrel-related liver and renal injury. **CONCLUSIONS:** These results demonstrate that differential expression of miRNAs in platelets and interactions with their target mRNAs in blood cells from ACS patients are associated with variability in platelet reactivity and clopidogrel response and drug-induced toxicity.

**Keywords***:* Antiplatelet Therapy; Pharmacogenomics; Bioinformatics

**Acknowledgment:** FAPESP, CNPq and CAPES