P011 THE HSA-MIR-150-3P MICRORNA IS UP-REGULATED IN GESTATIONAL DIABETES AND TARGETS THE *HLA-G* GENE

Eduardo A. Donadi [1], Nathalia J. Cézar [2], Jessica R. Plaça [3], Juliana D. Massaro [1], Luciana C. Veiga-Castelli [1], Erick C. Castelli [4], Claudia D. Polli [1], Wilson A. Silva-Jr [3], Elayne C. Moisés [5], Geraldo Duarte [5], Celso T. Mendes-Junior [6]. [1]Faculty of Medicine of Ribeirão Preto - University of São Paulo, Department of Clinical Medicine, Ribeirao Preto, Brazil; [2]Faculty of Medicine of Ribeirão Preto – University of São Paulo, Department of Genetics, Ribeirao Preto, Brazil; [3]Faculty of Medicine of Ribeirão Preto – University of São Paulo, Regional Blood Center, Ribeirao Preto, Brazil; [4]School of Medicine – UNESP São Paulo State University, Department of Pathology, Botucatu, Brazil; [5]Faculty of Medicine of Ribeirão Preto – University of São Paulo, Department of Gynecology and Obstetrics, Ribeirao Preto, Brazil; [6]Faculty of Philosophy, Sciences and Letters of Ribeirão Preto, University of São Paulo, Department of Chemistry, Ribeirao Preto, Brazil.

Some microRNAs (miRNA) have been described to be differentially modulated in gestational diabetes mellitus (GDM), the most common metabolic disorder observed during pregnancy.

Aim: Since HLA-G presents a crucial role on maternal tolerance to the fetus, we evaluated the differentially expressed miRNAs in GDM patients and their in silico targeting on the 3″ untranslated region (3′UTR) of the HLA-G gene.

Methods: The large scale miRNA expression was evaluated using Next-Generation sequencing (MiSeq-Illumina), and differentially expressed miRNAs between GDM and non-GDM pregnant women was detected using the DESeq2 package (http://bioconductor.org/biocLite.R). Variable and invariable HLA-G 3′UTR segments were used as targets for miRNA binding using three different algorithms (RNAhybrid, miRanda, PITA) with the aid of a package of Perl scripts named miRP (www.castelli-lab.net).

Results: RNASeq analysis revealed 15 differentially expressed miRNAs between GDM patients and healthy pregnant women ($P < 0.01$/FC > |1.4|). Of these, the miR-150-3p was up-regulated ($P = 0.005$/FC = 1.44) and showed strong affinity for the most frequent HLA-G UTRs at positions +2933 and +3098 (conserved), presenting the same intensity and specificity of ligation. In addition, miR-150-3p targeted a region that includes three polymorphic sites, +3010, +3027, +3035. In these sites, a very similar and stronger pattern of bind to some UTRs (1, 2, 3, 4 and 6) was evidenced. On the other hand, UTR-5 and UTR-7 were not considered as targets to miR-150-3p at this region. Although functional analyses are needed, this study showed that miR-150-3p can regulate many HLA-G UTRs. The fact that the miR-150-3p was up-regulated in GMD is consistent with the hypothesis of reduced HLA-G expression at the maternal-fetal interface during pregnancy.

Conclusion: This finding suggests that HLA-G post-transcriptional regulation may be related to development of GMD.