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THE miRNAs EXPRESSION PROFILE IN ACUTE MYOCARDIAL INFARCTION OF YOUNG ADULTS

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INTRODUCTION

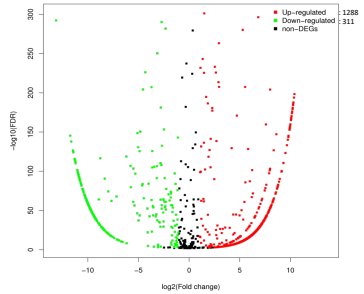
Acute myocardial infarction (AMI) is the most severe manifestation of coronary heart disease where Malaysians are getting AMI at younger age compared to well-developed countries. MicroRNAs (miRNAs) are short, non-coding RNAs that play important regulatory roles in development of human pathologies.

METHODOLOGY

This study investigated the miRNA expression profile in 3 Controls (age >18 years old), 3 Young AMI (age ≤ 45 years old) and 3 Mature AMI (age ≥46 years old) patients who were all Malay males with matching criteria, using RNA sequencing, followed by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses. miRNAs were considered significantly upregulated if relative expression showed a fold change (FC) ≥ 1 and $p \leq 0.05$; and considered significantly downregulated with FC ≤ -1 and $p \leq 0.05$.

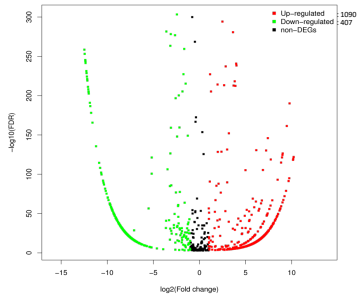
RESULT

Figure 1: Volcano plot of differential miRNA expression in Control group versus AMI (Young and Mature AMI) group.



A total of 1599 miRNAs were differentially expressed in AMI patients compared to Controls; 1288 miRNAs were upregulated and 311 miRNAs were downregulated.

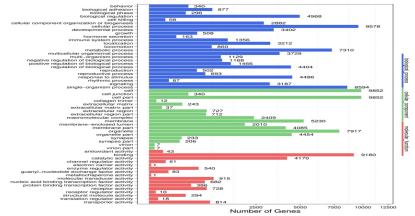
Figure 2: Volcano plot of differential miRNA expression in Young AMI group versus Mature AMI group.



A total of 1497 miRNAs were differentially expressed in Young AMI patients compared to Mature AMI patients; 1090 miRNAs were upregulated and 407 miRNAs were downregulated.

The top 5 upregulated miRNAs were miR-552, miR-4446-3p, miR-432-5p, miR-548j-5p and miR-219; while the top 5 downregulated were miR-16, miR-1064, miR-431, miR-790 and miR-1177.

Figure 3: GO analysis of differentially expressed miRNAs that covers 3 domains: biological process, cellular components & molecular function.



For these 1497 differentially expressed miRNAs, 34,195 target genes were predicted by GO analysis. The enrichment analysis revealed 11,199 involved in biological processes, 10,984 in molecular functions and 12,012 in cellular components. The most common GO categories were cellular process, metabolic process, cell, cell part, organelle, binding and catalytic activity (Figure 3).

Target genes of differently expressed miRNAs that were mapped in signal transduction pathway KEGG, revealed that 346 classes were enriched.

DISCUSSION

- miR-552 regulates catalytic activity, transcriptional regulation and binding (Zou et al., 2020) while miR-432-5p regulates TLR4 that causes cardiac hypertrophy (Li et al., 2018); miR-219 plays a role in acute inflammation (Liu et al., 2015) while miR-16 inhibits inflammatory pathway (Wang et al., 2020); down-regulation of miR-431 reduces the cell viability and promotes the cell apoptosis in the human cardiomyocytes (Zhou et al., 2021).
- There are limited studies on miR-4446-3p, miR-548j-5p, miR-1064, miR-790 and miR-1177 in atherosclerosis or AMI.
- Our findings showed that modulated miRNAs may regulate the functions of target genes in these signaling pathways during the formation and development of AMI in Young population.

CONCLUSION

The small RNA sequencing discovered new unknown miRNAs and suggested that these miRNAs regulatory mechanisms on gene expression are more closely involved in Young AMI. This could be an interim foundation study that requires further elaboration.

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