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Letter to the Editor

Can the cardioprotective effect of microRNA-103 inhibitors be extended to women with polycystic ovary syndrome?

Dear Editor,

Always on the lookout for articles from the *European Review for Medical and Pharmacological Sciences*, one, in particular, has attracted a lot of attention, because the scientific proposals and perspectives are fascinating. We think that the original research article published by Dr. Zaafan and Dr. Abdelhamid titled "The cardioprotective effect of microRNA-103 inhibitor against isoprenaline-induced myocardial infarction in mice through targeting FADD/RIPK pathway"[1] is another important piece demonstrating the complicated landscape of myocardial infarction and a mechanism to alleviate.

MicroRNAs (miRNAs) are evolutionarily conserved, non-coding, endogenous small (20~23 nucleotides) RNAs, which regulate post-transcriptional gene expression. Only recently, miRNAs have been suggested to be closely associated with myocardial cell death[2,3]. As we know, myocardial infarction (MI) is the irreversible death or necrosis of heart muscle secondary to prolonged ischemia and is responsible for 16% of the world's total deaths (World Health Organization, 2020)[4]. Even with a multimodal approach, the treatment is difficult in many cases, because it is "silent" and goes undetected, and in a later stage it could cause a catastrophic event and sudden death. Therefore, it is important to elucidate the underlying mechanism to improve the therapeutic strategy for MI and related conditions. To address this issue, Dr. Zaafan et al[1] focused their attention on protecting myocardial cells from experimentally induced programmed necrosis by employing the systemic miR-103 inhibitor to silence infarction. In summary, this paper showed that when experimentally myocardial infarction was induced in mice it increased the miR-103 expression, TNF-alpha, IL-6, NF-kB and RIPK in heart muscles and correspondingly decreased FADD expression. Whereas in the infarcted hearts of the mice treated with miR-103 inhibitor significantly inhibited miR-103 expression accompanied by markedly increased FADD expression and decreased expression of the other biomarkers and histological features of heart tissue was improved. Overall, the systemic application of miR-103 inhibitor significantly protects myocardial cells from dying via elevated FADD. We applaud the authors for pursuing the cardioprotective effect of systemic miR-103 inhibitors.

As per the prediction of the TargetScan v8 tool, it suggested miR-103-3p/107 targets 835 transcripts in humans. Several studies have shown that miR-103 overexpression worsens many cancers or adversely affects neurons[5-8]. However, inhibition of miR-103 expression has been shown to inhibit cancer cell proliferation[8] and exert neuroprotective effects[6] via regulating target genes/pathways. Interestingly, a recent study by Dr. Mu et al[9] demonstrated that miR-103 overexpression aggravates polycystic ovary syndrome (PCOS) development by disrupting PI3K/AKT pathway activation via targeting IRS1 in granulosa cells of the ovary. Inhibition of miR-103 attenuated PCOS progression and improved PCOS-related symptoms by inhibiting apoptosis and promoting proliferation of granulosa cells[9]. These data, therefore, suggests the systemic and organ specific application of miR-103 inhibitor could protect cells from undergoing apoptosis/necroptosis and promote proliferation depending on the organ and cell type via various pathways.

Corresponding Author: Palaniswamy Ramaswamy, Ph.D; e-mail: palani.swamy20@gmail.com

Some studies[10-12] showed that women with PCOS have an increased risk for cardiovascular events such as myocardial infarction. Also, international PCOS guidelines[13] recommend an assessment of cardiovascular risk factors and global CVD risk as part of long-term management of PCOS patients. Among patients with MI-obstructive coronary artery disease, women had higher mortality than men[11,12]. Considering these, can we hypothetically be able to treat or alleviate PCOS patients who are prone to cardiovascular events together and implicate the possible future application of miR-103 inhibitors in the clinic as a novel common therapeutic for both the conditions? To confirm the same hypothesis, we suggest that it will be interesting to note the effect of the systemic miR-103 inhibitor on experimentally induced MI on animals with PCOS and look for its cardioprotective effect and alleviating effect on polycystic ovary. Moreover, miRNA-based therapies have recently been explored, either alone or in combination with current targeted therapies. However, the strategy to use miRNAs for targeted therapy in the near future is probably over-optimistic, considering that therapeutic studies are still immature because of the pleiotropic effect of miRNAs on target genes. Nevertheless, the increasing capability of producing synthetic interfering miRNAs with higher affinity to the desired target in the specific organ could minimize this barrier.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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P. Ramaswamy[1], M.K. Sibin[2], P. Misra[2], R. Sahu[3]

[1]Multidisciplinary Research Unit (MRU), Armed Forces Medical College, Maharashtra, India
[2]Department of Biochemistry, Armed Forces Medical College, Maharashtra, India
[3]Department of Community Medicine, Armed Forces Medical College, Maharashtra, India