INTRODUCTION

Micro RNAs (miRNAs) are a class of single-stranded endogenous small non-coding RNAs (ncRNAs), with about 22 nucleotides in length. They are transcriptionally regulated similarly to messenger RNA (mRNA) and, when processed, can silence or downregulate the expression of their targets (Wojciechowska et al., 2017). Therefore, it is no surprise that miRNAs regulate various biological processes (Baltimore et al., 2008). In the cardiovascular system, miRNAs play a role in cardiomyocyte differentiation, growth and contractility and cardiac rhythm development and maintenance (Islas and Moreno-Cuevas, 2018).

CIRCULATING MICRORNAS AS NON-INVASIVE BIOMARKERS

In the clinical setting, biomarkers can help with the early diagnosis of diseases, evaluate and manage the response to therapy, and assess patient prognosis. miRNAs have numerous characteristics that potentially make them suitable non-invasive biomarkers (Fiedler et al., 2014).

Circulating miRNAs have been detected in peripheral blood and other body fluids such as saliva, urine and breast milk (Weber et al., 2010). They are highly stable and resistant to degradation (Mitchell et al., 2008). The expression of circulating miRNAs is analyzed by different methods such as real-time polymerase chain reaction (RT-qPCR) (Bellingham et al., 2017). The growing understanding of cardiac biology contributed to recognizing specific miRNAs as novel biomarkers for several cardiovascular diseases (Čakmak and Demir, 2020).

MICRORNAS IN THE DIAGNOSIS OF CARDIOVASCULAR DISEASES

Myxomatous mitral valve disease

Myxomatous mitral valve disease (MMVD) is the most common cardiac disease in dogs (Ettinger et al., 2017). As seen in table 1, several studies have already evaluated the changes in expression of some miRNAs in MMVD. A study identified several differentially expressed genes when characterizing the MMVD transcriptome, and 59 canine miRNA family members (ca-miRNA) were identified (Lu et al., 2015). Also, the miRNA expression profile in dogs with MMVD is different between ACVIM stage A (healthy), stage B1/B2 and stage C/D dogs, and it appears that expression changes are greater as the disease progresses (Li et al., 2015). Figure 1 shows which miRNAs are differentially expressed in dogs with MMVD known so far.

Dilated Cardiomyopathy

The most common cardiomyopathy in dogs is dilated cardiomyopathy (DCM). To this date, only one study evaluated which miRNAs were differently expressed in dogs with DCM. Its findings are summarized in table 1.

Diaphragmalysis

Heartworm disease, also called diaphragmalysis, is most caused by Dirofilaria immitis. In 2014, the presence of circulating filarial derived microRNAs in the host bloodstream was studied by Tritten et al. Their most relevant remarks are summarized in table 1. There was not a direct relation between miRNA copy numbers and microfilaria counts, which implies that adults also significantly release miRNAs into the bloodstream (Tritten et al., 2014).

Table 1 – Micro RNAs evaluation in canine cardiac diseases.

<table>
<thead>
<tr>
<th>miRNA</th>
<th>Change in expression</th>
<th>Purpose</th>
<th>Sample</th>
<th>Objective</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>hsa-141</td>
<td>↑</td>
<td>Cardiac disease monitoring</td>
<td>Plasma</td>
<td>Evaluation of the expression of circulating miRNAs in dogs with MMVD</td>
<td>Yang et al., 2017</td>
</tr>
<tr>
<td>hsa-miR-200b</td>
<td>↓</td>
<td>Therapeutic target</td>
<td>Cardiac tissue</td>
<td>Evaluation of miRNA expression in VCs isolated from MMVD (diseased) versus non-MMVD (control) canine cardiac valve tissues</td>
<td>Yang et al., 2018</td>
</tr>
<tr>
<td>hsa-miR-9</td>
<td>↑</td>
<td>Diagnosis, prognosis, or monitoring response to treatment</td>
<td>Serum</td>
<td>miRNA expression profile in dogs with MMVD stage B1/B2 or C/D compared with stage A dogs</td>
<td>Li et al., 2015</td>
</tr>
<tr>
<td>hsa-miR-1</td>
<td>↑</td>
<td>Diagnosis, prognosis, or monitoring response to treatment</td>
<td>Serum</td>
<td>miRNA expression profile in dogs with MMVD stage B1/B2 compared with stage C/D dogs</td>
<td>Li et al., 2015</td>
</tr>
<tr>
<td>hsa-miR-133</td>
<td>↓</td>
<td>Diagnosis</td>
<td>Plasma</td>
<td>Investigation of the presence of circulating miRNA profile released by filarial nematodes into the host bloodstream</td>
<td>Tritten et al., 2014</td>
</tr>
</tbody>
</table>

CONCLUSION

Although there is evidence regarding the potential role of miRNA as diagnostic and prognostic biomarkers, more studies are warranted to evaluate its role in canine heart disease.

REFERENCES


