

## **miR-21-5p up-expression are associated with the evolution of canine visceral leishmaniasis**

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Visceral leishmaniasis (VL) is an anthroponosis found in tropical and subtropical areas. VL is a chronic systemic disease, if untreated with an effective drug and in a timely manner, it can progress to death in 90% of cases. Domestic dogs are of great epidemiological importance since they are the main reservoirs of VL. The microRNAs (miRNAs) are small non-protein coding RNAs that play an important role in regulating gene expression. miRNAs, also, perform specialized functions in immune response. As the regulatory mechanisms of miRNAs in canine visceral leishmaniasis (CanVL) is poorly known, this study was aimed to investigate whether miRNA produced in dogs could be predictors of CanVL evolution. The expression profiles of 11 miRNA were assayed in 30 canine sera (14 from healthy dogs and 16 from dogs with CanVL), in order to verify a possible distinction between both groups. After miRNAs extraction in sera and subsequent cDNA synthesis, the expression profiles of miRNAs were determined by qPCR. The miRNA species evaluated were miR-21-5p, miR-146a-5p, miR-125b-5p, miR-144-3p, miR-194-5p, miR-346, miR-29c-3p, miR-155-5p, miR-24-3p, miR-181a-5p, miR-9-5p. Results were expressed in Relative Quantification (RQ), calculated by the comparative CT method ( $2^{-\Delta\Delta CT}$ ). RQ mean of health dogs (14 sera) were considered calibrators, which according to the method assumed the RQ mean value =1.0. The calibrators informed how many times the studied gene is more expressed. Sera of dogs

with CanVL up-expressed the miR-21-5p and miR-146a-5p. RQ values were 20.77 and 9.67, respectively, which represents how many times they were up expressed compared to healthy dogs. miR-125b-5p and miR-144-3p also were up-expressed in dogs with CanVL, but with less intensity. Mean RQ were 2.80 and 2.10, respectively, and higher expressed than healthy dogs. miR-194-5p, miR-155-5p, miR-24-3p, miR-181a-5p were similarly expressed in both groups of dogs. All dog sera studied were unable to express miR-29c-3p, miR-346, and miR-9-5p. These results and data from previous studies suggested that intense infection could promote the expression increase of miR-21-5p and miR-146a-5p in dogs, promoting anti-inflammatory response and reduced Th1 immune response by T cells and phagocytes. Thus, these miRNAs could cause a suppressor effect of the protective Th1 response in CanVL

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