

Developmental regulation of miRNA secretion in the filarial nematode *Litomosoides sigmodontis*

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The secretion of extracellular RNAs (exRNAs) by parasitic nematodes has opened new avenues for the development of novel biomarkers for helminthiases, including filariasis. These are catalogued as some of the major neglected tropical diseases, which together account for more than 120 million infections in tropical and subtropical regions. One outstanding question is whether the secretion of small RNAs is developmentally regulated in parasitic nematodes. Here, we present *in vitro* and *in vivo* data that show the presence of ubiquitous, as well as sex- and potentially stage-specific miRNA markers in Excretion/Secretion (ES) products from early larval and adult stages from the rodent filarial nematode *Litomosoides sigmodontis*. Moreover, a subset of these miRNAs, including female-specific miRNA markers, are found in biofluids from infected vertebrate hosts, including gerbils, mice and humans. Using infected BALB/c mice as a model for filarial infections, we tested the performance of a subset of circulating parasite-derived miRNAs as biomarkers and significantly discriminate between infected animals and naïve controls with high sensitivity/specificity (~80%/100%). Taken together, our data constitute the first report of a comprehensive characterisation of the miRNA secretion throughout filarial development *in vitro* and *in vivo*, and provides strong evidence to support the development of biomarkers to detect active reproductive filarial female worms.