Can many biomarkers make light work of ovine fasciolosis?

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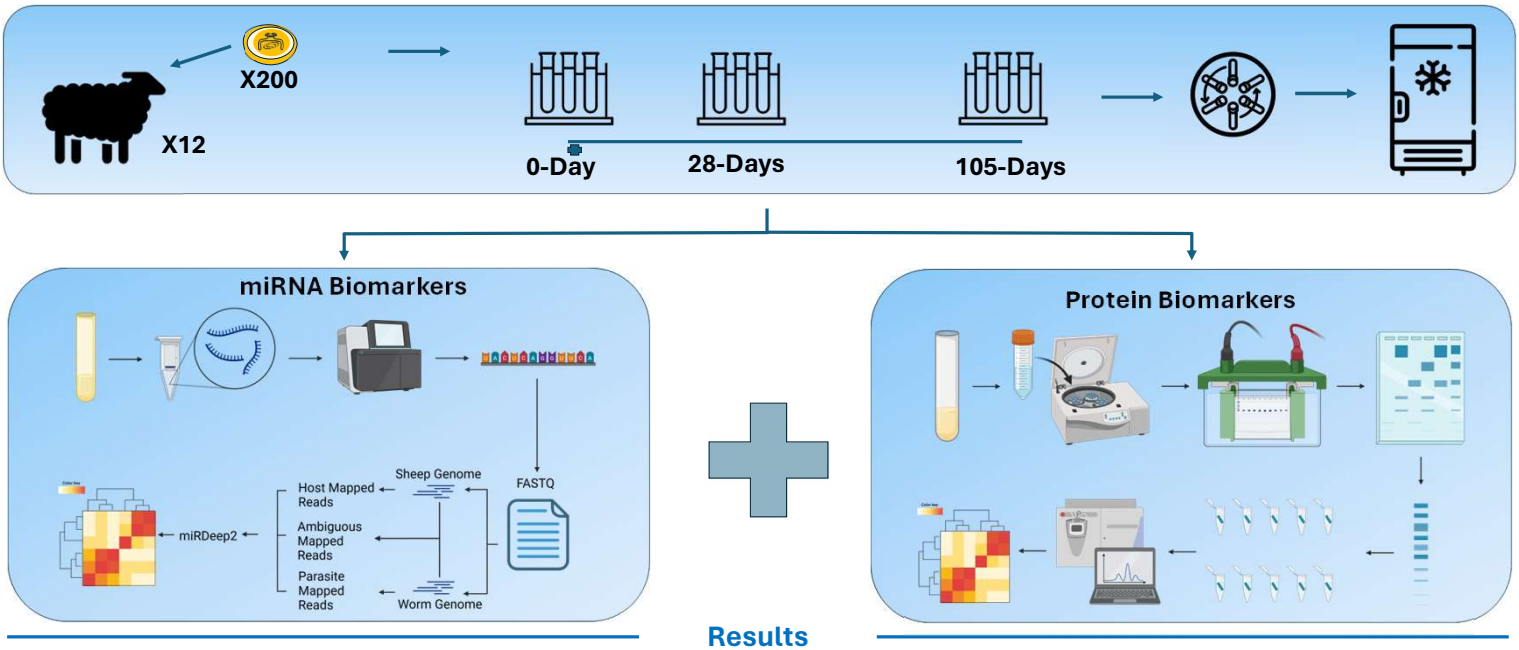
Introduction

- The liver fluke *Fasciola hepatica* is a highly successful trematode parasite and the causative agent of ovine fasciolosis
- The acute stage of infection, which occurs 3-6 weeks post infection, is of particular concern as it can cause mortality in extreme cases.
- In the absence of methods capable of diagnosing active acute infection, farmers often apply blanket chemical treatments called anthelmintics of which only one, triclabendazole, reliably treats acute infection.
- This is providing selection pressure for anthelmintic resistance which is increasingly common, demonstrating the need for novel methods capable of diagnosing acute infection[1].
- The interaction between parasite and host is known to involve a plethora of changes, both within the host and secreted by the parasite[23].
- We hypothesize that these biomarkers, particularly microRNAs (miRNAs) and proteins, could be used as the basis of novel diagnostics for ovine fasciolosis.

Methods

- Twelve sheep were experimentally infected with 200 *F. hepatica* metacercariae and blood samples were subsequently taken
- Blood samples were then clotted and spun to produce serum, which were stored at -80c.
- Three timepoints were chosen for analysis – 0-weeks (pre-infection), 4 weeks (acute-infection) and 12 weeks (chronic infection).
- RNA was extracted and small RNA sequencing was carried out whilst proteins were digested and then analysed using liquid chromatography mass spectrometry. In-house pipelines were used to profile miRNAs and proteins.



Results

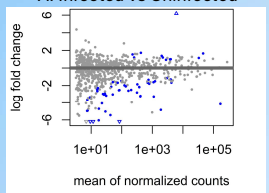
Parasite miRNAs are present in the sera of infected sheep

- All *Fasciola hepatica* miRNAs identified from sheep serum were found in the 105 DPI samples

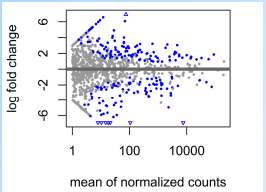
	No. Samples Present	Timepoint Present
miR 1	3	105 DPI
miR 2	2	105 DPI
miR 3	1	105 DPI
miR 4	1	105 DPI
miR 5	1	105 DPI
miR 6	2	105 DPI

Host circulating miRNAs are differentially expressed at distinct timepoints

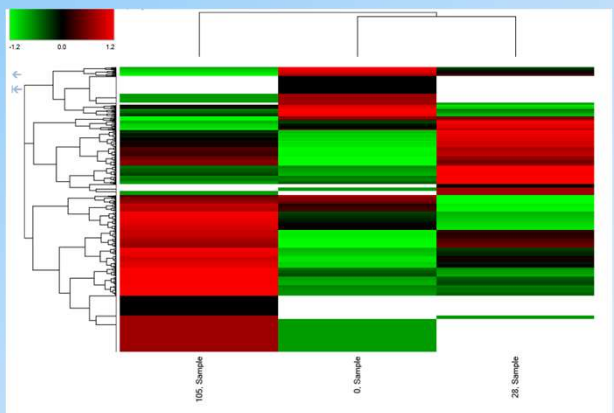
A. Infected vs Uninfected



28DPI vs 105 DPI



Host circulating proteins are differentially expressed at distinct timepoints



Conclusions

- Liver fluke miRNAs are detectable in the serum of infected sheep
- Hundreds of circulating host miRNA sequences are differentially expressed during infection at distinct timepoints
- Host proteins are differentially expressed at distinct timepoints associated with infection
- These biomarkers will be further tested and scrutinised to evaluate their diagnostic potential

References

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