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Transcriptome evaluation of equine sarcoid infected by bovine papillomavirus type-1

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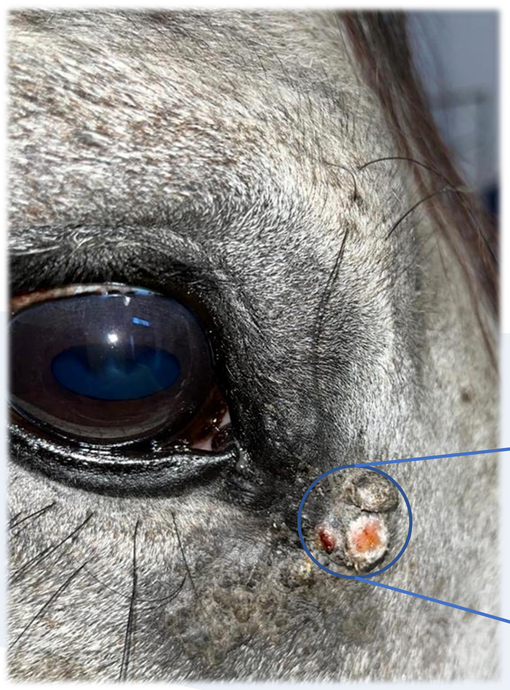
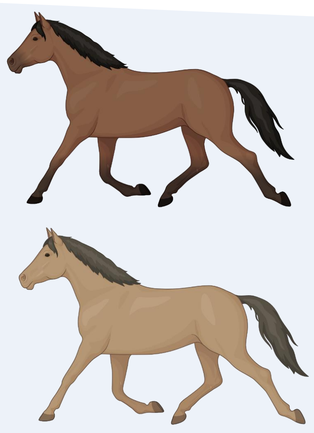


INTRODUCTION & AIM

- Sarcoids are the most common skin tumors in horses representing up to 90% (35-90%) of skin neoplasms in this species.
- They affect breeds of all ages and both sexes and can occur as single or multiple lesions in different forms, ranging from small, wart-like lesions to large, ulcerated, fibrous growths.
- Highly impacting pathology for the veterinary field due to the high incidence, resistance to therapy and frequent recurrence.
- The aim was to better understand the host pathogen interaction by implementing knowledge on transcriptomic tumor microenvironment.

MATERIALS & METHODS



12 sarcoids
2 margins

10 healthy skin

Real Time qPCR

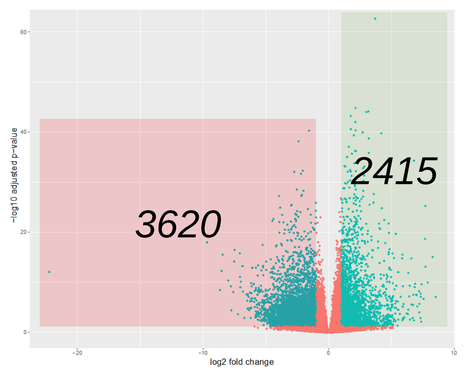
91,7% sarcoids **positive**
100% margins **positive**
90% healthy skin **negative**

RNA Extraction
&
Library preparation

mRNA-seq

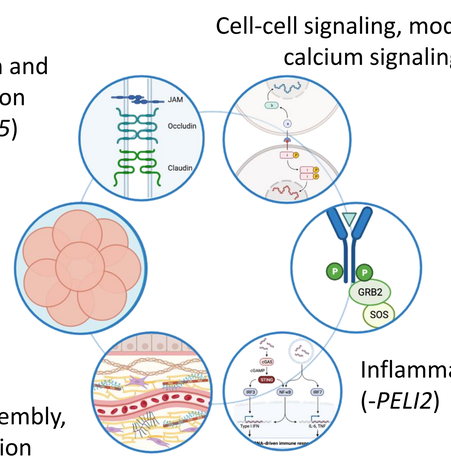
~63M paired-end reads per sample obtained from sequencing

~56M per sample on average were uniquely mapped on *EquCab3* genome



Differentially expressed genes (DEGs)
Sarcoids vs controls
log_2FoldChange > |1| and an adjusted p-value < 0.05

Functional analysis on DEGs: Gene Ontology (GO) *'Biological Processes'*



Cell junction organization and Regulation of cell migration (*+PRDX4, +TUSC3, -CLDN5*)

Cell-cell signaling, modulation of calcium signaling pathway (*-PIEZO2*)

Regulation of RTK signaling and Ras/Raf/MEK/ERK Pathway, Regulation of intracellular signal transduction (*+ETV1*)

Epithelial cell proliferation, Regulation of angiogenesis (*-FBXL22, +GPX8*)

Inflammatory response (*-PELI2*)

Extracellular matrix Assembly, Collagen fibril organization (+KDELR2, -FOXC1)

smallRNA-seq

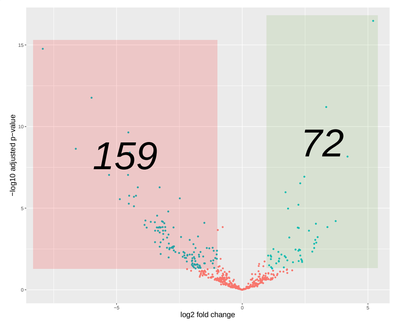
~20M single-end reads per sample obtained from sequencing

~18M per sample on average were clean and good quality-controlled

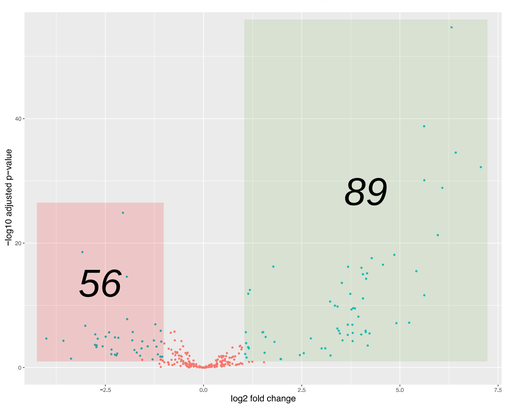
To retrieve the expressed micro RNAs (miRNAs), long non-coding RNAs (lncRNAs) and all the others smallRNAs, two sequential mapping steps were carried out:
- towards miRBase22 first
- then, the unmapped reads towards EquCab3 genome

Differentially expressed
Sarcoids vs controls (log_2FoldChange > |1| and an adjusted p-value < 0.05)

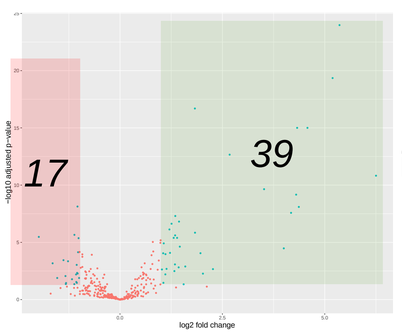
lncRNAs



miRNAs



All other smallRNAs

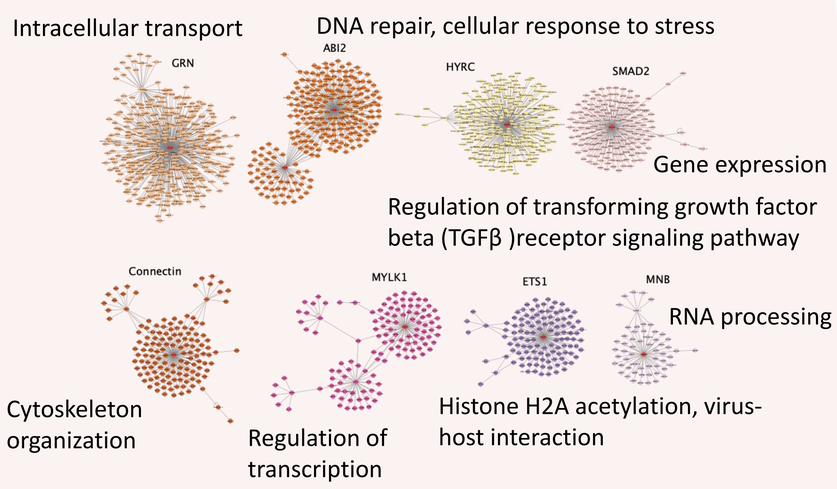


Functional analysis on targets of miRNAs: Gene Ontology (GO) *'Biological Processes'*

DISCUSSION AND CONCLUSIONS

- Our data identified a great discrepancy of transcription between sarcoid lesions and healthy skin with an overall enrichment for processes related to infection and cellular transformation.
- The gene expression analysis has highlighted huge differences between healthy and tumor tissues both in terms of active pathways and regulatory miRNAs.
- Genes involved in phosphorylation, cell adhesion and pathway of ERK1 and 2 are modulated.
- Of extreme interest, since we are dealing with a mesenchymal neoplasm, is the modulation of SMAD2 and HIF1AN, suggesting a complex regulatory system in the tumor microenvironment.
- A deeper exploration of the results is ongoing, including an integrated analysis of miRNA and mRNA as targets and relative biological processes.

Hub target genes of down-regulated miRNAs



Hub target genes of up-regulated miRNAs