Cerebrospinal fluid proteomic profiling for biomarker discovery in canine non-infectious meningoencephalitis

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Introduction

- **Canine non-infectious meningoencephalitis:**
  - Affects 1 in 4 dogs with neurologic disease
  - Presumably immune-mediated
- Diagnosis is problematic
  - Post-mortem via histopathology
  - Ante-mortem via ***brain biopsy***
    - Rarely performed in clinical practice
- Lack of antemortem diagnoses has mitigated improvements in patient care
- ***Critical need for ante-mortem diagnostic and therapeutic biomarkers!***

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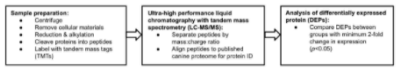
Aims and Methodology

Specific Aim:

1) Determine the CSF peptide signature of dogs with non-infectious meningoencephalitis relative to normal dogs and dogs with non-inflammatory neurologic disease using unbiased tandem mass spectrometry.

Archived CSF samples histopathologically confirmed cases:

- Normal (n=6)
- Granulomatous meningoencephalitis (GME; n=6)
- Necrotizing meningoencephalitis (NME; n=6)
- Oligodendroglioma (Oligo; n=5)



21 Viable Biomarker Candidates

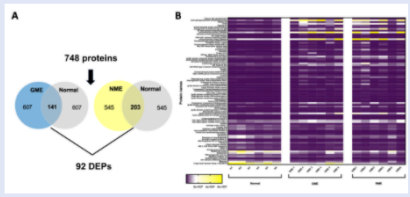


Fig 1: 92 DEPs in GME and NME relative to normal. (A), 748 annotated proteins were identified across all 4 groups. There are 141 DEPs in GME relative to normal, 203 DEPs in NME relative to normal, and 92 DEPs common in GME and NME relative to normal. **(B)** Expression patterns of 92 DEPs in GME and NME relative to normal represented by heat map.

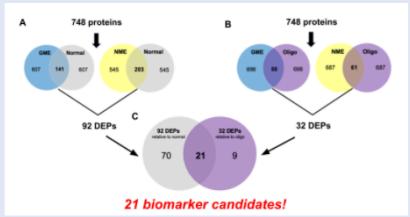


Fig 2: CSF proteomic profiling using mass spectrometry revealed 21 biomarker candidates for GME and NME. (A), There are 92 DEPs common in GME and NME relative to normal. **(B)**, There are 32 DEPs common in GME and NME relative to oligodendroglioma. **(C)**, There are 21 DEPs common in GME and NME relative to both normal and oligodendroglioma.

Top Biomarker Candidates: Acid Sphingomyelinase-like Phosphodiesterase & Chitinase-3-...

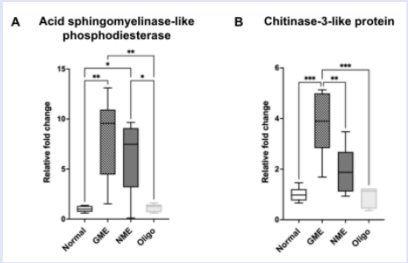


Fig 3: Expression patterns of top biomarker candidates for GME and NME. (A) Acid sphingomyelinase-like phosphodiesterase (ASLP) showed an 8-fold increase and 6.5-fold increase in GME and NME, respectively, relative to normal and oligodendroglioma. This suggests that ASLP may be a promising biomarker candidate for GME and NME. **(B),** Chitinase-3-like protein (C3LP) showed approximately a 3.7-fold increase in GME relative to normal and oligodendroglioma, and a 2-fold increase in GME relative to NME. This suggests that C3LP may be a promising biomarker for differentiating GME and NME.

*Data are represented by box and whisker plot. Whiskers represent group minimum and maximum, while the box represents 25th through 7th quartile. *p<0.05 **p<0.01 ***p<0.001*

Conclusion

- CSF proteomic profiling using mass spectrometry:
  - Reference library for canine proteome
  - Viable biomarker discovery platform in canines
    - Identified 21 biomarker candidates
- Rationale for validation of top biomarker candidates via ELISA:
  - **Acid sphingomyelinase-like phosphodiesterase**
  - **Chitinase-3-like protein**

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