



CAESAR KLEBERG  
WILDLIFE RESEARCH INSTITUTE  
TEXAS A&M UNIVERSITY - KINGSVILLE®

# Investigating potential inhibitory roles of organic copper and zinc in CWD prion protein misfolding and propagation



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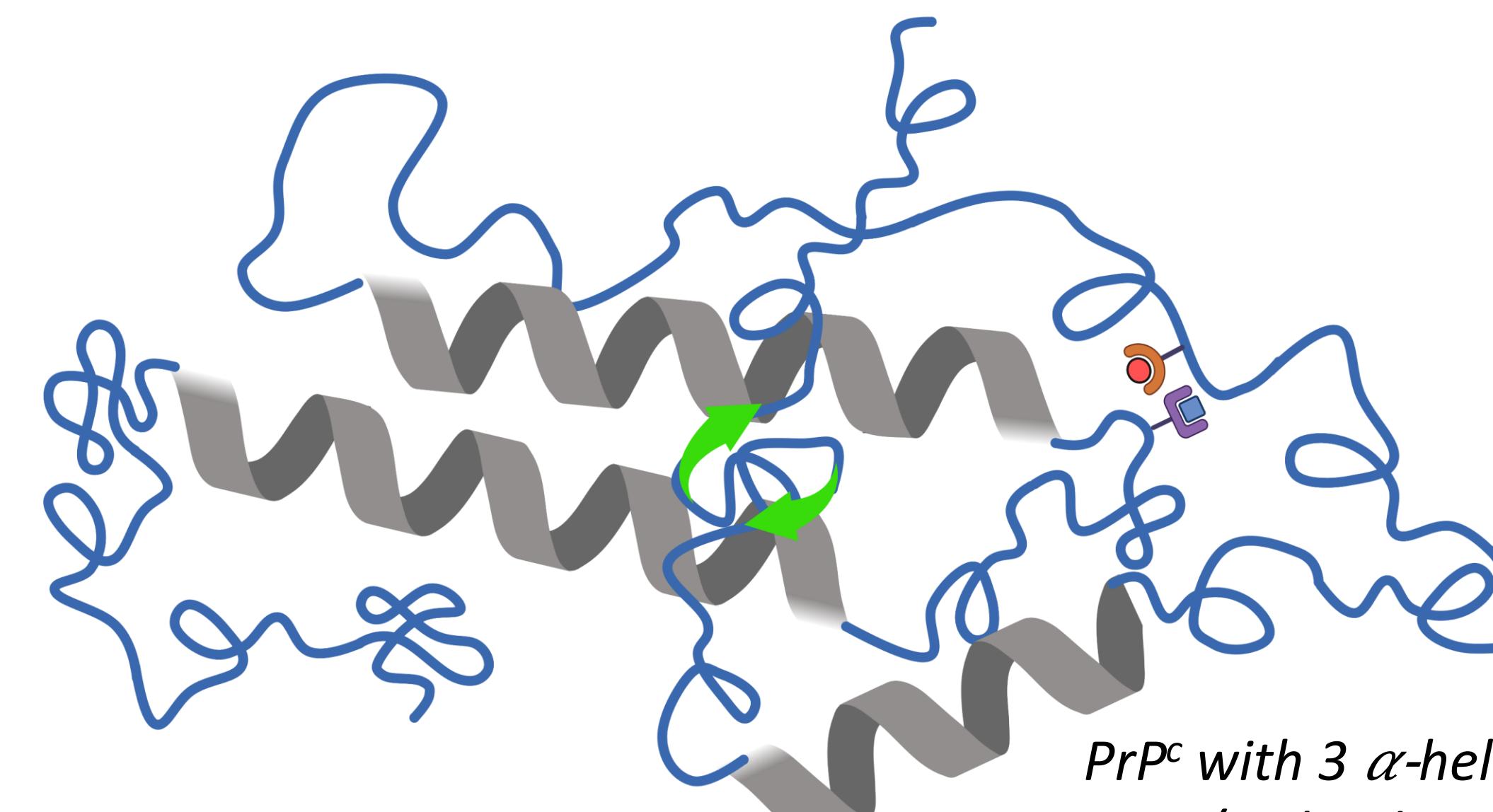
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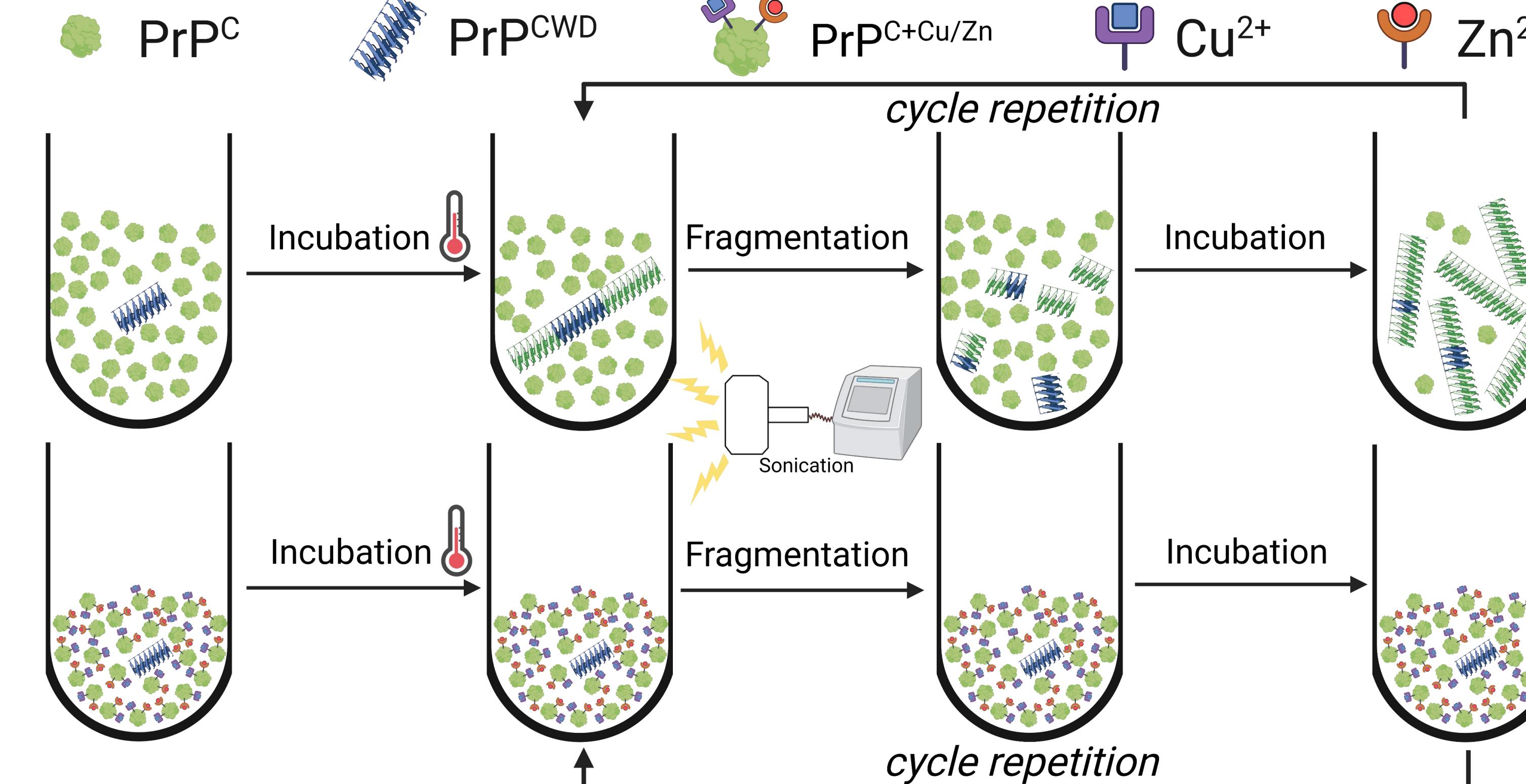
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## Introduction

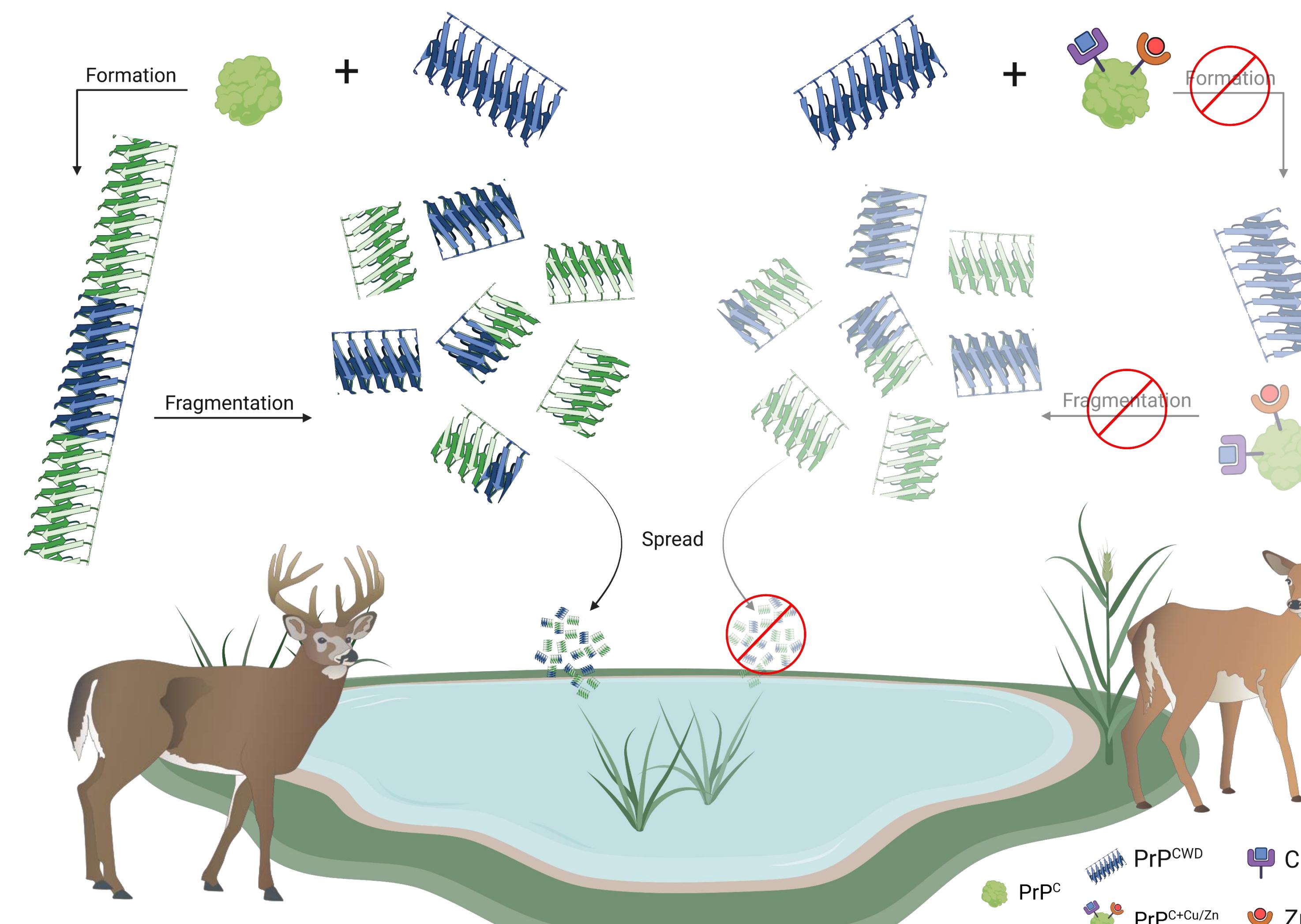
- CWD spreads rapidly with no treatment in sight
- Copper ( $\text{Cu}^{2+}$ ) and zinc ( $\text{Zn}^{2+}$ ) prevent  $\text{PrP}^{\text{C}}$  misfolding
- Mineral status related to CWD progression is unknown



$\text{PrP}^{\text{C}}$  with 3  $\alpha$ -helices, 1 anti-parallel  $\beta$ -sheet, Cu/Zn binding at N-terminal octa-repeat



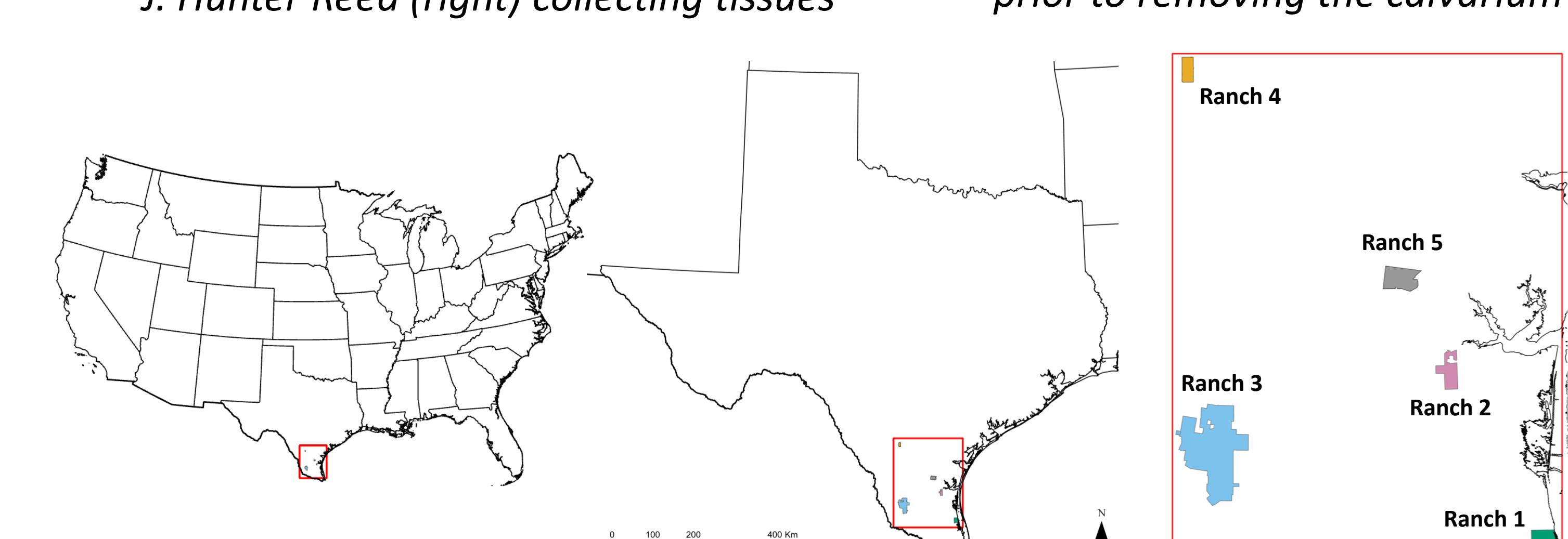
Top: lack of  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ ,  $\text{PrP}^{\text{C}}$  misfolds and propagates with PMCA  
Bottom:  $\text{PrP}^{\text{C}}$  bound  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$ , no  $\text{PrP}^{\text{C}}$  misfolding



Left:  $\text{PrP}^{\text{CWD}}$  binds  $\text{PrP}^{\text{C}}$  leading to misfolding, continuing spread  
Right:  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  binding to  $\text{PrP}^{\text{C}}$ , no misfolding, no spread

## Objectives

- Collect brain, ileum, lymph nodes, & liver from deer
- Genotype single nucleotide polymorphisms
- Evaluate tissue  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  with spectrophotometry
- Confirm CWD status with RT-QuIC on all harvested deer
- Evaluate effect of mineral status on  $\text{PrP}^{\text{CWD}}$  with PMCA

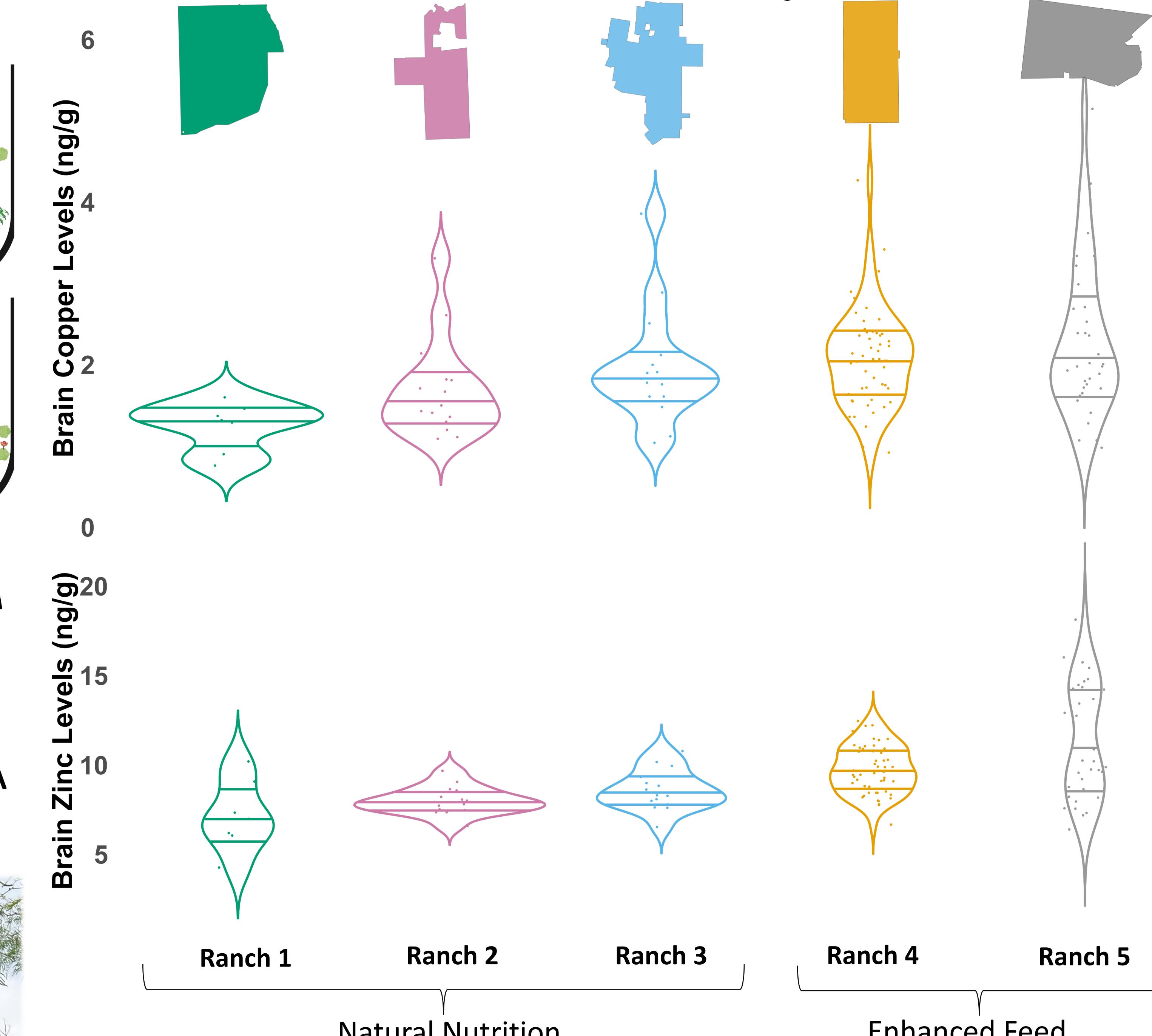


5 ranches spanning a gradient of bioavailable  $\text{Cu}^{2+}$ ,  $\text{Zn}^{2+}$  in Texas, USA

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## Brain Mineral Levels by Ranch



Violin plots represent the distribution of samples, the points represent individuals, the horizontal lines indicate the 25%, 50%, and 75% quartiles

## Discussion

- Large gradient in brain  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  levels across South Texas ranches to perform PMCA
- $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  of natural nutrition group consistent with historical soil quality metrics

## Future directions

RT-QuIC

Genotype codon 96S

PMCA

Trace mineral analysis

## Acknowledgements

- Texas ranchers and landowners
- East Foundation and their employees
- Patton Center for Deer Research
- Biorender.com



ABSTRACT