Effects of Panobinostat, a Histone Deacetylase Inhibitor, on NETs Formation in Canine Neutrophils

Stephanie S. Han, Jennifer L. Willcox, Ngii Nguyen, Wan Khoon Avalene Tan, Ronald H. L. Li
Department of Veterinary Surgical and Radiological Science, School of Veterinary Medicine, University of California, Davis, California, USA

Introduction
Neutrophils play an important role in innate immunity by formation of neutrophil extracellular traps (NETosis).

![Fig. 1](image1)

Overzealous inflammation and NET formation can also occur in people, NETs have been shown to contribute to tumor progression and metastasis.

Materials and Methods
Eligibility Criteria:
- Dogs deemed healthy, > 1 year of age, > 10 kg, no vaccination within 30 days of enrollment, no comorbidities or medications
- Normal complete blood count within reference intervals

Results

![Fig. 2](image2)

![Fig. 3](image3)

![Fig. 4](image4)

![Fig. 5](image5)

Conclusion/Future Directions
Conclusions:
- Panobinostat modulated NETosis in canine neutrophils in a dose-dependent manner
- Unlike human neutrophils, panobinostat did not further stimulate NETosis
- Inhibition of NETosis by panobinostat may be secondary to a reduction in histone citrullination

Future Directions:
- Assessment of apoptosis in panobinostat-treated canine neutrophils
- Western blot analysis to evaluate histone citrullination and acetylation
- Future pharmacodynamic studies to assess if panobinostat decreases NETosis in dogs with cancer

Rationale/Hypothesis/Objectives
Rationale:
- Cancer is the leading cause of death in older dogs and new therapeutic options are needed.
- Given the potential role NETs may play in cancer progression, treatment strategies targeting their formation should be pursued.
- This study is the first step to determine if HDACis may reduce NETosis in dogs and provides the basis for future in vivo studies.

Hypothesis:
The HDACi, panobinostat, will dose-dependently modulate NET formation in canine neutrophils induced by phorbol myristate acetate (PMA) or A23187, by inhibiting histone citrullination.

Objectives:
1. Evaluate if increasing concentrations of panobinostat would modulate in vitro NETs formation by PMA or A23187
2. Evaluate if panobinostat inhibits PMA or A23187-induced NETosis by inhibiting histone citrullination

References
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