A Unique Isotope and Targeting Molecule to Treat Equine Laminitis

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Objective

Sn-117m is a unique isotope that emits both a gamma photon which is used in detection and imaging, as well as conversion electron (C.E.) energy that is being used experimentally to treat human inflammatory vascular diseases, and commercially to treat canine osteoarthritis. We have shown that the use of a radionuclide conjugate, such as Sn-117m attached to or linked into a chelating agent and conjugated to a macrophage targeting agent such as annexin V, annexin A1, or T-DPA, is effective at decreasing macrophage mediated inflammation. We postulate that Sn-117m-based products may be developed to treat and image inflammatory conditions such as equine laminitis (EL) in ungulates. EL causes pathological changes in the hoof including separation of the hoof lamina from the coffin bone (pedal bone) leading to long lasting, crippling deterioration in function, and pain for which there is inadequate medical treatment (Figure 1). A radionuclide conjugate may be systemically administered for delivery to the hoof of an ungulate with EL, binding to inflammatory cells of the hoof lamina and reversing the inflammatory destructive laminitis without affecting tissue adjacent to the area of interest. The radionuclide conjugate may include [Sn-117m]-DOTA-annexin V, [Sn-117m]-DOTA-[T-DPA], [Sn-117m]-DOTA-annexin A1 (lipocortin 1). Other chelating agents may be used in place of DOTA.

Materials & Methods

The radionuclide conjugate is infused, such as with a direct arterial injection, into the lateral palmar artery or other vascular infusion methods, to target infiltrating macrophages that exacerbate the relentless inflammatory process underlying laminitis (Figure 2). Administering the radionuclide conjugate is anticipated to ameliorate the inflammatory cycle and allow the tissue to heal. Infusions of the radionuclide conjugate may not only treat the afflicted area but also should allow imaging of the laminitis due to the existence of the Sn-117m gamma photon. Imaging may be performed with a gamma camera or with single photon emission computerized tomography (SPECT). Annexin V is a naturally occurring human protein that binds to specific cell membrane chemicals that are expressed on macrophages that cause the inflammatory conditions in equine laminitis. When conjugated to Sn-117m, the resulting Sn-annexin molecule has been shown to specifically bind to inflammatory cells in human vulnerable plaque and has successfully localized to inflammatory fibrocalcific disease (3). We expect this conjugate to similarly bind to inflammatory cells in equine laminitis and induce apoptosis. Sn-annexin binds to the inflammatory cell outer membrane leaflet onto phosphatidylserine A.

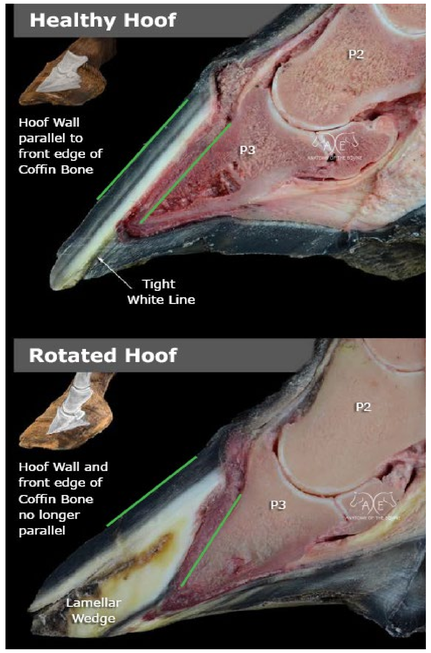

Figure 1. Anatomy of Equine Laminitis. Top panel: Normal anatomy. Bottom panel: Delamination causing separation of the hoof from the coffin bone (1).

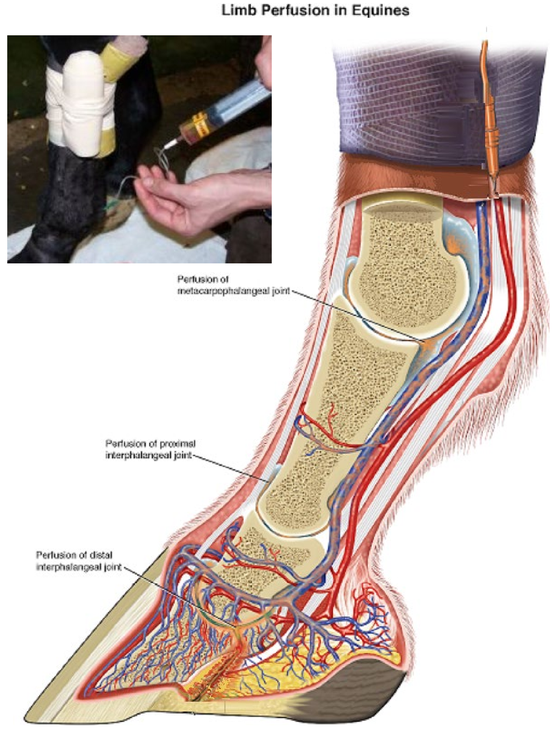

Figure 2. Infusion Into the Distal Equine Limb. A pneumatic tourniquet at 600 mm Hg is placed at the proximal metacarpus and infusion occurs in the lateral palmar artery (2).

Results

Sn-117m was successfully conjugated to a targeting molecule that localizes to the outer cell membrane of inflammatory cells resulting in the apoptotic death of these cells. Inflammation is considered a significant contributor to laminitis, especially at its onset. The systemic injection of our inflammation targeting agent [Sn-117m]-DOTA-annexin V has been studied in several animal models (3). Imaging of human pathologic inflammatory cell collections *in vivo* as well as animal therapeutic trials in inflammatory states suggest that [Sn-117m]-DOTA-annexin V may be used as a laminitis therapeutic agent.

Conclusions

Equine laminitis is a crippling and costly disorder with inadequate therapy despite decades of extensive research. The etiologies of this condition are diverse but in many presentations of laminitis there appears to be an inflammatory component. The active therapeutic agent proposed in this overview is the unique C.E. energy emitted from the isotope Sn-117m. Sn-117m has been successfully chemically linked to an inflammatory cell targeting large molecule (i.e., annexin V) with statistically significant induction of macrophage apoptosis.

References

1) www.anatomy-of-the-equine.com
2) https://inkymousestudios.com/portfolio-item/equine-limb-perfusion-step-3-perfusion-of-the-limb/
3) *"Simultaneous localization and treatment of vulnerable plaque by tin-117m conversion electrons: First-in-human results"*, R Virmani, TCT ('Innovations' session): Oct 22, 2012

Disclosures

All authors are employed by and/or own stock in Serene, LLC