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The role of MMP-1 in equine sarcoids - a potential therapeutic target?

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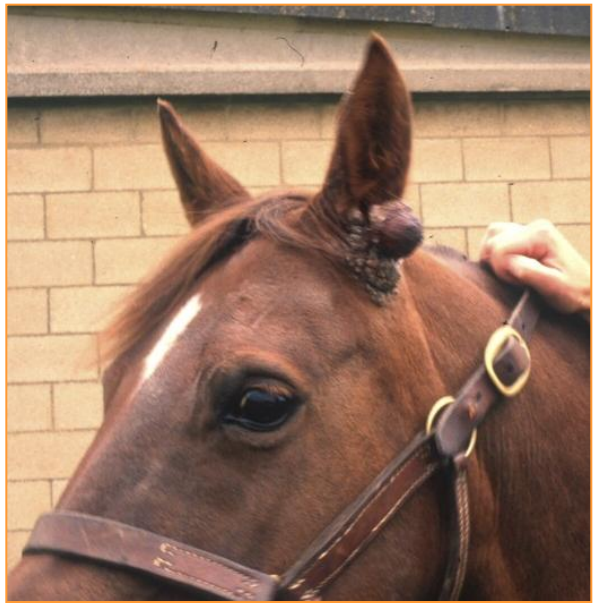
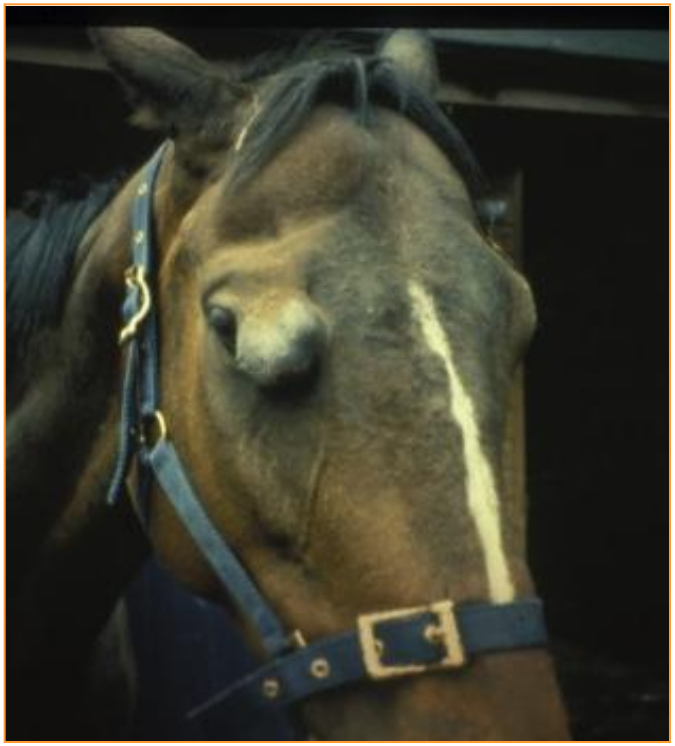
Equine Sarcoids (1)

- Sarcoids are the most common skin tumour in horses.
- The predominant causal agent is Bovine Papillomavirus-1 (BPV-1).
- They can occur as isolated lesions anywhere on the body, although the commonest sites include the face, chest, groin and sheath, or there may be numerous lesions occurring at multiple sites.



Equine Sarcoids (2)

- They do not spread to internal organs but invade and damage nearby tissues and structures.
- The overall effect of sarcoids depends upon the severity of the disease and its location.
- It can also affect the horse's value.



Equine Sarcoids (3)

- The presence of a single sarcoid at any location is an indication of an individual's susceptibility to the disease and the likelihood that lesions will develop elsewhere.

- Over the years, numerous treatment methods have been attempted, such as surgical excision, cryosurgery, BCG injection, topical application of various creams, irradiation and other methods.

- No single treatment has been identified as being universally successful in all cases.

Matrix metalloproteinase (MMP)

- Matrix metalloproteinase (MMP) proteins are naturally occurring enzymes, which are involved in the breakdown of extracellular matrix both as a normal physiological process and also as part of various different disease processes, such as in the development of sarcoids.
- MMP-1, one of the MMP family, has been implicated in the development of sarcoids, specifically the local infiltration of sarcoid cells into surrounding tissues.
- Previous work in our laboratory has shown that there is increased activity of MMP-1 in sarcoid tissue when compared to normal skin tissue.

Reasons for the study

- Does MMP-1 make sarcoid cells more invasive?
- Does *Bovine Papillomavirus type 1 (*BPV-1) increase the levels of MMP-1?
  - If so, by what mechanism?
- Can siRNA inhibit the production of MMP-1?
  - These are a group of agents with antiviral properties that act by blocking viral genes.

What we did

- In our laboratory, we used cellular models (invasion and degradation tests) to assess the invasive nature of sarcoid derived cells lines under different conditions.

What we found

- MMP-1 does enhance the invasive nature of sarcoid cells
- BPV-1 proteins do increase the levels of MMP-1. An activator protein (AP-1) is shown to be crucial in this process.
- The antiviral agents, siRNA, do reduce MMP production resulting in inhibition of invasion and cell growth.

Conclusions

- This study shows that inhibition of viral gene expression by siRNAs is a useful approach for the treatment of equine sarcoids.

- This project gives a clearer understanding of the specific pathological processes and pathways involved in the local invasion of sarcoids and has provided preliminary evidence in the identification of medication for their treatment.