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Are specific changes in mucus biochemistry associated with respiratory dysfunction in the racing Thoroughbred?

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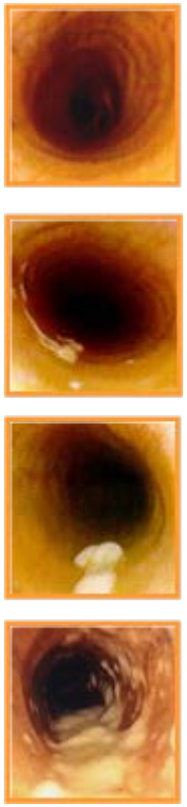
Prj:

Inflammatory Airway Disease (IAD)

- Between 7% and 30% of racehorses are unable to race due to IAD
- Most frequent in young race horses in training – bacterial or viral aetiology
- Underlying problem is mucus accumulation
- Manifests as poor racing performance and failure to train

Mucus score



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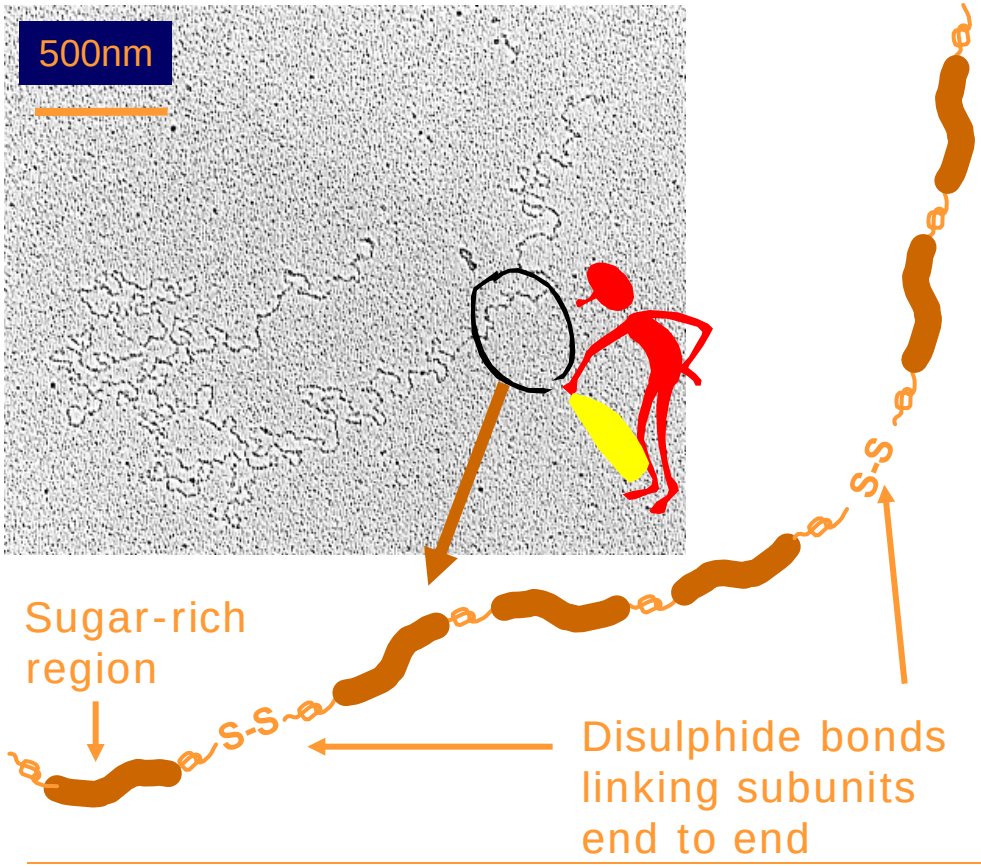
Gel-forming mucins are enormous polymeric glycoproteins



Key features of mucins

- 80% by weight sugar (glycan) – 1000s of glycans attached to a single mucin
- Glycans provide specific binding sites for bacteria and viruses
- Mucins entangle and interact to form mucus gel

Hypothesis and objectives

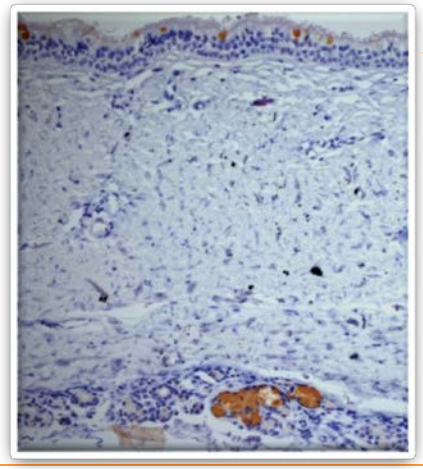
"Gel-forming mucins play a key role in determining the properties of mucus in health and disease"

Our aims were to:

- Identify the major gel-forming mucins in equine airways mucus
- Determine their molecular properties
- Investigate changes in the amounts of the mucins in IAD

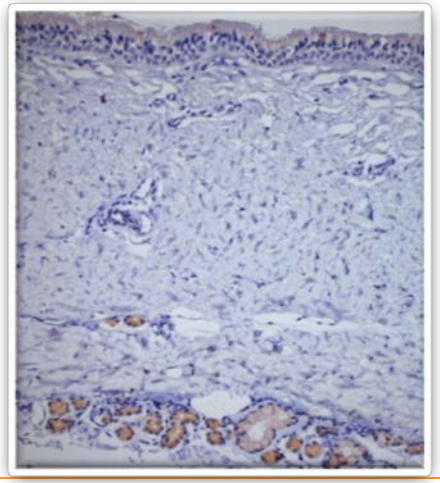
Equine airways mucus is a mixture of mucins

- Airways mucus contains two gel-forming mucins: Muc5b & Muc5ac
- We derived novel antibody probes to Muc5ac and Muc5b
- In the trachea Muc5b and Muc5ac are produced by surface epithelial goblet cells and mucous cells in submucosal glands



◀ Surface epithelium ▶

◀ Submucosal glands ▶

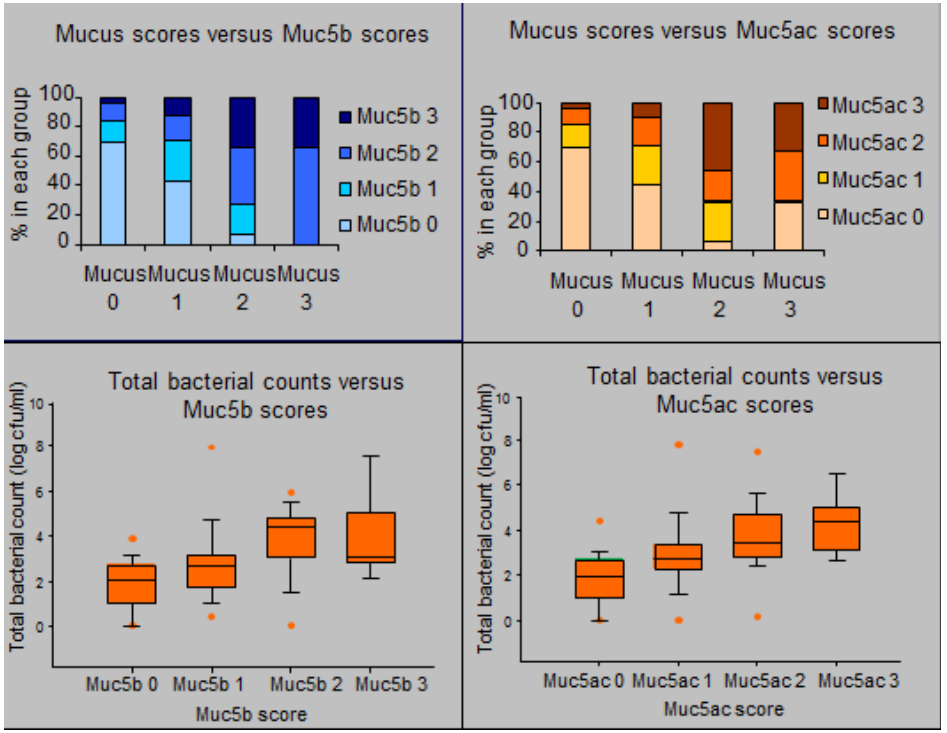


Muc5b

Muc5ac

Gel-forming mucins in IAD

- Muc5ac and Muc5b are increased in IAD
- In most, but not all cases, the amount of Muc5ac and Muc5b correlates with mucus score at endoscopy
- The increase in Muc5b and Muc5ac was significantly associated with bacterial numbers and measures of inflammation



Implications of findings

- Initial evidence that measuring absolute mucin levels provides more information on IAD than traditional endoscopic examination.
- Further study needed to study effects of specific pathogens on mucin/mucus production
- Both the epithelial cells and glands will need to be targeted to reduce mucus production in the airways
- Studies of horses in training are now required to identify whether quantification of absolute mucin levels in tracheal mucus can be used to identify horses at risk of poor performance due to IAD