Investigation of cell free DNA as a biomarker of NETosis in airway lavage samples from horses with neutrophilic asthma

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Equine asthma is an inflammatory disease that causes increased airway mucus, cough and bronchoconstriction. It is highly prevalent, with mild/moderate EA (mEA) reportedly affecting 60-100% of certain groups of horses including young racehorses, and severe EA (sEA) reportedly affecting 10-20% of adult horses in the northern hemisphere. Mild/moderate EA negatively affects the welfare and performance of young racehorses. Retired racehorses, as with older horses of other breeds, can also develop sEA, which has more profound impacts on exercise tolerance, health, quality of life and longevity. Currently, diagnosis of EA relies on sending airway samples to a lab for cellular analysis, which can take several days. More rapid diagnosis could be achieved with the identification of biomarkers that could be measured immediately and on the farm.

Our proposed research will investigate a novel biomarker for neutrophilic EA, with the goal of establishing this biomarker 1. as a diagnostic that can be measured on the farm, and 2. as a potential target for new therapeutic strategies for EA. The novel biomarker is cell-free DNA (cfDNA). Cell free DNA is known to be increased in airway samples from people with asthma because of increased release of neutrophil extracellular traps (NETs). Research has also shown that NETs are increased in airway samples from horses with sEA, but is currently unknown if NETs are increased in airway samples from horses with neutrophilic mEA, and cfDNA measurement has not been reported in equine airway samples. Our study will measure both NETs and cfDNA in airway samples from horses with mEA and sEA and compare them with healthy horses. Excitingly, we will make these measurements with a small, portable and economical device that could one day be used to measure airway cfDNA on the farm. We will also use antibody-based testing to determine whether the cfDNA in equine airways is coming from NETosis, dying cells (apoptosis), or dead cells (necrosis). With the successful completion of this project, we will show that cfDNA is a novel biomarker for neutrophilic EA that can be measured in airway samples on the farm, and we will link airway cfDNA to levels of airway neutrophil activation, which could help to inform future research on novel therapeutic targets for EA. We assert that these outcomes will benefit stakeholders at all levels of the equine industry.