Appendix 5: Lay Summaries of Research Projects for 2021-2022

New Projects:

Arroyo, L. - Improving fecal transplantation in horses: determining optimal conditions for preparation and storage

The development of new DNA sequencing technologies has revealed that the interaction between intestinal bacteria and the host is extremely important to health maintenance. In fact, an altered composition of the intestinal bacteria (called dysbiosis) is present in horses with intestinal diseases such as colitis and colic and during treatment with antimicrobial drugs. The correction of dysbiosis to decrease inflammation and to resolve diarrhea faster. Different methods can be attempted to resolve dysbiosis including probiotics, supplements, or fecal microbiota transplantation (FMT), which is the transferring of all microorganisms and metabolites present in the feces of a healthy donor to a sick patient. FMT has been used with great success in humans and dogs, resolving over 95% of cases of diarrhea in people with Clostridioides difficile infection, which is also a leading cause of diarrhea in horses. FMT has been given to horses with diarrhea, but so far, scientific evidences indicates that FMT is not so efficient in horses. Our preliminary data show that the current recommendations of FMT to correct dysbiosis in horses has no evident impact on the microbiota of horses. This might be related to the fact that FMT cannot be given by enema, as in other species, because of the horse's anatomy and the administration via naso-gastric tube drastically decreases the viability of the transferred bacteria. Furthermore, it has been shown that over 80% of the bacteria present in feces die during FMT preparation because of exposure to Oxygen and freezing. Therefore, increasing bacterial viability in the transplanted solution is fundamental to improve FMT efficacy in horses. The objectives of this study are to optimize bacterial viability of FMT using anaerobic conditions and to identify microbiota patterns associated with higher resistance to storage.

Arroyo, L. - The longitudinal development of the fecal microbiome and metabolome in neonatal foals

Neonatal diarrhea is a common occurrence in foals that can develop into a life-threatening condition. However, at present the etiology is poorly understood and it is unclear why diarrhea progresses in some foals whereas others recover without additional symptoms. The microbial environment within the neonatal gut rapidly becomes colonized following birth. However, several factors influence the particular microbes that are present such as location, maternal diet, and even breed, making comparisons between individuals challenging. Therefore, the metabolic activity of gut microbes may provide a more analogous comparison and improve our understanding of bacterial function at this critical stage of gastrointestinal development. Integrating both microbial and metabolic data will enable a comprehensive understanding of how the gut environment matures in horses and what key aspects denote health. This research will also begin to reveal potential deviations from health that occur during critical bouts of diarrhea in foals. Understanding the gut microbial development in foals will advance the field of equine neonatal care and move it towards personalized treatments and therapeutics.

Arroyo, L. - Comparative Anatomy: Equine Pulmonary Arterial Structure and Function

During their career, more than 80% of racehorses can be expected to develop Exercise-Induced Pulmonary Haemorrhage (EIPH). This disease, which occurs mainly in the most upper and rearward region of the lungs, is characterized by blood leaving the microvasculature of the lungs and entering the airways. The management and treatment of EIPH has a substantial economic impact to the equine industry, with the cost of treating EIPH estimated to exceed $100 million annually in the United States alone. The cause of EIPH has not been determined, consequently current treatment and mitigation measures are empiric and speculative. There is intense interest

in understanding the relationship between the anatomy and mechanical properties of the large arteries and the manifestation of microvascular diseases in humans. Arterial anatomy and elasticity determine the nature of the pulse wave which transmits pulsatile energy to the microvasculature. Pulse wave energy transmission is viewed as a fundamental aspect underlying the development of microvascular diseases. Studying the pulse wave in horse lungs is an important step in understanding what causes EIPH and will improve the potential to develop effective treatment outcomes and mitigation strategies. Detailed knowledge of the physical dimensions (anatomy), mechanical properties (strength, elasticity) and structural composition of arteries is required. This information is poorly described or unknown for the equine pulmonary vascular system. Comparative information between these properties in lung regions typically affected and unaffected by EIPH will be obtained from five horses and analysed for differences which will guide continued research into the cause of EIPH.

Gomez, D. - Enteroinsular axis in healthy horses and horses with gastrointestinal diseases during hospitalization

Endotoxemia are conditions where bacteria and their products gain access to the blood and set up widespread infections, often leading to death. Consequences of sepsis and endotoxemia include organ failure, loss of hormonal control, and metabolic/electrolyte derangements, including high glucose (hyperglycemia). These abnormalities are linked to severity of illness and death. Recent research has shown that hormones from the intestine (known as incretins) are important to control glucose levels and the ability of the pancreas to produce insulin. However, there is no information on the incretins in horses with gastrointestinal disease. The goal of this study is to investigate incretins (GLP-1, GLP-2, GIP) and insulin in healthy horses and horses with colic and diarrhea and determine their association with clinical findings, severity of disease, and likelihood of mortality. This information will have clinical implications in the diagnosis, treatment, and prognosis of critically ill horses.

Koch, T. - Mesenchymal stromal cells for the treatment of equine tendonitis

Tendon and ligament injuries are common in the equine athlete. These types of soft tissue injuries result in significant economic loss to the equine industry each year as a result of decreased performance prolonged rehabilitation, and recurrent injury. Even though tendons do heal with rest, the fibroelastic scar tissue formed is functionally deficient in comparison to more flexible tissue of normal tendons. The result is compromised performance of the horse and high re-injury rates.
Currently, tendon injuries are treated in numerous ways including simple lay-off and rest, controlled rehabilitation exercise programs, shock-wave therapy, and biologics such platelet rich plasma and so-called stem cell therapies to name the most common therapies. This range of treatments reflects that no treatment has proven superior, and that adequate tendon repair remains an unmet clinical need. Culture expanded mesenchymal stromal cells (MSC) have shown promise in reducing the re-injury rate in horses suffering from tendonitis. Improved MSC efficacy may be achieved by extending the dwell time of the cells within the tendon tissue. This has the prospect of healing more horses and extending the careers of more horses suffering from tendon injuries. Improved MSC efficacy may be achieved by extending the dwell-time of the cells within the tendon tissue. Hyaluronic acid (HA) is used to extend dwell-time of cells within synovial joints. This increased dwell-time is expected to be associated with increased inflammatory modulation within the tissue and improved tissue healing.

Koenig, J. - Mesenchymal stromal cells for the treatment of equine osteoarthritis

Mesenchymal Stromal Cells (MSC) has been shown to alleviate pain in mild to moderate osteoarthritis (OA) of the fetlock joint. To date, these cells have been from single donor animals which makes the therapeutic response less standardized. We hypothesize that equine umbilical cord blood (eCB) MSC are safe and effective in treating joint pain and inflammation in an injury-

induced equine model compared to placebo treatment. Our objectives are: 1) To compare the clinical safety and efficacy of eCB-MSC with that of saline in an equine fetlock-chip model; 2) To compare joint response to treatment on a molecular level to gain insights into possible mode of action of the eCB-MSCs. These feasibility studies will be conducted in research horses, and the horses will be returned to the research herd upon completion of the study. We expect that the tested cell formulation will not trigger significant adverse reactions following multiple injections. These results will set the stage for testing in horses with lameness due to fetlock OA.

Valverde, A. - Comparison of two intraoperative lidocaine constant rate infusions on cardiorespiratory function and quality of recovery in healthy isoflurane-anesthetized horses undergoing elective surgery

Delivery of general anesthesia using a combination of at least 1 injectable anesthetic drug during maintenance with inhalational anesthetics is nowadays very common in equine anesthesia and known as balanced anesthesia or partial intravenous anesthesia. Reduced doses of individual anesthetic drugs are possible with balanced anesthesia techniques because of synergistic or additive effects between the different drugs and often result in better analgesia and relaxation, less cardiorespiratory depression, and in horses may contribute to a better quality of recovery.

Anesthetic mortality in horses is the highest among domestic species and recent studies show that most of the fatal outcomes occur in the postoperative period, including the recovery phase from anesthesia; therefore, the impact of intraoperative anesthetic drugs on the quality of recovery should be thoroughly considered.

Lidocaine, routinely used intraoperatively in balanced techniques, has a sparing effect on the required concentration of inhalational anesthetic through analgesic and central nervous depression effects, which promotes a more stable cardiorespiratory function and a lighter plane of anesthesia. A negative association of lidocaine with the quality of recovery can outweigh these benefits by causing ataxia and visual dysfunction, especially if the infusion of lidocaine is not stopped for at least 30 minutes before the end of surgery, since plasma and tissue concentrations can be high at the time the horse attempts to recover and interfere with motor function and coordination. This study will investigate the feasibility of a higher rate of lidocaine and its effects during anesthesia and the recovery period.

zur Linden, Alex - Equine Pulmonary Biopsy: Improving Safety and Efficacy

Percutaneous lung biopsy is a common method for obtaining diagnostic samples of lung tissue abnormalities in humans and other species. Due to blood vessels and airways that run throughout the lung tissue, complications can arise due to puncture of high flow structures during biopsy. Currently there has been no characterization of the detailed branching of either airways or blood vessels within the equine lung. Because anatomy differs between individuals, and anomalies of anatomy may occur, a preventative strategy will further increase safety of the procedure. Filling the biopsy tract with a material to reduce bleeding and air leakage, shows promising results but is not yet standard practice. By using data collected from dissection and multi detector computed tomography (MDCT) of cadaver horse lungs, we plan to elucidate the paths of major vessels and airways within the equine lung. Correlation of regions of minimal functional importance with external anatomical landmarks on adult equine cadavers will allow us to make recommendations on the safest locations for biopsy. These recommendations will be provided as landmarks easily identified by clinicians to improve the safety of the procedure in adult horses, which due to size, must be performed without imaging guidance. Development of a preventative step following biopsy will begin with testing gel foam embolization techniques for air and blood leakage in ventilated and perfused cadaver lungs. We hypothesize that greater anatomical knowledge, recommendations for biopsy locations, and preventative strategies will increase the safety and efficacy of blind percutaneous lung biopsy in horses.