Mapping the equine cardiac channelome – elucidation of molecular targets of electrophysiological function in horses with and without cardiac rhythm abnormalities

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Horses have a unique ability to dramatically alter their heart rate to cope with increased energy demand, with 7-8 fold increases at peak exercise performance. Such increases in heart rate are unattainable in other mammals, where they would be considered damaging, with a very high likelihood of mortality. The electrical excitability of the heart plays an important role in modulating its activity and in providing this unique capacity to cope with strenuous exercise. However, the mechanisms by which electrical activity is controlled are unknown in the horse.

Each year horses die on the racetrack, leading to public outcry and negative publicity for the equine racing industry. Irregular heart rhythms are an important cause of sudden cardiac death (SCD) in horses. In humans, these abnormal rhythms are typically associated with alterations in ion channels (particularly their number and location within the heart), which conduct electrical activity across the heart. Human investigations have focused on understanding these ion channels in healthy humans and humans with abnormal heart rhythms, in order to produce novel and more effective drugs. However, this important knowledge is not available to equine veterinarians and researchers.

Here we will use advanced molecular methods to study ion channels and how there are distributed across the entire equine heart and compare hearts from horses without abnormal rhythms to those that have abnormal heart rhythms. We will then correlate this with the different ways the proteins are made, modified and regulated in the different areas of the heart to determine how the path of conduction is altered to cause the rhythm abnormality.

This will enable us to identify the specific changes which occur in those genes and proteins responsible for cardiac conduction in horses and determine how this influences the function of the heart. This will vastly increase our knowledge of these critically important channels, and will lead to improved ability to diagnose, treat, and prevent potentially fatal dysrhythmias in horses The ultimate aim of the research will be to fundamentally better understand how the horses' heart functions allowing for better management, prevention and treatment of disease and conditions related to the equine heart, particularly those linked to SCD. Given the importance of reducing the rate of SCD for the equine industry, this study represents a critical first step to understanding why certain horses develop dysrhythmias. Ultimately, this proposal is a key first step to reducing the rate of SCD in equine athletes.