Developing novel tools towards the reduction of antibiotic usage and against antimicrobial resistance in equine infection, by using stem cell approaches

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Alarming messages from WHO, and various other entities around the world, alert to the urgency of implementing strong measures towards effective reduction on the usage and dependence of antibiotics to treat bacterial infections, in order to combat the global growing problem of antimicrobial resistance (AMR). At the current pace, loss of antimicrobial efficacy, namely to treat infections caused by multidrug-resistant bacteria (MDR) which are resistant to multiple antibiotics, is set to have major impact on thoroughbred health and welfare in the future, as currently treatable infections may become life-threatening, and veterinarians are increasingly aware of this grave problem. To ensure good veterinary practice and the welfare of the horse while addressing this challenging issue, it is essential that new anti-infective therapies are developed. This is true for infections affecting the thoroughbred, including respiratory, such as strangles, which is highly contagious and difficult to eliminate in carrier animals, and those leading to low performance and loss of training time in the racing horse or associated with post-operative complications.

This proposal aims to explore the potential of Mesenchymal Stem Cells (MSCs) products, an established therapeutic tool, as novel anti-infectives. This will be achieved by testing the antimicrobial effects of conditioned media from equine MSCs (MSC-CM), which is the MSC cell culture medium, both alone and in the presence of common antibiotics used in veterinary practice (penicillin, amoxicillin, trimethoprim sulphonamides and gentamycin), against relevant pathogenic bacteria (Streptococcus equi and Streptococcus zooepidemics, Staphylococcus aureus and Escherichia coli), using susceptible bacteria to antibiotics and AMR/MDR isolates of each species. Analysis of the protein content of the MSC-CM will be carried out to identify key molecules underpinning the effects of MSC-CM, providing relevant information on the antimicrobial mechanisms of these preparations, and on specific effectors that can be used in future studies for standardization and improvement of preparations.

The findings of this project will provide the basis for larger studies to test the efficacy of MSC-CM preparations in the context of clinically relevant infections in equine patients. This will provide an important step-forward towards our ultimate aim of developing commercial MSC-based cell-free preparations as effective off-the-shelf anti-infectives that can help reducing antibiotic usage and address the serious emerging problem of antimicrobial resistance in horses.