



PREVENTION AND TREATMENT OF OSTEOMYELITIS USING LOCALLY ADMINISTERED VANCOMYCIN IN AN IN-VIVO RAT MODEL

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Osteomyelitis (i.e., bone infection), caused by methicillin-resistant *Staphylococcus aureus* (MRSA) bacteria, has traditionally been treated with systemic administration of vancomycin. However, typical intravenous injections have their problems. When vancomycin is systemically administered, it is filtered out of the circulatory system quickly by the kidneys and in order for the vancomycin to maintain a therapeutic concentration, more vancomycin has to be injected. If the concentration of vancomycin is too high the drug becomes toxic to the kidneys (i.e. nephrotoxic) and the patient can suffer from renal failure. In order to resolve these problems, we hypothesized that high concentrations of locally administered vancomycin would prevent and treat osteomyelitis without resulting in high toxic levels of the drug in the circulatory system.

To test this, *in-vivo* rat models were used. To determine the effectiveness of locally administered vancomycin to prevent the development of osteomyelitis, we inoculated rats with *Staphylococcus aureus* in their tibia and either: simultaneously treated half with local delivery of vancomycin (i.e., intraosseously), or left the other half with their inoculated tibias untreated. We found that the rats treated with the vancomycin locally, remained 'uninfected' at the end of the study. However, rats that were not treated developed osteomyelitis within 2 weeks. The presence of bacteria in the bone was confirmed through bioluminescent imaging, and osteomyelitis was determined using X-ray imaging. Treated rats had no bioluminescence from the bacteria whereas those left untreated did. High-performance liquid chromatography (HPLC) analysis of the explanted bone, muscle, and blood from the treated rats showed that vancomycin was only found within the bone therefore showing that this type of treatment has the potential to reduce undesirable side-effects from this antibiotic.

To determine the effectiveness of locally administered vancomycin to treat osteomyelitis, we tested to see if it could treat a *Staphylococcus aureus* infection that had been allowed to develop in the rat tibia for 2 weeks. Once the infection develops, half of the rats would be treated with local vancomycin (i.e., intraosseously) and the other half would be left untreated. Preliminary results from this study show the bioluminescent imaging of the rats treated with vancomycin have very little to no bioluminescence. However, the rats that have been left untreated have a lot of bioluminescence. The study period for this model is 42 days post infection and we are still in the middle of our investigations. We anticipate obtaining all results for this study by the end of next semester.

