## COMBATTING FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

# Sustained Delivery Of Vancomycin Over Time Using Quickgel Click Hydrogel For The Treatment Of Surgical Site Infections

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Background: Surgical site infections (SSIs) are significant complications post-operatively, leading to increased mortality and healthcare costs for the wounded warfighter and civilian patients. Current systemic antibiotic treatments are cleared from the body within 2 hours and often fail due to impaired drug delivery at the surgical site with limited access to deep musculoskeletal tissues. Methicillin sensitive Staphylococcus aureus (MSSA) and Methicillin resistant Staphylococcus aureus (MRSA) are common causes of SSIs and are sensitive to vancomycin. Vancomycin cannot be administered orally and is usually administered intravenously. Current surgical practice includes packing vancomycin powder directly into the surgical site prior to closure. No product yet exists to provided sustained, localized, and controlled antibiotic release targeted to a surgical space. We have developed an injectable, biorthogonal, PEG-based Cu++-free click chemistry hydrogel that rapidly polymerizes (QuickGel) in situ to provide a tunable and sustained localized delivery of biologic agents. Purpose and Objective: This study evaluates the effectiveness of injectable QuickGel, a novel PEG-based, biodegradable hydrogel, for localized, sustained antibiotic delivery in the prevention of SSIs. Rationale: The injectable QuickGel is cleared from the body in 5-7 days in mice. This gel is space-filling and rapidly polymerizes without the generation of heat or toxic products. The unique biocompatible and biodegradable properties of QuickGel enable direct application and sustained release of antibiotics to surgical sites, potentially overcoming the limitations of systemic antibiotic delivery. Currently, there are no FDA-approved products that offer localized and sustained antibiotic release to musculoskeletal soft tissues. Methods:
-In Vitro: The hydrogel's ability to release antibiotics was assessed in vitro. The release of vancomycin from the hydrogel was tested using a Kirby Bauer Disc Inhibition assay against MSSA and MRSA. The release kinetics of vancomycin were determined using a spectrofluorometric measurement of vancomycin concentration.
-In Vivo: A rat muscle pouch model was used to model SSIs infected with MRSA. The hydrogel incorporated with vancomycin was applied into the pouch to evaluate infection prevention over 14 days. Preliminary Results: In vitro assays demonstrated complete release of vancomycin within 24 hours, achieving effective inhibition zones. The in vivo rat study will demonstrate if there is significant reduction in infection rates in treated subjects compared to controls. Preliminary Conclusions: QuickGel Click Hydrogel effectively delivers and sustains antibiotic levels at the surgical site, indicating its potential to significantly reduce SSIs. The hydrogel is injectable and space-filling, offering promising attributes for use in complex wounds.
Impact: This technology aligns with the DTRA JSTO mission to enhance the Joint Force’s capabilities by potentially reducing the incidence and severity of infections in post-surgical recoveries, thereby improving warfighter health and readiness. This study has economic and health implications for the wounded warfighter as well as for civilian patients. Future Directions: Further studies will focus on optimizing hydrogel formulation for various surgical applications and expanding antibiotic choices.

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