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"Investigating the feasibility of utilizing bacteriophages as a novel diagnostic platform for the rapid detection of slow growing organisms causing peri-prosthetic joint infections"

Periprosthetic joint infection (PJI) is the leading cause of failure after total joint replacement. Rapid and accurate detection of the organism causing the infection is crucial to achieve a successful treatment. The current gold standard method to diagnose PJI is to sample tissue surrounding the infected implant then culture it to detect bacterial growth. The conventional method of tissue culture has a limited sensitivity of up to 10-20% of infections being "false-negative" cultures. This low sensitivity can be caused by slow growing pathogens that are difficult to culture, such as *Cutibacterium acnes* (*C. acnes*). *C. acnes* is reported in over 24% of infections related to implanted medical devices and in 0.9–1.9% of PJI cases. *C. acnes* also requires up to 14 days to grow in culture. Delayed diagnosis leads to implant failure, sepsis and chronic pain. Alternative non-culture base molecular and proteomic strategies, such as next generation sequencing, are currently available. However, they rely on identifying genetic or molecular byproducts of the pathogen. These methods have their limitations due to their inability to distinguish between live or dead bacterial cells. Therefore, exploring new diagnostic platforms that don't rely on culturing and that are more sensitive and accurate in detecting viable bacterial cells can help improve treatment outcomes. Bacteriophages (phages) are naturally occurring viruses that specifically infect viable bacterial cells and can differentiate between various bacterial species and strains. Phages can also be modified to express fluorescent or luminescent markers to enhance the detection of bacterial cells [11,12]. In the food industry, phages have shown to be a reliable and rapid diagnostic tool in detecting the presence of low bacterial counts in processed food products [8, 13]. Overall aim of this proposal is to provide preliminary scientific proof of principle that it is feasible to utilize phages as a diagnostic tool to detect slow growing and difficult to culture bacterial infections, such as *C. acnes*. The long-term aim of this research proposal is to design a high-throughput diagnostic platform that utilizes phages as an adjunct tool to current diagnostic methods to improve the rapid detection of difficult to diagnose organisms. *Model organism:* *C. acnes* has been selected as the pathogen of choice for this study due to its relative prevalence in causing culture-negative PJI. Further research is also required to build the diagnostic capacity of this reporter phage platform to identify organisms causing polymicrobial infections.