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Title: A Vaccine Targeting Urinary Tract Infections using SimCells, Safe, genome-free, non-replicating bacteria cells with high immunogenicity

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Globally, Urinary Tract Infections (UTIs) affect over 400M people each year and cause around 237K deaths. Associated treatment costs exceed €6B annually. Despite a clear clinical need for vaccines against UTIs, no FDA or EMA-approved vaccines are currently available. Consequently, 15% of antibiotics prescribed in the US and EU are to treat UTIs, exacerbating the global spread of antimicrobial resistance. Here, we described a proof-of-concept study to manufacture a UTI vaccine using SimCell technology. SimCells are genome-free bacterial cells that can be used as a safe and immunogenic inactivated whole-cell vaccine. We produced *Escherichia coli* SimCells at lab scale with a purity of <1 viable cell per 1 billion SimCells. Nucleic acid staining and qPCR revealed that SimCells contain significantly less DNA than their wild-type counterparts. Analysis by SDS-PAGE and SEM suggests the genome-shearing process involved in SimCell production better preserves cellular proteins and surface features compared to conventional bacterial inactivation methods, such as chemical, thermal, or irradiative inactivation. In an *in vivo* immunogenicity study, *E. coli* SimCells were administered via intravenous and intramuscular routes to immunocompetent mice. Mice administered with *E. coli* SimCells produced significantly higher *E. coli*-specific antibodies compared to the vehicle control. This study lays the foundation for the development of a human *E. coli* vaccine and demonstrate the potential of SimCells to act as effective vaccines against AMR pathogens for which antibiotic countermeasures do not exist.