Docket #: S22-258

Nanoparticle agent to eradicate drug resistant bacteria in the growth arrest phase

Stanford researchers have developed a method to eliminate antibiotic resistant gram-negative bacteria in the growth arrest phase. The increase in relapsing bacterial infections and the rise of drug resistant bacteria are significant global health problems. Stanford researchers in the Santa Maria Lab have developed a gold nanocluster (AuNC) functionalized with adenosine triphosphate (AuNC@ATP) that kills drug-resistant (XDR) strains of E. coli, K. pneumoniae and P. aeruginosa in vitro. This nanoparticle eradicates bacteria in the growth arrest phase by disrupting cytoplasmic Mg2+ homeostasis through augmentation of Mg2+-chelating ATP at a non-physiological cytoplasmic concentration. The AuNC is also expected to inhibit FtsH proteolysis activity. Initial gastrointestinal safety studies of AuNCs coated with either hydroxyl (AuNC@PEG-OH)- or amine (AuNC@PEG-NH2)-functionalized poly(ethylene glycol) indicate the gold nanocluster is non-toxic. Stanford research of this promising antimicrobial nanoparticle is ongoing.

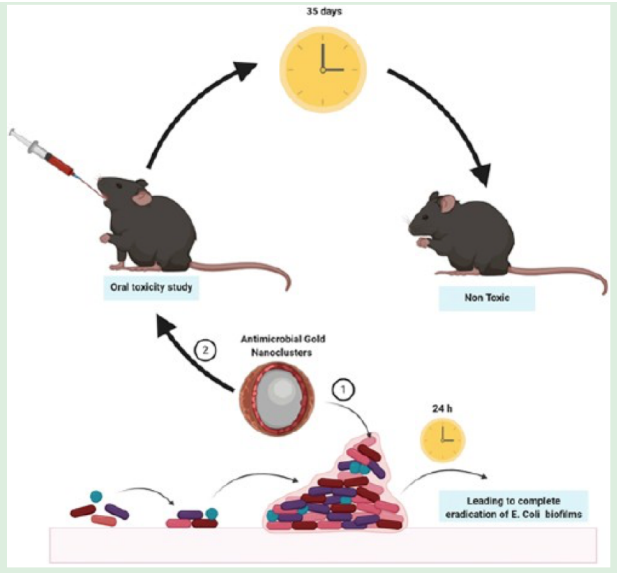

Image courtesy the Santa Maria Lab

Stage of Development – Pre-Clinical
Researchers continue to develop strategies to prevent relapse in chronic bacterial infections and evaluate the potential for antibiotic resistance development. Safety and in vivo efficacy studies are ongoing.

Applications

- **Treatment of chronic (gram-negative) bacterial or fungal infections** such as, tuberculosis, cystic fibrosis lung infections, middle ear infections, chronic skin wounds, urinary tract infections or a biofilm associated infections (e.g., catheter-associated infections, central line-associated infections, endotracheal tube-associated infections, implantable devices-associated infections including prosthetic joint infections)
- Cancer treatment - support antitumor immunity

Advantages

- Gold nanocluster functionalized with adenosine triphosphate (AuNC@ATP) exhibits **excellent antimicrobial activity against growth arrest cells and kills drug-resistant (XDR) strains** of E. coli, K. pneumoniae and P. aeruginosa in vitro.

- **Less adverse side effects** than other anti-cancer drugs re-purposed to treat chronic relapsing bacterial infections.
- **Potential to reduce cytotoxicity of certain cancer treatments** – prevents premature degradation of ATP, and thereby lowers dosage required.

Publications

- Cao, Z., Chen, J., Tran, J., Chen, X., Bacacao, B., Bekale, L. A., & Santa Maria, P. L. (2020). Antimicrobial gold nanoclusters eradicate Escherichia coli biofilms and are nontoxic by oral administration. *ACS Applied Bio Materials, 3*(8), 5275-5286. https://doi.org/10.1021/acsabm.0c00641

Patents

- Published Application: WO2024044636

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