Mycobacterial Diseases
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Commentary

Photonic Advances in Mycobacterial Disease Management

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DESCRIPTION

TB, other mycobacterial species like *Mycobacterium smegmatis* are often studied as model organisms due to their genetic and physiological similarities to *Mycobacterium tuberculosis* *Mycobacterium tuberculosis (M. tb)*. Traditional treatments for mycobacterial infections rely heavily on antibiotics, which are increasingly compromised by the emergence of Multidrug Resistant (MDR) and Extensively Drug Resistant (XDR) strains. This underscores the urgent need for alternative therapies that can effectively target mycobacteria. One promising approach is Photodynamic Therapy (PDT), which employs light to inactivate microorganisms. Among the various wavelengths explored for photoinactivation, Near Infrared Radiation (NIR) has garnered attention due to its deep tissue penetration and minimal damage to surrounding tissues. Recent research has demonstrated that NIR radiation can effectively inactivate bacterial pathogens, including mycobacteria, either alone or in combination with photosensitizing agents.

Mechanism of photoinactivation and efficacy against mycobacteria

Photoinactivation through NIR radiation leverages photothermal and photochemical effects to disrupt bacterial cell integrity. While bacteria are generally less susceptible to direct photothermal damage due to their small size and limited capacity to absorb NIR wavelengths, the introduction of exogenous photosensitizers can significantly enhance their vulnerability. Photosensitizers are molecules that absorb light energy and transfer it to molecular oxygen, generating Reactive Oxygen Species (ROS) such as singlet oxygen and free radicals. These ROS inflict oxidative damage on essential cellular components, including lipids, proteins, and DNA, ultimately leading to cell death. Mycobacteria possess a unique cell wall structure rich in mycolic acids, which confers robustness against environmental stress and antimicrobial agents. This characteristic also makes them challenging to target with conventional therapies. However, NIR radiation, especially in the presence of photosensitizers, has shown potential in overcoming these barriers. Studies have demonstrated that NIR radiation at specific wavelengths (typically between 700-900 nm) can effectively inactivate *M. tb* and *M. smegmatis*. In these studies, photosensitizers such as porphyrins, phthalocyanines, and phenothiazines have been employed to enhance the photoinactivation process. Upon NIR exposure, these agents generate ROS that compromise the integrity of the mycobacterial cell wall and membrane, facilitating the entry of light energy and further accelerating microbial inactivation.

Advantages and challenges of NIR photoinactivation

NIR radiation penetrates tissues more deeply than visible light, enabling its use for treating infections located in deeper tissues or organs. Unlike antibiotics, photoinactivation relies on physical and chemical mechanisms rather than specific molecular targets, reducing the likelihood of resistance development. By using photosensitizers that preferentially bind to bacterial cells over host cells, NIR photoinactivation can achieve selective microbial killing with minimal collateral damage. NIR photoinactivation can complement existing antibiotic therapies, potentially lowering required drug doses and mitigating side effects. Despite its potential, NIR photoinactivation faces several challenges, include determining the ideal NIR wavelength, intensity, and exposure duration is important to maximizing efficacy while minimizing potential damage to host tissues. Ensuring efficient delivery and retention of photosensitizers at infection sites remains a technical hurdle. Nanotechnology-based carriers and targeting ligands are being explored to address this issue. Although NIR radiation is generally considered safe, excessive exposure or inappropriate dosages may cause thermal damage to surrounding tissues. Photoinactivation systems involving specialized light sources and photosensitizers may be costly, limiting their widespread adoption, particularly in resource-limited settings where TB prevalence is high. To fully realize the potential of NIR photoinactivation against mycobacterial infections, several areas of research need to be prioritized, understanding the precise molecular mechanisms underlying NIR-induced bacterial inactivation will help refine treatment protocols and identify

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synergies with existing therapies. Rigorous clinical studies are needed to evaluate the safety, efficacy, and feasibility of NIR photoinactivation in treating TB and other mycobacterial infections. Designing photosensitizers with higher specificity, efficiency, and biocompatibility will enhance the practicality of NIR photoinactivation. Combining NIR photoinactivation with advanced diagnostic tools like imaging techniques can enable real-time monitoring of treatment efficacy and infection clearance.

CONCLUSION

The photoinactivation of M *.tb* and M. *smegmatis* using near-infrared radiation represents a promising alternative to traditional antimicrobial strategies. Its non-invasive nature, deep tissue penetration, and ability to mitigate resistance development make it a compelling option for addressing the global challenge of TB and other mycobacterial infections. While there are challenges to overcome, ongoing advancements in photodynamic technology, materials science, and microbiology are likely to pave the way for its clinical application. As research progresses, NIR photoinactivation has the potential to become a transformative tool in the fight against mycobacterial diseases.