Nanotechnology: Targeting Tuberculosis in the Developing World

1. INTRODUCTION

The introduction of nanotheranostics, a combined therapeutic and diagnostic system for use in personalised medicine, has shown promise. Success has been demonstrated tackling some cancers with the use of nanoflares and targeted drug delivery [1]. This has encouraged the application of this technology for other diseases. This essay will explore and analyse the potential effectiveness of nanotechnology targeting typical third world diseases, with specific reference to mycobacterium tuberculosis (TB).

2. CLINICAL NEED

According to the World Health Organisation (WHO) [2], 10 million people were afflicted with TB in 2018. Over 95% of cases and deaths occurred in developing countries, with 87% of new cases occurring in high burden countries, situated in Asia and Africa. With mortality rates at 15% in 2018, and multi-drug resistant strains of TB emerging, global efforts to eradicate TB have always been strong [2]. Despite this, reductions of TB cases have only been at 2% in recent years, with significant increases needed to meet the 2030 Sustainable Development Goal of eradicating TB [2].

3. CURRENT TESTING

Assuming a patient contracts TB and their immune system is unable to eliminate it; two possibilities follow. The first is that the bacteria are controlled in a dormant state, known as latent TB infection (LTBI) [3]. The second is that the LTBI is not controlled and becomes active TB; this happens in 10% of LTBI cases. Two approaches are available for diagnosing LTBI, the tuberculin skin test, and the interferon-γ release assay [3]. Both tests rely on an immunological response from memory cells, though the latter is more practical as the result given is specific to TB bacteria alone [3].

Active TB would be identified most commonly using the Ziehl-Neelsen strain stained smears and conventional light microscopy from patient sputum samples [3]. As a low-cost method that achieves results quickly, this is a WHO forefront control strategy. However, the sensitivity of this test, compared to conventional fluorescent microscopy is low, but the latter is a more expensive option and unlikely to be adopted in the developing world due to the need for expensive equipment [3]. X-rays have also been used to diagnose TB, as sputum testing is often stigmatized [4].

Rapid and accurate TB testing would notably reduce deaths, decrease transmission, and allow for better patient care in a timely manner. Progress in molecular science has shown potential for rapid diagnosis using nucleic acid probe kits that can identify mycobacteria in culture [3]. Several medical devices have also made use of silicon semiconductors successfully, leading to more interest in low cost production using the same [5]. Similarly, the encouragement of 400,000 potential lives saved, in the developing world from rapid TB testing, has led to research exploring inexpensive sensor arrays for metabolomic profiling, that would allow for disease detection through non-invasive means [6].

4. CURRENT TREATMENT

Treatment is dependent upon the pathogenic strain, of which there are three types; drug susceptible, multi-drug resistant, and extremely drug resistant. First line drugs include ethambutol, isoniazid, pyrazinamide, and rifampicin [7]. Second line drugs include fluoroquinolines and injectables, including

aminoglycosides [7, 8]. First line drugs are for the treatment of the first two strains, while the second line differentiates between the second and third strain [7]. Treatment for all three strains is extensive, with a minimum therapy time of six months [7, 8].

In the developing world, the therapies available for TB, have been relatively unsuccessful. Poor compliance from patients is a substantial challenge [9]. The high frequency and high doses required, due to deficient bioavailability of the drugs, prolongs the treatment and therefore, the negative side effects of the drugs. On an institutional level, drug research and development for poverty linked diseases is not at adequate levels to effectively respond to the impact from the diseases [9].

5. NANOTECHNOLOGY APPROACHES

Nanotechnology refers to technology in the order of one billionth of a metre. Converging this with modern biology has given rise to nanobiotechnology and subsequently nanomedicine [10]. This has allowed healthcare interventions in both the diagnostic and therapeutic field to interact with the human body at the atomic and molecular level, using specialist systems designed at this level [10].

Current limitations with regular therapy approaches include poor retention, limited cellular penetration, and low bioavailability. The need for targeted drug delivery for sustained periods of time and cell membrane barrier removal is paramount to the future of healthcare [11].

The use of nanoparticles in drug development has shown success, with biocompatibility being overcome via a number of materials. These include polymethacrylic acid, poly (lactic-co-glycolic acid) (PLGA), and a number of natural polymers such as lipid, silica, and chitosan [11]. PLGA has been researched further and has demonstrated favourable biodegradability, mechanical properties, and degradation kinetics [11]. Its potential use in targeted drug delivery for TB is immense, as its been used to safely encapsulate some anti-cancer and anti-bacterial drugs. [12]. This suggests it can be extended to TB specific drugs too, thereby improving therapeutic efficacy and minimizing side effects as less drug is required.

Using nanoparticles has the potential to eliminate other challenges affecting effective TB therapy. [13]. Some metal nanoparticles, like graphene/zinc oxide nanocomposites, have shown effective antimicrobial properties that also help in stopping the formation of biofilms, which enhance microbial resistance [13]. However, cytotoxicity concerns over nanoparticles and uncertainty over TB drug behaviour at the nano level has slowed the wider acceptance of nanotechnology therapy methods [11, 14].

Present barriers to diagnostics comprise of stigma, time taken with results, and lack of resources for improvement. The nanotechnology approach offers diagnostic bio-nano-sensors [10]. These can sense biochemical or biophysical signals relating to diseases at molecular or cellular levels. These could be used both in vitro and in vivo offering more accurate diagnostic information [10]. The greater sensitivity and significantly reduced size of the sensors allows for greater flexibility in the integration of diagnostic devices into portable, wearable, or implantable devices, or extending their use to other technologies like lab-on-chip systems [10]. In the developing world this could allow for remote monitoring of patients without fears of clinic congestion and transmission. An alternate diagnostic method involves using rolling circle amplification to detect the pathogenic DNA [15, 16]. This method employs the use of short DNA strands to detect the disease. Though promise has been shown for this to be low cost and portable, there is still more research to be undertaken

before this is a widely used method in biosensors and in disease detection in the developing world [15, 16].

6. CONCLUSION

In this essay, the potential for TB therapy and diagnostics to move away from their conventional means has been presented and discussed. Though the full potential of nanotechnology has not been explored, several studies and emerging projects show promise. While numerous challenges are still present, it is a viable option for developing countries to experiment with, as the impact of TB remains profound. It is clear that current diagnostic and therapy means are no longer as effective as they need to be. Nanotechnology provides a new and novel route that needs to be taken in order to curb the effects of TB globally.

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