

Editorial on Special Issue “Tuberculosis Drug Discovery and Development 2019”

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1. Introduction

Mycobacterium tuberculosis, the etiological agent of human tuberculosis (TB), represents a global challenge to human health since it is the main cause of death by an infectious disease worldwide. Estimations by the World Health Organization (WHO) reported that the tubercle bacillus latently infects approximately one fourth of the world's population, and it is responsible for more than one million deaths every year [1]. Additional factors such as immunodeficiencies [2] and diabetes [3] increase the risk of developing active TB.

The currently available anti-TB therapy is composed of four antibiotics (rifampicin, isoniazid, pyrazinamide and ethambutol) that must be administered for at least 6 months to patients affected by drug-sensitive pulmonary TB [4]. However, the increasing number of multi- and extensively drug-resistant TB cases [5] requires the use of second- or even third-line anti-TB medications, which are characterized by frequent severe side-effects that reduce patients' compliance [6].

Feeding the drug discovery pipeline with the identification of novel chemical entities and promoting the development of those candidate drugs that are presently in clinical trials are therefore of outmost importance in order to shorten anti-TB treatment.

In this Special Issue of Applied Sciences dedicated to “Tuberculosis Drug Discovery and Development”, we review the most recent achievements in drug and target identification and present an update on the clinical development of two candidate compounds (macozinone and delpazolid). An overview of technical advancements is included, together with a summary of the anti-TB vaccines which are either in the discovery or clinical phases.

2. The Present Special Issue on “Tuberculosis Drug Discovery and Development 2019”

This Special Issue of Applied Sciences dedicated to “Tuberculosis Drug Discovery and Development” starts with a review article by Bandodkar and colleagues [7] where several drug discovery approaches, which led to the identification of the TB drug candidates currently in the pipeline, are presented. In addition, the authors describe validated and promiscuous drug targets in the context of their experience at AstraZeneca R&D, Bangalore, India. In their article, Lienhardt and Raviglione discuss the ambitious aim of the WHO to reduce TB incidence by 90% by the year 2030 [8], whereas Iacobino and co-authors review the increasing global challenge represented by drug-resistant TB [9]. An interesting paper by Mazzarello closes the initial section by presenting a historical perspective focused on Carlo Forlanini, who invented pneumothorax for TB treatment in 1882, in the same year when Robert Koch identified *M. tuberculosis* as the causative agent of human TB [10].

The Special Issue then features a series of articles dedicated to the most relevant and frequently explored drug targets: the cell wall of *M. tuberculosis* is reviewed by Vilchèze [11], DprE1 and MmpL3

are described by Degiacomi and co-workers [12], and the oxidative phosphorylation pathways are presented by Foo and colleagues [13]. In addition, Gries et al. report on the most recent advances in host-directed therapies and anti-virulence compounds, which could represent a helpful complement to current anti-TB approaches [14]. In the context of additional approaches to standard antibiotic treatment, an article by Visca et al. reviews the importance of post-TB treatment with the roles of surgery and rehabilitation [15]. Two candidate compounds which are in the advanced stages of development complete the section dedicated to novel medications: macozinone [16] and delpazolid [17].

Three papers describe state-of-the-art approaches to TB drug discovery. The first one by van Wijk and co-authors deals with quantitative pharmacology models including machine learning and artificial intelligence [18]; the second one by Bruch and colleagues discusses structure- and target-based approaches to TB drug design [19]; the last one explores the -omics technologies and how they have been exploited so far in TB drug discovery [20].

The Special Issue closes with an Editorial by Rappuoli who highlights the need for new drugs and vaccines to eradicate TB [21] and introduces the final article by Martin and colleagues [22] who wrote an update on the TB vaccine pipeline.

Overall, this Special Issue has gathered together most of the globally known TB professionals, including clinicians, academic staff as well as researchers from the private sector, and provides an extensive overview of the currently available tools and compounds that can help in the fight against TB.

3. Conclusions

The research work described in these sixteen reviews that constitute the Applied Sciences Special Issue provides an extremely useful example of the achieved results in the field of tuberculosis drug development. Moreover, readers can find information regarding the new approaches that are in progress to identify new antitubercular drugs, as well as novel drug targets.

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