100 years of the Bacillus Calmette-Guerin vaccine

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Editorial

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On July 18, 2021, the world celebrated the 100th anniversary of the first administration of Bacillus Calmette-Guérin (BCG), the only licensed vaccine against tuberculosis (TB) to date. Since its introduction a century ago, billions of people have been vaccinated with BCG, leading to an extraordinary drop in overall infant mortality, likely not only due to a reduction in TB, but also, other infections. Yet, although the efficacy of BCG to prevent TB meningitis and disseminated TB in children is well established, its efficacy to prevent contagious TB in adolescents and adults is uncertain, and novel TB vaccines are urgently needed.

Extraordinary progress has been made during the past century in life sciences, with the knowledge about BCG increasing in parallel, as witnessed by more than 30,000 citations found on PubMed. From efficacy studies against TB to treatment of bladder cancer, BCG changed the world and still has plenty to offer. Yet, the exact mechanism that induces protection as well as the correlates of protection against TB are still poorly defined. With the current COVID-19 pandemic, BCG has re-gained increased attention due to its potential heterologous effects against non-mycobacterial pathogens, including SARS-CoV-2.

In this Special Issue, we present papers that discuss the strengths and limitations of this vaccine, the diversity of applications, its broad protection against a plethora of diseases and the current efforts to improve it. The Special Issue contains various types of articles, including research articles, review articles, editorials and a meeting report, covering a variety of topics, from historical perspectives on BCG and TB vaccine candidates to the most recent advances in BCG research and new TB vaccine strategies to modify, improve or boost BCG. Also, the immunology of BCG and the non-specific effects of BCG vaccination, both against heterologous infectious agents and non-infectious diseases, are discussed. Combined with the increasing problem of vaccine hesitancy throughout the world, this is a most relevant and timely topic, and a unique opportunity to show that vaccination works, requires further refinement and has a great future ahead.

Specifically, the issue focuses in the following topics: (i) a meeting report on the Virtual Global Forum on Tuberculosis Vaccines which includes historical perspectives on BCG and TB vaccine candidates [1]; (ii) heterologous effects of BCG against leprosy [2], SARS-CoV-2 [3] and Buruli ulcer [4]; (iii) Pre/post-exposure vaccination (including therapeutic vaccination): new vaccination strategies to modify or improve BCG [5], sex differences in the protective efficacy of BCG [6], and a novel vaccine candidate (MTBVAC) which is on the cusp of initiating efficacy trials [7]; (iv) The effects of neonatal BCG vaccination on mortality up to 1 year of age [8]; (v) Unconventional T cells & BCG vaccination: How important are Donor Unrestricted T cells (DURT) in protection? To what extent does BCG induce or limit DURT expansion? [9]; (vi) Usage of BCG in diverse therapeutic settings including bladder cancer [10–12], more broadly as oncotherapy [13], as well as allergic asthma [14] and endometriosis [15].

Currently, there are more than 12 vaccines against TB in clinical trials, including repeated BCG vaccination, which is the confirmation that despite being 100 years old, the BCG vaccine is here to stay. Altogether, we hope that this special issue will stimulate future research in TB vaccine development.

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