

# Bacillus Calmette-Guerin (BCG) Vaccine-Induced Trained Immunity Against Respiratory Illness and Plausible Protection Against COVID-19 †

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† Presented at Virtual symposium to observe World Antimicrobial Awareness week “Applications of biotechnology and microbiology with special emphasis on Antimicrobial resistance”, 18-24 November 2020, Chennai, India

**Received: 10.11.2020; Revised: 15.11.2020; Accepted: 17.11.2020; Published: 10.01.2021**

**Abstract:** COVID-19 pandemic has caused an unprecedented impact on physical and mental health where all countries are not equally affected. The observed disparities in SARS-CoV-2 infection incidences and COVID-19 fatalities are concomitant with country-specific mitigation efforts. During the pandemic’s initial phase, the per capita COVID-19 incidences were high among high-income countries, whereas lower- and middle-income countries (LCMIs) reported a low burden. The underlying root causes of this anomaly are not well understood. One hypothesis suggests that LCMIs having implemented mandatory BCG vaccination provide non-specific trained immunity protection against COVID-19. Many ecological studies reported an association between concurrent COVID-19 incidences and global BCG vaccination coverage. BCG vaccination is proven to mediate non-specific protection against many respiratory illnesses. However, there is no direct evidence on BCG vaccination-mediated immune protection against SARS-CoV-2 infection. More than 20 vaccine trials are underway, enrolling healthcare workers and the general population to evaluate BCG vaccine safety, efficacy, and immune protection against COVID-19. Herewith, this manuscript highlights BCG vaccine trained immunity in respiratory illnesses and deciphers its concomitant relevance in COVID-19.

**Keywords:** COVID-19; BCG; SARS-CoV-2; trained immunity.

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## Funding

This research received no external funding.

## Acknowledgments

This research has no acknowledgment.

## Conflicts of Interest

The authors declare no conflict of interest.