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Back to the Basics: The Good Old BCG for COVID-19?

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A R T I C L E I N F O

Letter to the Editor

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The outbreak of SARS-CoV-2 from Wuhan, China in late 2019 and the subsequent worldwide pandemic in 2020 [1] are pushing scientists to look for urgent and efficient ways of protecting patients and managing positive cases, and a real "race for a cure" is running forward, but also backward! In fact, several epidemiological data in humans suggest that live vaccines (e.g., Bacillus Calmette–Guérin (BCG), measles, oral polio and vaccinia) may enhance nonspecific resistance to other non-targeted infections [2]. Several epidemiological studies have notably shown that BCG vaccine is capable of providing protection against numerous infections, unrelated to tuberculosis in an innate-immune dependent manner [3]. Such non-specific effects implicate both adaptive and innate immune mechanisms, and recent evidence suggests that epigenetic reprogramming of monocytes termed 'trained immunity' is a key mechanism which acts as a boosting effect on the innate immune memory [3-6].

Observations suggest that the innate immune system exhibits memory-like features, remembering the first exposure to the vaccine and responds with an emphasized reaction to future infections [3-4]. Particularly, Natural Killer (NK) cells may contribute to these indirect beneficial effects as BCG immunization enhances the cytokine production by human NK cells [7]. Different clinical trials (e.g., BRACE trial in Australia, NCT04327206) are currently underway to investigate the potential benefits of BCG immunization to confer such protection [8]. These trials, due to several paradigms, are essentially restricted to health care providers as an initial step [9].

Moreover, an interesting monocentric trial in the United Arab Emirates was recently published with encouraging results. It compared two groups, comprised of BCG booster-vaccinated healthcare professionals versus unvaccinated professionals. The rate of SARS-CoV-2 infection was compared between the groups, more than 3 months later. The results indicated that the infection rate in the unvaccinated cohort was 8.6% versus 0% in the booster vaccinated cohort (Fisher's exact test *P-value* = 0.004), highlighting the potential efficiency of this booster BCG vaccine [10]. Finally, regarding the safety of this potential BCG revaccination, a 2021 systematic review encompassing 24 studies has concluded this strategy had no serious adverse events in immuno-competent patients and that such revaccination carries only minimal risks of mild local and systemic reactions [11]. The near future will tell us whether this century-aged BCG vaccine could be a cure of youth for COVID-19 pandemic.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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