REVIEW

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COVID-19 vaccination clinical trials should consider multiple doses of BCG

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Vaccine repositioning is a hot research topic as an alternative to the traditional vaccine approach, which is a costly and time-consuming process due to the availability of previous safety and toxicology data. Multiple-dose BCG vaccine repurposing for COVID-19 will be an uprising breakthrough of vaccine discovery with safer outcomes. BCG induces cross-protection that might not be related to the target disease as innate immune cells, including monocytes and natural killer cells, contribute to this immune protection as known as "trained immunity" (Covián et al. 2019). BCG had multifaceted protection against TB, leprosy, and heterogeneous pathogens (Yamazaki-Nakashimada et al. 2020). Moreover, it was repositioned as a treatment for type-1 diabetes, many types of cancer, and multiple sclerosis (Yamazaki-Nakashimada et al. 2020). BCG vaccine accelerates the "resetting" of the immune system (Kühtreiber and Faustmann 2019) or "turn on" immunity mechanism that agrees with its pleiotropic repurposing for many diseases. Multiple-dose BCG vaccine was used for reversing type-1 diabetes and for treating bladder cancer (Kühtreiber et al. 2018; Pettenati and Ingersoll 2018). While intravesical multiple doses of BCG for bladder cancer showed many complications (Waked et al. 2020; Yong et al. 2020), intradermal multiple doses of BCG for diabetes showed high safety profile (Kühtreiber et al. 2018).

As recent studies have shown that upon certain vaccinations, human innate immune cells can undergo extensive metabolic and epigenetic reprogramming, which results in enhanced immune responses upon heterologous re-infection, a process termed trained immunity (Mourits et al. 2018); The author recommends that COVID-19 vaccination clinical trials should consider multiple doses of BCG. After reviewing the recent COVID-19 literature, although some preliminary studies suggested BCG to fight COVID-19 (de Vriese 2020; Max-Planck-Gesellschaft 2020; Sparrow 2020; The Brussels Times 2020), they did not consider the use of multiple intradermal BCG vaccination (at least 2 doses, 4 weeks apart (Kühtreiber et al. 2018) for the prophylaxis of COVID-19 outbreak. I do recommend that diabetic patients should participate in clinical trials to benefit from the reported BCG anti-hyperglycemic effect (Kühtreiber et al. 2018). What if safe multiple doses of BCG turned on the immunity and protected people from COVID-19 more efficiently than a single dose?

Conflict of interest: None declared.

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