



Commentary

A new step toward tuberculosis vaccine?

Chiara Tersigni^a, Luisa Galli^{a,b,*}^a Department of Health Sciences, University of Florence, Viale Pieraccini 24, 50139 Florence, Italy^b Pediatric Infectious Disease Unit, Meyer Children University Hospital, Florence, Italy

ARTICLE INFO

Article History:

Received 4 August 2020

Accepted 4 August 2020

Understanding the role of the immune system in controlling tuberculosis (TB) infection is pivotal to reach the goal of full elimination of the disease by 2050, as highlighted by World Health Organization (WHO) [1]. TB diagnosis in children is particularly challenging, especially in limited resource settings, and studies which aim to identify target population to address efforts are crucial. Host's characteristics in determining disease control and its severity are increasingly studied, with the main aim to identify biomarkers of TB "resistance", especially in the pediatric age.

Basu Roy et al. recently published on EBioMedicine a study on a cohort of Gambian pairs of children ($n = 58$) exposed to the same index case with different infection status (infected and uninfected). This study emphasizes the importance that a discordant infection status could be related to the unique characteristics of the individual to inhibit mycobacterial growth [2]. The selection process of included children and the elimination of possible confounding factors give strength to what can be considered as an important milestone surrounding this fundamental topic [2]. Using a mycobacterial growth inhibition assay, bacterial growth was evaluated at baseline and at 96 h and a quantitative analysis of IL-1 α , IL-1 β , IL-10, IFN- γ and TNF- α was performed [2]. The used test, an autoluminescent BCG growth monitoring in whole blood, has been described by the same groups of authors in a recent publication [3]. It permits, with a small amount of blood (225 μ l) to obtain serial measurements (after 1 h and at 24, 48, 72 and 96 h) with the quantification of luminescence related to bacterial colony forming units (CFUs) [3].

While mycobacterial control was superior in uninfected children at one hour, suggesting the role of both adaptive and innate immune response, on the other hand, children with mycobacterial infection showed a superior control at 96 h with a greater role of adaptive responses [2]. Regarding cytokine production, uninfected children

produced less BCG-specific interferon gamma compared to infected children, mirroring the infection status [2]. Moreover, infected children were statistically significant older than uninfected, with a longer smear-positive index case exposure. Historically, the most important role regarding tuberculosis immunity has been attributed to T-cell-mediated response, with CD4+ T cells playing a crucial role both for the control of infection and the tissue damage during TB infection [4,5]. Together with adaptive immune response, innate immune cells are crucial for TB infection control [4,5]. Nevertheless, unanswered questions remain. In fact, as stated by the authors, the complete knowledge of immune response to TB is still lacking and consequently, the way to find an effective vaccine is still far away. It is well known that the only available vaccine, the Bacillus Calmette-Guèrin (BCG), used for the first time in 1921, confers a significant protection against TB meningitis and miliary tuberculosis, especially in children under 5 years of age, with a different level of protection against pulmonary TB, ranging from 0 to 80% [6]. In addition, BCG scarring has been associated with a lower morbidity and mortality compared to children not having a scar [7,8]. Up to now, several new TB vaccines are in the pipeline with incomplete results regarding safety and efficacy in the pediatric age [9]. Mechanisms required for mycobacterial killing are still under investigation and large studies in different populations are needed to help vaccine development. Intriguing results provided by this study, using a tool which helps to understand the *in vivo* interactions between the host and the *Mycobacterium spp*, pave the way for new studies regarding TB vaccine development with a direct applicability in the clinical practice.

Contributors

CT and LG both conceived and wrote the manuscript. LG approved the final version.

Declaration of Interests

The authors have nothing to declare.

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DOI of original article: <http://dx.doi.org/10.1016/j.ebiom.2020.102891>.

* Corresponding author at: Department of Health Sciences, University of Florence, Viale Pieraccini 24, 50139 Florence, Italy.

E-mail addresses: luisa.galli@unifi.it, l.galli@meyer.it (L. Galli).

<https://doi.org/10.1016/j.ebiom.2020.102965>

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