Available online at www.sciencedirect.com

ScienceDirect

Procedia in Vaccinology 2 (2010) 172–177

Procedia in Vaccinology

www.elsevier.com/locate/ procedia

Ninth Global Vaccine Research Forum and Parallel Satellite Symposia
Bamako, Mali, 6-9 December 2009

Antibodies in the protection against mycobacterial infections: what have we learned?

Yamile López *, Gustavo Falero-Díaz, Daniel Yero, Rosa L. Solís, Maria E Sarmiento, Armando Acosta

Finlay Institute, Ave. 17 esquina 198, Reparto Siboney Playa, Havana, Cuba

Abstract

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*. Despite of the massive global use of BCG, there is a need for other TB vaccines. Newer animal models are needed to test candidate vaccine efficacy to protect animals against challenge with *M. tuberculosis* virulent strains in more realistic scenarios than currently done. Also, the elucidation of the importance of humoral immune defenses against intracellular pathogens constitutes a priority to improve the rational design of new vaccines. Our group has been actively testing the protective role of antibodies in different models of pulmonary TB infection through evaluation of bacterial loads and morphometric and histological changes in the lungs of infected mice. Results presented here suggest a protective role for antibodies and the humoral response against tuberculosis infection.

Keywords: *tuberculosis, mice model, antibodies, 16 kDa protein*

1. Introduction

Through all of history, tuberculosis (TB) has been a health problem for humanity. At the beginnings of civilization the disease was probably occasional, but with the increment of population densities, in the XVII-XIXth centuries, it took epidemic proportions [5,7,16].

In spite of the use of the live attenuated vaccine developed by Calmette and Guerin (BCG) and in spite of effective therapy with antibiotics like isoniazid, rifampicin and streptomycin, the number of TB cases has not ceased to increase until our days. The World Health Organization estimates that approximately a third of the world population

* *Corresponding author. E-mail address: ylopez@finlay.edu.cu*

1877-282X © 2010 Published by Elsevier Ltd.
doi:10.1016/j.provac.2010.07.011

is infected and that about eight million people acquire TB yearly. Without an adequate treatment, over 60% of the people with TB would be condemned to death [36].

In order to implement strategies to increase the effectiveness of BCG vaccine, or to replace it by a more effective vaccine, an important point is to try to elucidate the effector immune mechanisms at work in the fight against intracellular pathogens. For many years, cell-mediated immunity was attributed an exclusive role in the defense against intracellular pathogens. The Th1/Th2 paradigm prevailed for a long time and directed the development of most vaccines. In recent years, many experiments have however challenged this concept. Nowadays, it is well accepted that a combination of both arms of the immune system is optimal for fighting intracellular as well as extracellular pathogens [15].

2. A role for IgG antibodies

With the scientific development of hybridomas technology and the production of monoclonal antibodies, evidence that support a clear role of antibodies in the fight against intracellular pathogens such as fungi, viruses, parasites and bacteria has been accumulating [1]. The availability of new technologies for the study of antibody-mediated immunity and the need for new therapies for the control of re-emergent diseases had pushed forward the discovery of new functions of antibodies, such as their role as direct microbicide molecules [2,29,39] or as interactive and unique effector molecules [38].

In the specific case of *M tuberculosis*, initial work was developed using anti-arabinomanan (AM), anti-lipoarabinomanan (LAM), anti-heparin-binding haemaglutinin adhesin (HBHA) or anti- Mtb83 monoclonal antibodies [4,12,13,17,18,30]. These antibodies, which are usually able to opsonize mycobacteria, were administered to infected mice by different routes, yielding results such as prolonged host survival, increased serum clearance, diminished mycobacteria dissemination and reduction of colony forming units in the lungs and spleen.
The interest of the scientific community in the elucidation of the real role of antibodies mediating protective immunity against TB began to increase, as illustrated in **Figure 1**.

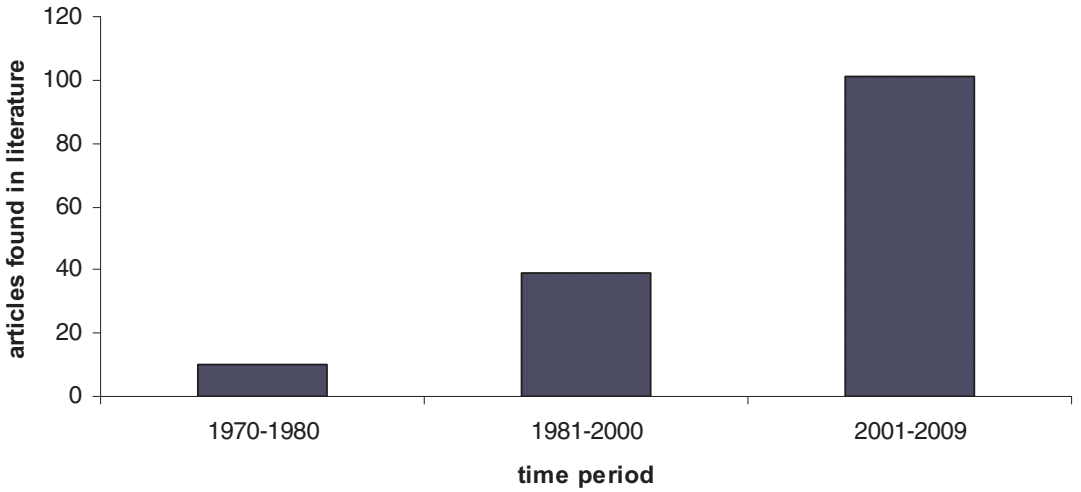

Figure 1: Antibodies and *M tuberculosis*. Data for this graphic were obtained by searches in Medline and PubMed and references from relevant articles.