

## Antibody mediated immunity — a missed opportunity in the fight against tuberculosis?

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Dear Editor,

Tuberculosis is one of the leading causes of mortality produced by a single infectious agent. Each year 8 million new cases and between 2 to 3 million deaths are reported. One-third of the human population is already infected with *Mycobacterium tuberculosis* — the causative agent of tuberculosis. The disease is increasing at a worrying rate primarily due to the absence of an effective vaccine, the emergence of multi-drug resistant strains, as well as co-infection with HIV; coupled with the low diagnostic and therapeutic coverage in many developing countries.

The role of cell-mediated immunity against mycobacteria, and in particular, *M. tuberculosis* has been fully established. Up to now all the efforts for the development of new or improved vaccines against tuberculosis have been directed toward the induction of an effective cell-mediated immune response. However, the potential role of antibodies for protection against *M. tuberculosis* infection have been underestimated on the assumption that they have limited effect, if any, against intracellular pathogens.

*M. tuberculosis* gains access to the host through the mucosa of lung alveoli, thus the presence of specific antibodies in mucosal secretions could inhibit bacterial colonization. In fact, our group has demonstrated the protective capacity of secretory IgA monoclonal antibodies directed against *M. tuberculosis* antigens as well as formulations of human gammaglobulins against models of infection with BCG and *M. tuberculosis* in mice (1,2,3). Similar results have been obtained with human secretory IgA in the same animal model (unpublished observations). Using different animal models and antibody formulations, other groups have reported the protective role of antibodies in *M. tuberculosis* infection (4).

Potential mechanisms by which antibodies could modify the outcome of mycobacterial infection could be mediated by interference with adhesion, toxin neutralization, opsonization, activation of complement, increase in cytokine

expression, enhancement of phagosome-lysosome fusion, and enhancement of antigen presentation among others (5).

Future applications of antibody formulations for the control of tuberculosis may include: treatment of patients infected with multidrug resistant strains, combination with the standard treatment in order to achieve shorter therapeutic regimes, and administration to recent contacts of tuberculosis patients and risk groups. Since BCG, the current vaccine against tuberculosis is only protective in the severe forms of the infection in childhood and is not protective against the pulmonary disease in adults — the most common form of the disease. Hence the development of new tuberculosis vaccines is urgently required (6).

The induction of specific antibody responses by vaccination in addition to the stimulation of cell-mediated immunity could be a novel strategy for the development of new generation prophylactic and therapeutic vaccines against tuberculosis. Taking into consideration this possibility, our group has been working on recombinant BCG strains expressing T and B epitopes of *M. tuberculosis*, with some encouraging results with respect to immunogenicity and protection in mice (unpublished results).

Accumulated reports in favour of the protective role of specific antibodies in tuberculosis provide us with potential improvements in prophylactic, therapeutic, and diagnostic methods to enhance future control measures against the disease.

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