Adjuvanted Recombinant BCG Vaccine increases protection against TB

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Vaccination against *Mycobacterium tuberculosis* (TB) has been only partially successful based on the vaccine *M. bovis* Bacillus Calmette-Gué rin (BCG), protecting children efficiently against early manifestations of TB. However, its protective immunity wanes in 10-20 years, being limited against adult pulmonary TB. Therefore several strategies are being pursued for the development of improved vaccines against TB. It is considered that to obtain a high protection level against TB, it is necessary to induce a high Th1 cellular immune response against the mycobacteria. Most of the strategies attempt to increase the CD4+ - Th1 and CD8+ characteristics of the immune response. Assays evaluate the efficacy of TB vaccines in experimental animals by pulmonary challenge with MTB in mice and then in Guinea pigs. Universally, BCG provides a 1 log reduction in lung colonization in mice at 1 month, considered to be partially protective. The most promising vaccines being evaluated have been based on different forms of recombinant mycobacteria or the BCG-prime and boost with different antigens. We investigated whether the well-know adjuvant properties of bacterial toxins and toxin derivatives are maintained when expressed in BCG. We have observed that the expression of these derivatives in recombinant BCG could modulate the immune response induced against the co-administered rBCG strains towards a Th2 or Th1 pattern depending on the derivative. Therefore, we investigated the effect of the expression in rBCG of a very potent Th1-driving toxin derivative - the E. coli heat labile enterotoxin derivative, LTK63. The immunization of mice with the rBCG-LTK63 strain induced a very strong Th1-predominant immune response against the mycobacteria, with production of high levels of IFN-γ and TNF-α . This resulted in a 2 log reduction in bacterial colonization in mice following challenge with MTB, or
1 log reduction in comparison to BCG. We have now expressed LTA-K63 in BCG, which resulted in a 1.3 log reduction in relation to BCG immunization, following challenge with MTB. These results confirm that the expression of Th1 driving adjuvants in BCG can modulate the immune response induced against the mycobacteria, inducing higher protection against TB

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The EMBO conference series "Tuberculosis 2012" is an international congress on Tuberculosis and its causative organism Mycobacterium tuberculosis to be held from September 11-15, 2012 at the Conference Centre of the Institut Pasteur, Paris.

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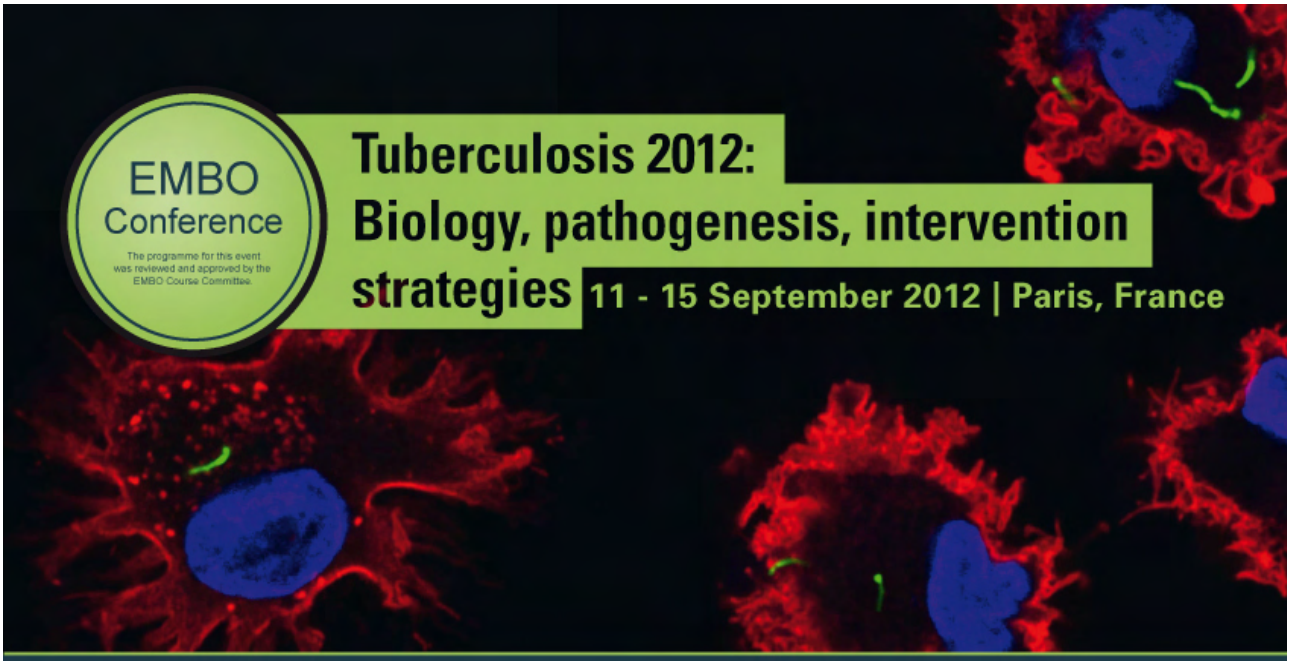

EMBO Conference

The programme for this event was reviewed and approved by the EMBO Course Committee

Tuberculosis 2012: Biology, pathogenesis, intervention strategies

11 - 15 September 2012 | Paris, France

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Early registration deadline:
15 June 2012

Abstract submission deadline:
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PROGRAM AND ABSTRACT BOOK