detect due to the paucity of immunodominant antigens. Currently, the most widely used biomarkers are based on elevated frequencies of CD4 T cells producing IFNγ. Increasing evidence questions the value of IFNγ as correlate of protection in TB (9,10). Undoubtedly IFNγ does play a crucial role in defense against MTB (11), but determination of IFNγ alone can no longer be considered as a reliable marker of protective immunity.

A recombinant BCG strain expressing a phagolysosomal escape domain is described in WO 99/101496, the content of which is herein incorporated by reference. The phagolysosomal escape domain enables the strain to escape from the phagosome of infected host cells by perforating the membrane of the phagosome. In order to provide an acidic phagosomal pH for optimal phagolysosomal escape activity, a urease-deficient recombinant strain was developed. This strain is disclosed in WO2004/094469, the content of which is herein incorporated.

A recombinant Δ*ure*C *Hly*$^+$ rBCG (rBCG) strain expressing membrane-perforating listeriolysin (Hly) of *Listeria monocytogenes* and devoid of urease C induces superior protection against aerogenic challenge with MTB as compared to parental BCG (pBCG) in a preclinical model (12). This vaccine construct has successfully proven safety and immunogenicity in a phase I clinical trial (US 61/384,375), the content of which is herein incorporated by reference.

In the present study, it is shown that rBCG and pBCG induce marked Th1 immune responses, whilst only rBCG elicits are profound Th17 response in addition. It was also observed earlier recruitment of antigen-specific T lymphocytes to the lung upon MTB infection of rBCG-vaccinated mice. These T cells produced abundant Th1 cytokines after restimulation. Superior protective efficacy of rBCG was apparently dependent on IL17. Elevated IL17 production after rBCG, but not pBCG vaccination, was also detected in healthy volunteers during a phase I clinical trial. Our findings identify a general immunologic pathway as a marker for improved vaccination

Claims

1. A recombinant Mycobacterium cell which comprises a recombinant nucleic acid molecule encoding a fusion polypeptide comprising:
(a) a domain capable of eliciting an immune response, and
(b) a phagolysosomal escape domain
for use as vaccine for generating a Th17 immune response.

2. The cell of claim 1 which is a urease-deficient cell.

3. The cell of claim 1 or 2 which is a recombinant *M. bovis* cell, particularly a recombinant *M. bovis* cell from strain Danish subtype Prague.

4. The cell of any one of claims 1-3, wherein the domain capable of eliciting an immune response is selected from immunogenic peptides or polypeptides from *M. bovis* or *M. tuberculosis*.

5. The cell of any one of claims 1-4 for generating a Th17 immune response in a mammalian, e.g. human subject.

6. The cell of any one of claims 1-5 for generating a Th17 immune response in a Mycobacterium-naïve subject or a subject pre-exposed to Mycobacterium challenge.

7. The cell of any one of claims 1-6 for use in a vaccine against a disorder selected from:
(i) tuberculosis,
(ii) bladder cancer,
(iii) an autoimmune disorder, and
(iv) leprosy.

8. The cell of any one of claims 1-7 for use as a vaccine for generating a Th17 and a Th1 immune response.

9. A method for generating a Th17 immune response in a subject in need thereof, comprising administering to said subject a recombinant nucleic acid molecule encoding a fusion polypeptide comprising:
(a) a domain capable of eliciting an immune response, and
(b) a phagolysosomal escape domain.

detect due to the paucity of immunodominant antigens. Currently, the most widely used biomarkers are based on elevated frequencies of CD4 T cells producing IFNγ. Increasing evidence questions the value of IFNγ as correlate of protection in TB (9,10). Undoubtedly IFNγ does play a crucial role in defense against MTB (11), but determination of IFNγ alone can no longer be considered as a reliable marker of protective immunity.

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Claims

1. A recombinant Mycobacterium cell, which is a urease-deficient cell and which comprises a recombinant nucleic acid molecule encoding a fusion polypeptide comprising:
   (a) a domain from a mycobacterium polypeptide capable of eliciting an immune response, and
   (b) a listeria phagolysosomal escape domain
   for use as vaccine against tuberculosis for generating a Th17 immune response.

2. The cell of claim 1 which is a recombinant *M. bovis* cell, particularly a recombinant *M. bovis* cell from strain Danish subtype Prague.

3. The cell of claim 1 or 2, wherein the domain capable of eliciting an immune response is selected from immunogenic peptides or polypeptides from *M. bovis* or *M. tuberculosis*.

4. The cell of any one of claims 1-3 for generating a Th17 immune response in a mammalian, e.g. human subject.

5. The cell of any one of claims 1-4 for generating a Th17 immune response in a Mycobacterium-naïve subject or a subject pre-exposed to Mycobacterium challenge.

6. The cell of any one of claims 1-5 for use as a vaccine for generating a Th17 and a Th1 immune response.

7. Use of a recombinant Mycobacterium cell, which is a urease-deficient cell, in the manufacture of a vaccine against tuberculosis, which comprises a recombinant nucleic acid molecule encoding a fusion polypeptide comprising:
   (a) a domain from a mycobacterium polypeptide capable of eliciting an immune response, and

(b) a listeria phagolysosomal escape domain

for generating a Th17 immune response in a subject in need thereof.