

**Figure S1. BCG vaccination induces expansion of memory-like NK cells.** C57BL/6 mice (5 mice per group) were given 100  $\mu$ l of PBS (unimmunized) or immunized subcutaneously with  $10^6$  CFU of BCG in 100  $\mu$ l of PBS. One and three months after vaccination, spleen, and peripheral lymph node cells were isolated, pooled, and cultured, with  $\gamma$ -irradiated *M. tb* H37Rv or Ag85a. After 5 days, CD3-NKp46+CD27+ and CD3-NKp46+CD27+KLRG1+ cells were measured by flow cytometry. **(A)** Expansion of CD3-NKp46+CD27+ cells one month after BCG vaccination. **(B)** Expansion of CD3-NKp46+CD27+ cells three months after BCG vaccination. **(C)** Expansion of CD3-NKp46+CD27+KLRG1+ cells one month after BCG vaccination. **(D)** Expansion of CD3-NKp46+CD27+KLRG1+ cells three month after BCG vaccination. Mean values and SEs are shown. Data are representative of two independent experiments.

**Figure S2. Memory-like NK cells expand after BCG vaccination and challenge with *M. tb* H37Rv.** C57BL/6 mice (20 mice per group) were given 100  $\mu$ l of PBS or immunized subcutaneously with  $10^6$  CFU of BCG in 100  $\mu$ l of PBS. After thirty days, mice were challenged with 75-100 CFU of *M. tb* H37Rv by aerosol. At weekly intervals up to 4 weeks, five mice in each group were sacrificed, and absolute number of CD3-NKp46+27+ cells was determined by flow cytometry and fold change compared to uninfected control mice was shown. **(A)** Lung **(B)** spleen. Mean values and SEs are shown. Data are representative of two independent experiments..

**Figure S3. Expansion of memory-like NK cells in BCG-vaccinated mice depends on IL-21.** **(A)** C57BL/6 mice were treated with PBS or immunized subcutaneously with  $10^6$  CFU of BCG in 100  $\mu$ l of PBS. Three month after vaccination, spleen, and peripheral lymph node cells were pooled and cells were cultured with or without Ag85, in the presence of isotype-matched control antibodies or neutralizing antibodies to IL-21. After five days, expansion of CD3-

NKp46+CD27+ cells were measured by flow cytometry. **(B)** C57BL/6 mice were treated with PBS or immunized subcutaneously with  $10^6$  CFU of *BCG* in 100  $\mu$ l of PBS. Three month after vaccination, spleen, and peripheral lymph node cells were pooled and transfected with either IL-21 or scrambled siRNA (control siRNA) and cultured with or without Ag85. After 72 hrs, cells were lysed and IL-21 mRNA levels was measured real time PCR. **(C)** Wild type C57BL/6 mice were sacrificed and spleen, and peripheral lymph node cells were pooled and cultured with or without Ag85, in the presence or absence of rIL-21. Mean values and SEs are shown. Data are representative of two independent experiments.

**Figure S4. Memory-like NK cells enhance cytokine and anti-microbial peptide expression in *M. tb*-infected mice lungs.** C57BL/6 mice (5 mice per group) were immunized subcutaneously with  $10^6$  CFU of BCG in 100  $\mu$ l of PBS. After one month, NK cells from pooled spleens and peripheral lymph node cells were isolated and adoptively transferred ( $1 \times 10^6$  cells once on day 0 of infection) to *M. tb* H37Rv-infected C57BL/6 mice. Infected mice in all panels were sacrificed thirty days after infection, RNA was extracted from lungs cytokine and anti-microbial peptide mRNA was quantified by real-time PCR. Data are representative of two independent experiments.

**Figure S5. Expansion of memory-like NK cells in individuals with LTBI depends on IL-21.** PBMC from 5 individuals with LTBI and 5 individuals without LTBI were cultured, with or without ESAT-6. **(A)** After 5 days, the percentages of proliferating CD3-NKp46+CD27+KLRG1+ cells were measured by flow cytometry. **(B)** PBMC were transfected with either IL-21 or scrambled siRNA (control siRNA) and cultured with or without ESAT-6. After five days, expansion of CD3-NKp46+CD27+KLRG1+ cells were measured by flow cytometry. **(C)** PBMC were cultured same as in panel B and cells were lysed and IL-21 mRNA levels was measured real time PCR. Five independent experiments were performed. Mean values and SEs are shown. **Table. S1:** List of mouse primers used for the study

S. No.	Name of the Gene	Primer Sequence

1.	CD3	Forward: ATGCGGTGGAACACTTTCTGG Reverse: GCACGTCAACTCTACACTGGT
2.	$\beta$ -Defensin	Forward: TCTTGTTCTTGGTGCCTGCT Reverse: CGACCGCTATTAGAACATCGAC
3.	IL-21	Forward: GCCTCCTGATTAGACTTCGTAC Reverse: CAGGCAAAGCTGCATGCTCAC
4.	$\beta$ -actin	Forward: CTCTGGCTCCTAGCACCATGAAGA Reverse: GTAAAACGAAGCTCAGTAACAGTCCG
5.	IL-1 $\beta$	Forward: CAACCAACAAGTGATATTCTCCATG Reverse: GATCCACACTCTCCAGCT
6.	IL-12	Forward: CTTAGCCAGTCCCGAAACCT Reverse: TTGGTCCCGTGTGATGTCT
7.	IL-18	Forward: GCCTCAAACCTTCCAAATCA Reverse: TGGATCCATTTCTCAAAGG
8.	TNF- $\alpha$	Forward: CATCTTCTCAAATTCGAGTGACAA Reverse: TGGGAGTAGACAAGGTACAACCC
9	<i>IFN-<math>\gamma</math></i>	Forward: TCAAGTGGCATAGATGTGGAAGAA Reverse: TGGCTCTGCAGGATTTTCATG