

# Long-term activation of lung-resident macrophages by mucosal BCG

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GLOBAL FORUM  
ON TB VACCINES

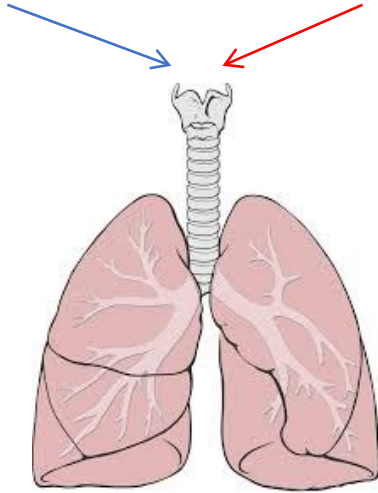


Universidad  
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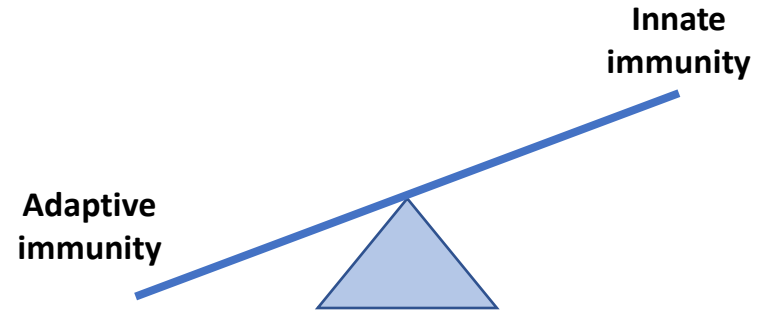
No conflicts of interest to declare

BCG

TB infection



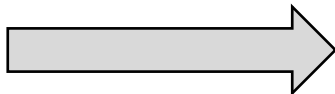
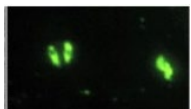
Superior efficacy compared to canonical route in mouse, guinea pig and NHP models



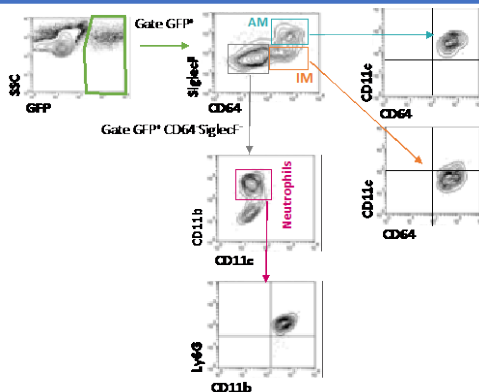
CONTRIBUTION OF INNATE RESPONSE TO MUCOSAL BCG-INDUCED PROTECTIVE EFFICACY?

# EVALUATION OF INFECTED POPULATIONS FOLLOWING Mtb RESPIRATORY INFECTION

GFP-tagged H37Rv



Specific Markers

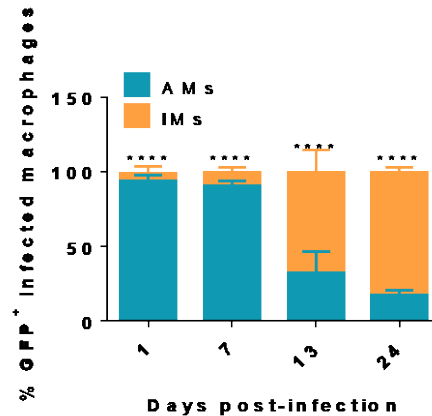
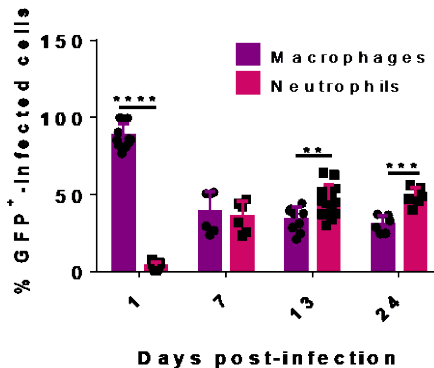
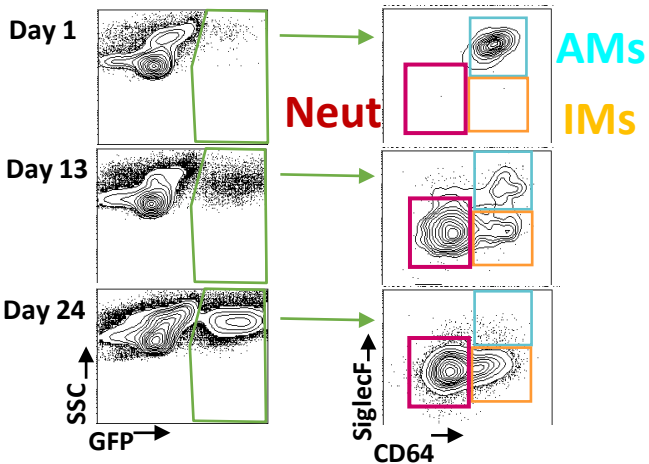


Alveolar Macrophages

Interstitial Macrophages

Neutrophils

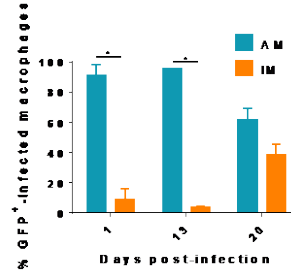
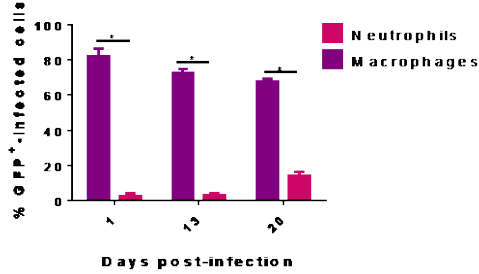
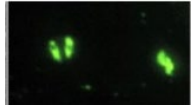
>90%  
infected cells



Mtb spread from AMs to neutrophils and IMs

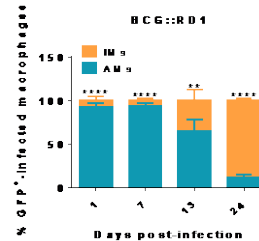
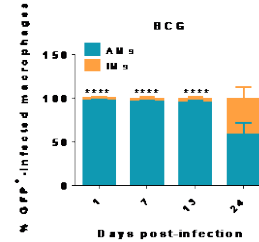
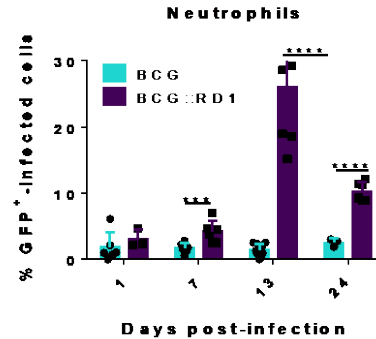
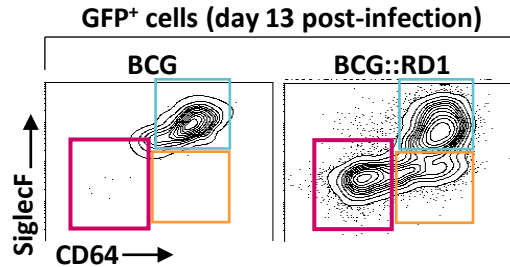
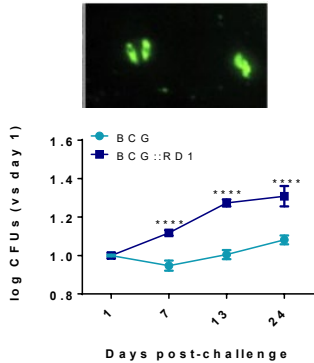
# IS Mtb CELLULAR SPREAD A MECHANISM OF VIRULENCE?

GFP-tagged BCG



BCG is mostly retained by AMs

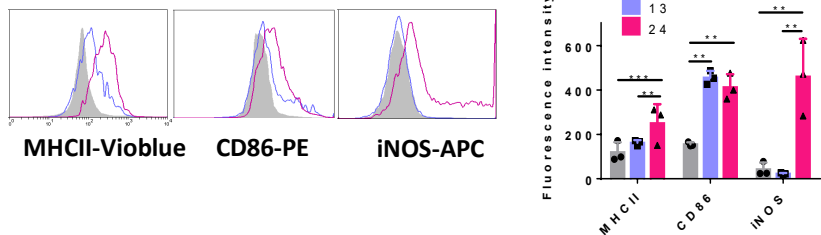
- GFP-tagged BCG
- GFP-tagged BCG::RD1



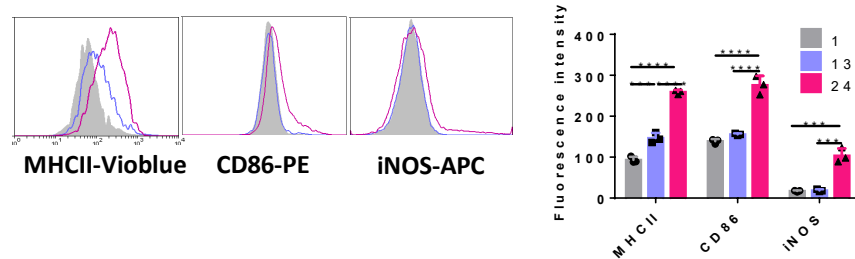
Cellular spread characteristic of virulent strains

# ALVEOLAR MACROPHAGE ACTIVATION BY MUCOSAL BCG

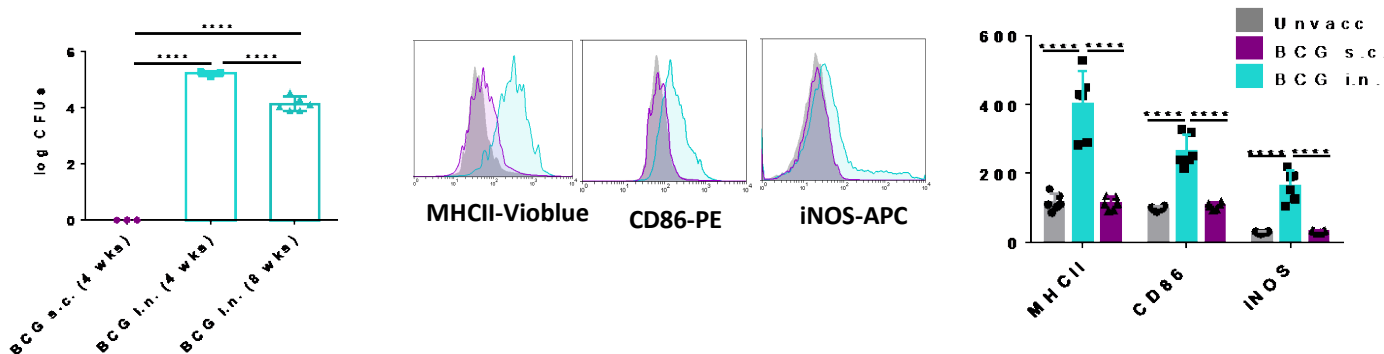
## INFECTED AMs (GFP+)



## NON-INFECTED AMs (GFP-)

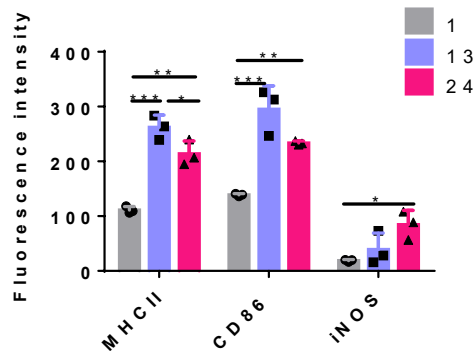
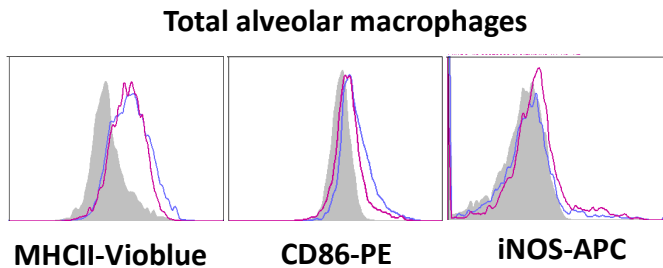


## COMPARISON BETWEEN INTRANASAL AND SUBCUTANEOUS BCG ADMINISTRATION ROUTES

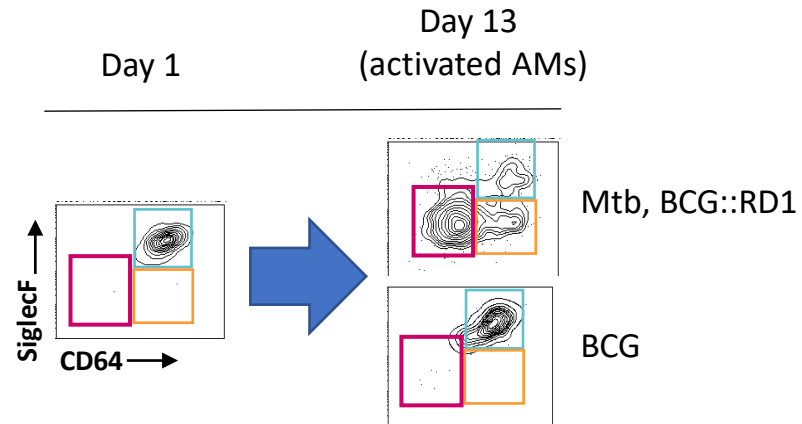


Respiratory, but not subcutaneous BCG vaccination induces AMs activation

# ALVEOLAR MACROPHAGE ACTIVATION BY Mtb



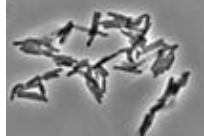
**Mtb induces AMs activation**



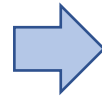
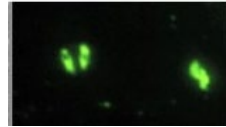
**Virulent strains, but not BCG, escape from AMs before they acquire an activated phenotype**

# IS BCG-INDUCED AMs ACTIVATION RELEVANT FOR VACCINE PROTECTIVE EFFICACY?

Non-fluorescent BCG  
(s.c. vs i.n.)

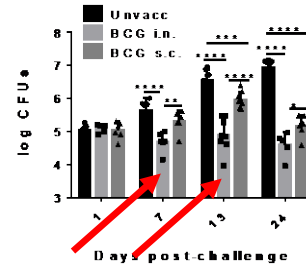
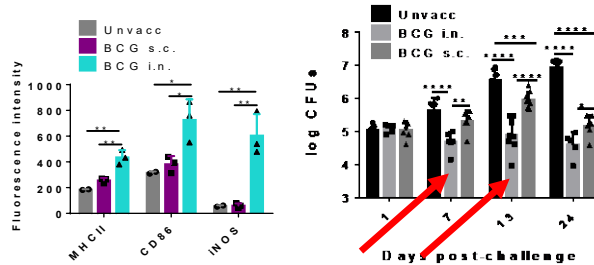
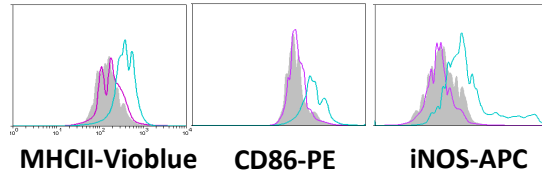


GFP-tagged H37Rv



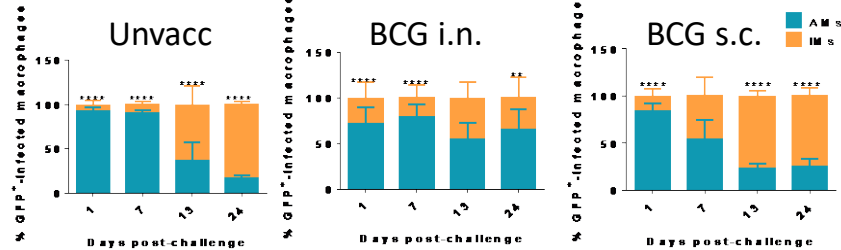
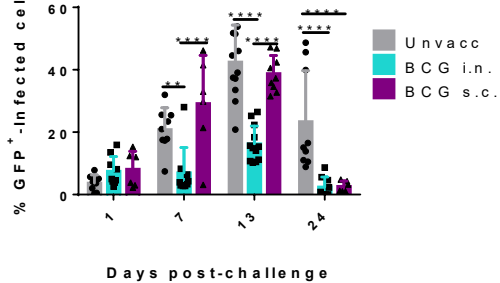
Status of Mtb-infected cells in naïve or BCG vaccination scenarios

GFP<sup>+</sup> lung macrophages day 1 post-H37Rv challenge



AMs that initially engulfed Mtb are pre-activated at the time of pathogen encounter, which correlates with an early control of bacterial replication

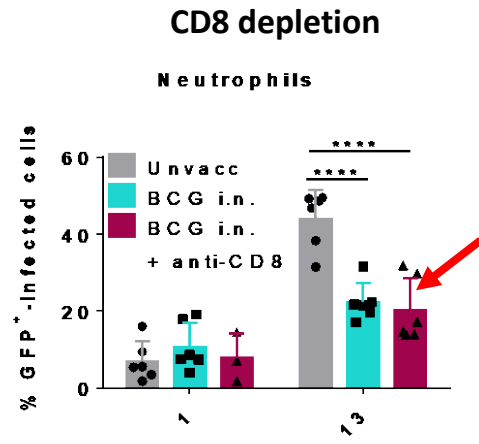
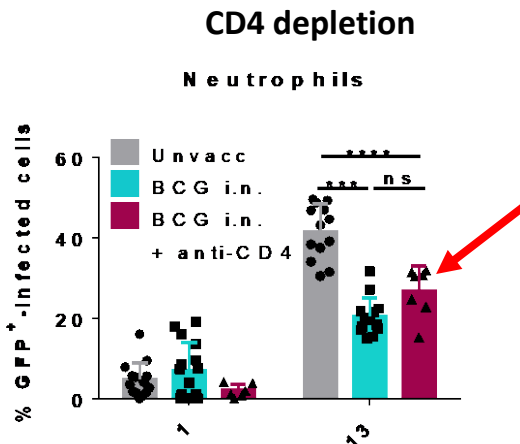
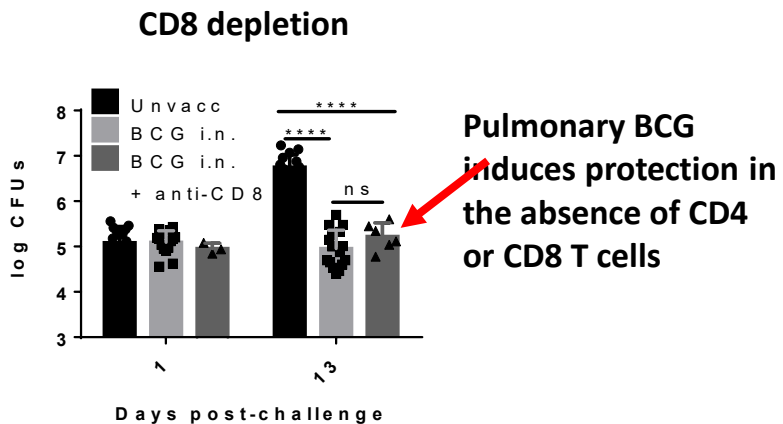
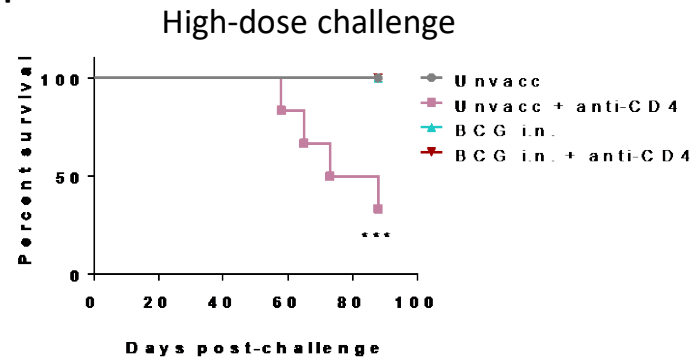
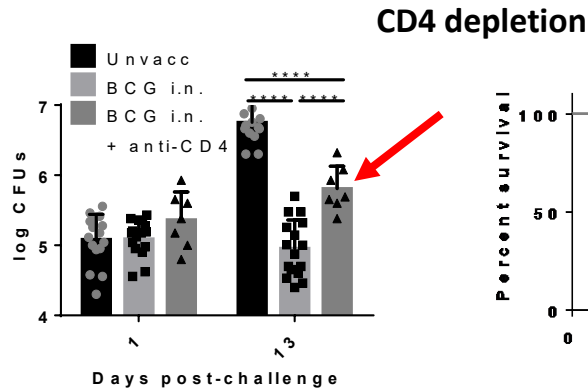
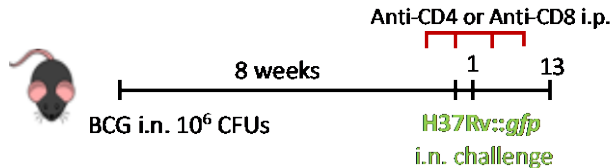
Neutrophils



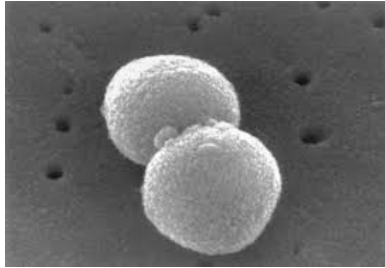
Mtb is mostly retained by AMs in BCG-vaccinated individuals



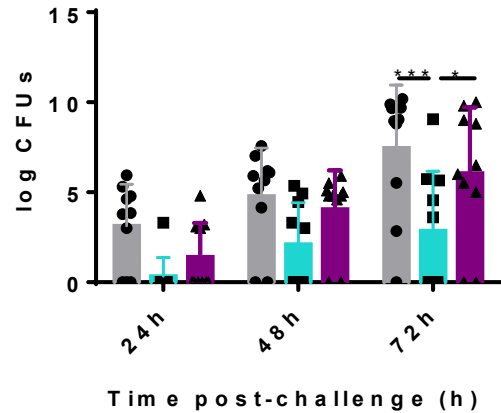
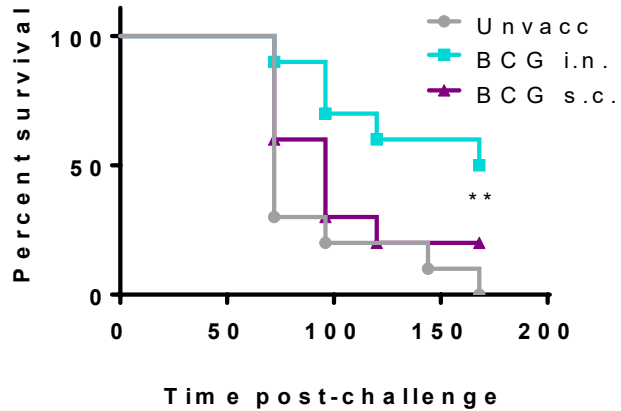
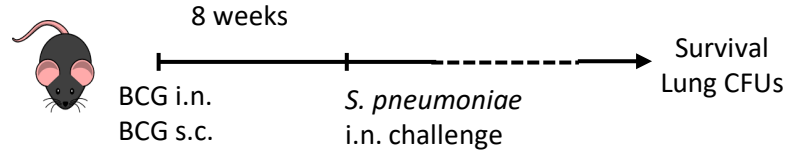
# BCG-INDUCED PROTECTION IN THE ABSENCE OF T CELLS



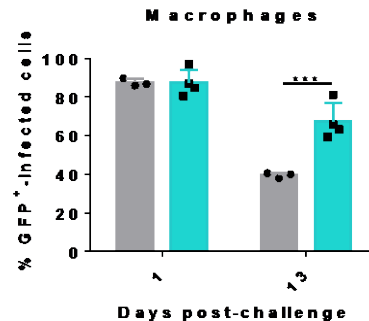
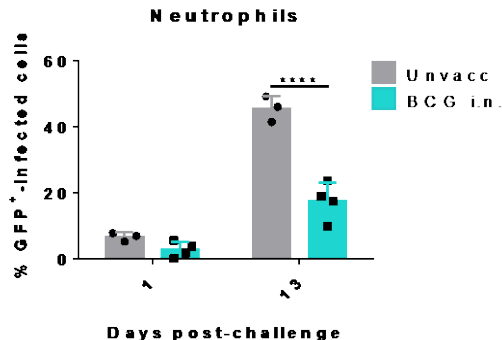
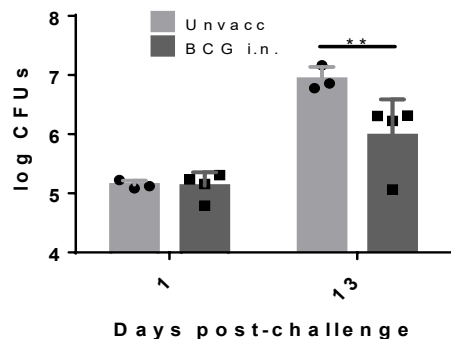
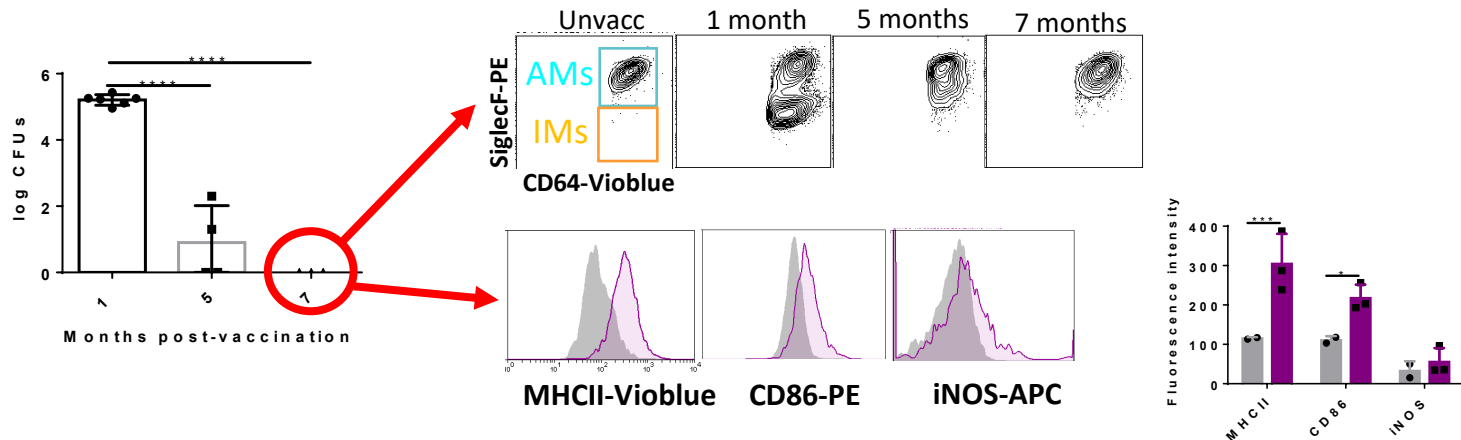
# HETEROLOGOUS PROTECTION OF PULMONARY BCG



Streptococcus pneumoniae

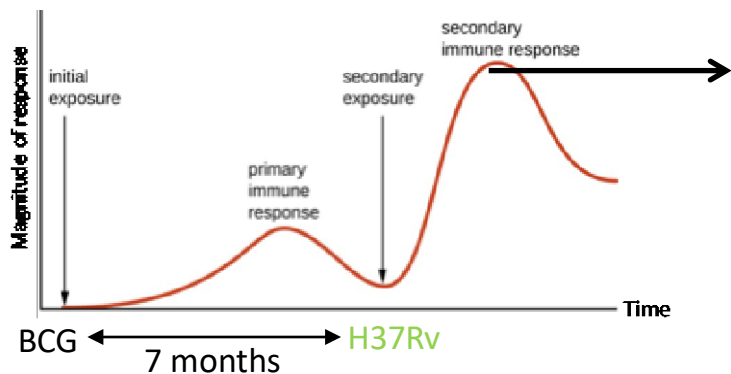


# PULMONARY BCG INDUCES LONG-TERM ACTIVATION OF ALVEOLAR MACROPHAGES



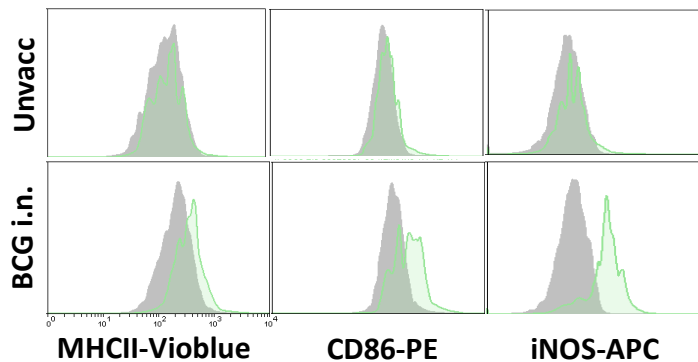
AMs show an activated phenotype after BCG clearance, which correlates with a better early control of Mtb infection

# PULMONARY BCG INDUCES A MEMORY-LIKE RESPONSE IN ALVEOLAR MACROPHAGES

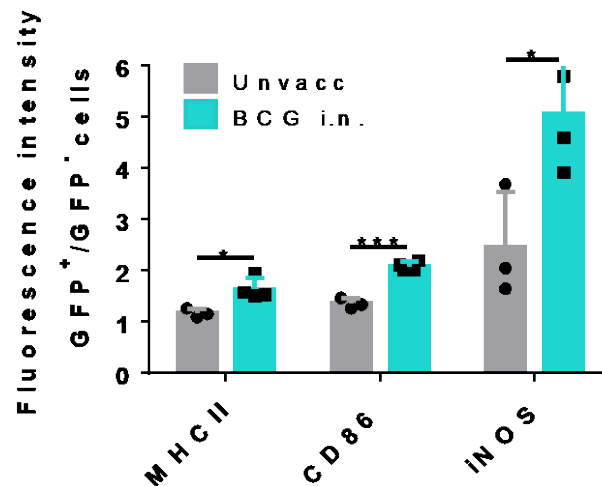


Comparison between GFP- and GFP+ cells at day 1 post-challenge:

- GFP- : not exposed to secondary stimulus
- GFP+ : exposed to secondary stimulus



— GFP-Non infected cells  
— GFP+-Infected cells



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